Formation and Function of the
Department of Molecular, Cellular, and Developmental Biology
University of Colorado Boulder: 1962 - 2015

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Chapter 1 The Institute for Developmental Biology and the Founding of Modern Biology at the University of Colorado Boulder

The arrival of Meredith Runner in 1962 might be viewed as the moment when the University of Colorado (CU) finally made a commitment to modernize biological science education and research on its campus at Boulder. Runner was recruited to be the chair of the existing biology department at Boulder. He seemed an excellent choice, since he came with both many years of experience as a university professor and several years as a program director at the National Science Foundation and as a consultant at the National Institutes of Health. To say that Meredith Runner was familiar with how biology was changing and how government-run agencies now funded science at the university-level would be an understatement.\(^1\)

Meredith Runner earned his Ph.D. in biology in 1942 from Indiana University. Upon graduating he moved to the University of Connecticut as an instructor and later as an assistant professor. He stayed at Connecticut until 1946, then moved to the Roscoe B. Jackson Memorial Laboratory, a non-profit biomedical research institute focused on studying system genetics and aging, located in Bar Harbor, Maine. While at that laboratory, a major center for mouse genetics, Runner continued his research on morphogenesis and molecular epigenesis, which led him to closely look at the influences of various environmental factors on embryonic development at the cellular and tissue level, including the role of maternal metabolism, in promoting and preventing abnormal development. Much of Runner’s research, with its focus on the mouse, was concerned with looking at and discovering the mechanisms of biological processes, and the causes and preventions of abnormalities in mammalian development (also known as teratology). His appointment to chair of the biology department at Boulder appears to have been a major first move by the university’s administration to change how biology was taught at the university.

The biology department, at the time of Runner’s arrival, was woefully under-funded and over-crowded. Moreover, both its research and its courses focused on more traditional aspects of biology, such as systematics, zoology, and botany, and where

\(^1\) Information from Meredith Runner’s Curriculum Vitae – MCDB department archives, FF IDB Miscellaneous 1966-67, summary of grant proposal to the national science foundation, September 23, 1966.
students learned field techniques through the study of ecology. This focus was reflected in the degrees that the department offered to its undergraduate and graduate students: zoology, botany, and a general biology degree for students destined to teach public high school science. The arrival of Runner, while heralded by the university’s administration and medical school, was hardly welcomed by the existing faculty in biology. Indeed, his presence appears to have been a source of major discontent and stress, to the point that shortly after his arrival the existing faculty initiated new departmental rules and regulations that reduced the power of its chair in the selection of new faculty. Runner remained as the chair of the biology department for only one year, resigning this position in the summer of 1963. If the biology department faculty had hoped this would remove Runner from the campus, however, they were seriously mistaken.

Prior to Runner’s arrival at Boulder, the administration had sought funding from the National Institute of Health (NIH) for a new psychology and biology building. The grant was submitted to the NIH in March of 1962, but during the review process it was determined that the NIH would fund only a psychology building. The reasons for not funding the construction of a new biology building can only be guessed at, but the appointment of Runner as Chair of the Biology Department appears to have been in response to the NIH’s refusal to fund biology at the university.

Shortly after Runner’s arrival at Boulder, the university administration, with the urging of the university’s president Quigg Newton, submitted an application to the National Science Foundation (NSF) to acquire matching funds for a new graduate level training building for biology. The administration knew that the existing facilities in the biology department were inadequate if they were going to improve biology training at the university, but they also recognized that the existing faculty’s research focus was firmly planted in traditional biology. The university determined that a new building on the East Campus would not only provide more experimental laboratory space to pursue modern biology, but would also act as a “carrot” to entice to Boulder biologists who were

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2 Joe Daniel took over as acting chair of the department in August 1963. Letter to Joe Daniel from Dean Briggs in College of Arts and Sciences Dean Archives, Box 10, Biology Department -Folder 10, Norlin Archives, University of Colorado Boulder. Information on Runner’s resignation can be found in the Runner Archives finding aid in the Norlin Archives.

more focused on the modern concerns of biology: cellular, molecular, and developmental biology. Moreover, the creation of a new building for modern biology could be construed as evidence that the university was serious about, and committed to modernize the teaching of biology.

In the March of 1963, the university received the NSF funds and construction on the new building began almost immediately. After his resignation as chair of the biology department, Runner joined the committee tasked with managing, designing, and equipping the new building. Two years later, in 1965, the Life Sciences Research Building #1 (LSRB#1) was ready for occupancy. But Runner’s involvement in modernizing biology training at the university didn’t end there, much to the chagrin of the biology department faculty. Runner became the proverbial thorn in their side when in 1964 he became involved in the Centers of Excellence Award committee. As part of the federal government’s attempt to improve science education at the university level, the NSF introduced a Centers of Excellence Award, of which seven would be awarded to either four-year colleges or universities that proposed major changes to how undergraduate science was taught in the lecture halls and laboratories.

The existing biology department lacked space to expand and improve its laboratory space. It also would need financial support to hire faculty focused on more modern questions in biology. The financial shortfall meant that modern equipment with which to undertake experiments could not be purchased and space could not be found. But the lack of space and financial support were only part of the problem; the rest of it lay firmly in the intellectual focus of the existing biology faculty and their reluctance to acknowledge the changing face of biology. As mentioned previously, the biology department remained focused on more traditional research research subjects, such as taxonomy, evolution, biological diversity, and plant and animal ecology. Research questions focused on molecular and cellular biology, they believed, represented: “nothing more than a "narrow field of Biology" [with] no demonstrable heavy demand

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4 See correspondence to the administration in the Meredith Runner Collection, Box 2, National Science Foundation Proposal 1964 Folder, Norlin Archives. These letters and memoranda reveal the discontent of the existing biology department faculty, as expressed by the new Chair of the Biology Department Robert Pennak, for the omittance of their suggestions for improving the quality of biology education at the university in the proposal to the National Science Foundation. And also memoranda contained in Department of Biology Reports Folder, Box 2 Meredith Runner Collection.

5 Improving education at all levels was one of the major goals of Lyndon B. Johnson’s Great Society presidency.
for molecular biologists in the 1500 senior colleges and universities of the United States.” The tensions between scientists who studied biology from the more traditional approach of ecology and taxonomy and those who studied biology at the cellular or molecular level has been explored by historians of science. Some, like Joel Hagen, suggested that the epistemological rift between the two different approaches to biology was not as great as other historians have argued, but the situation at Boulder would suggest otherwise. Perhaps the practice of science is influenced more by particular localities and situations than by actual differences between the two approaches.

It is clear that in the 1960s, the existing biology faculty, under the leadership of the new Department Chair, Robert Pennak, did not believe that molecular and cellular biology would become important disciplines within biological research. Instead, Pennak and his colleagues wanted the university to support the biology department’s suggestion of expanding environmental biology. He suggested that new, cross-disciplinary research, such as biochemistry and biophysics, should be limited to the existing departments of chemistry and physics. The antagonism that surrounded the formation of a new department of biology continued well into the 1990s, but by then, the distrust of the faculty was less about intellectual biases and more based on resentment concerning the amount of money the “new” department had received over the years, as well as inequity of teaching loads between the two departments. Leslie Leinwand, the Chair of MCDB from 1995 - 2007, commented that on her arrival at CU she tried to reach out to the original department, then known as Environmental, Population, and Organismic Biology (EPOB), in an attempt to streamline and improve biology education at CU, but her attempts were met with antipathy, so she moved her focus elsewhere. In reality, there was a need for both biology departments at the university, but early intellectual biases blinded faculty to this fact.

Despite Pennak’s complaints of and admonishments to the Institutional Science

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6 Memorandum to Members of the Institutional Science Development Committee from Robert Pennak, Chair of Bio Dept. dated 23 June 1964. Meredith Runner Collection, Box 2, Department of Biology Reports Folder, Norlin Archives.
8 Interview with Leslie Leinwand, July 2, 2014. Interview deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
Development Committee, the final grant proposal that was submitted to the NSF for a Center of Excellence Award excluded any requests for the existing biology department to expand its teaching in environmental biology. Instead, the proposal petitioned for money to support the teaching of experimental and developmental biology at the new LSRB#1 on East Campus and the formation of a new institute to be known as the Institute for Developmental Biology (IDB).

The creation of the new institute made the biology department and Robert Pennak angry and bitter, leading Pennak to ask: "I have been trying to decide what serious mistakes I have made during the past nine months that may have contributed to the present situation."9 The formation of the IDB came out of a period of extensive internal review by the university administrators. It reflected the major changes happening in biology and challenges facing science education in four-year institutions all over the country; it was not due to some personal vendetta by Meredith Runner against the biology department or Robert Pennak. What Pennak had failed to do was recognize the importance of molecular and cellular biology to the entire science of biology and to the understanding of the mechanisms involved in the formation and evolution of organisms at the cellular and molecular level. This failure represented a fundamental intellectual difference between the "traditional biologists" at the university and the changing face of biology nationally and internationally. It was exactly this type of failure that the NSF hoped to correct by granting Centers of Excellence Awards.10 Runner recognized this from his years working as a program director at the NSF.

The university administration remained adamant that more needed to be done to improve life sciences at the university, so President Joseph Smiley and Dean Thurston Manning assembled a committee to investigate the teaching of life sciences.11 The formation of the All University Life Sciences Committee (1965-1966) sought to uncover the true state of life sciences education at the university. The committee members represented the existing departments of biology, psychology, and physics, plus Meredith

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9 See Memorandum to all Biology Faculty Members from Robert Pennak dated 29 May 1964, CC President Smiley, Acting Dean of Faculties, Wahlstrom, Acting Dean of the College of Arts and sciences Briggs: Meredith Runner Collection, Box 2, Department Biology Reports Folder.
10 See Introduction for the importance of the NSF to science education development.
Runner as head of IDB, Peter Albersheim representing biochemistry, and Lloyd Kozloff from the medical school in Denver. The group undertook extensive surveys of existing biology departments within universities and four-year colleges in the United States, as well as interviewing faculty on the medical school campus. They spent many months analyzing the state of biology at the Boulder campus and at the medical school in Denver. Based on input from the university’s faculty, and on extensive discussions with other faculty around the United States, the committee presented its findings to the university’s administration. The proposal was not only a scathing attack on the existing biology department, which had failed to “keep up” with current trends in modern biology, but it also highlighted the failure of the university to support modern science at this level of education.

Two important developments came out of the Institutional Science Development Committee report and the All University Life Sciences Committee report. First, that an Institute for Developmental Biology should be instigated immediately; and second, that a new department for Molecular and Cellular Biology should be established as soon as possible. Both reports recognized the need to modernize biology at the university if the university was to establish itself as an important center of modern science education and research in the West.

The Life Sciences Research Building #1 and the Formation of the Institute for Developmental Biology

The construction of the Life Sciences Research Building #1 (LSRB #1), financed by the NSF grant in 1963, represented much more than a space for experimental biology and psychology; it represented a commitment by the university to improve its life sciences education program on the Boulder campus. The building created new spaces

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12 Meredith Runner Collection, Box 8: Folder-The All University Life Sciences Report: 1965-1966, Norlin Archives.
for experimental biology research and housing for laboratory mammals and was intended to be the home of experimental biologists working in developmental biology and others working in the life sciences. It was not intended to be a teaching facility, but rather a space where basic biological, psychological, and related sciences could be coordinated into a "physical system to maximize the opportunities for interdisciplinary exchange and cooperation and to reduce the need for duplication of costly facilities." The administration hoped that the new facility would focus on taxonomic, ecological, behavioral, learning, physiological, and genetic characteristics of living organisms and be a space for collaboration among the various researchers who would eventually use the new space. In short, the new facilities would ensure that biology at Boulder would not lag even further behind the rest of the United States, and would also be seen by the various funding agencies as a solid commitment by the university to improve its life sciences programs.14

During the process of putting together the proposal for the NSF Centers of Excellence Award (Science Development Program), Meredith Runner and Joe Daniel (both still listed in the Department of Biology) investigated the possibility of setting up a Developmental Biology Research Center (DBRC) in the new building (LSRB#1) located on the East Campus at Boulder.15 The two biologists had tentatively approached the idea in late 1963, shortly after the first grant to construct LSRB#1 had been received. With the completion of the NSF proposal imminent, however, they both realized that the administration’s goal of improving life sciences education at the university could only be achieved with the introduction of a new graduate program that would be cross-disciplinary in nature, satisfying the needs of developmental biology.

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13 Meredith Runner Collection: Box 8; folder Facilities Development Grant – LSRB#1 Committee Program Requirements, pg.2. Norlin Archives.
14 Meredith Runner Collection: Box 8; folder Facilities Development Grant – LSRB#1 Committee Program Requirements, Norlin Archives.
15 Proposal to NSF for support of Graduate Training Grant and Establishment of Research Institute, CU Proposal# 65.5.266, Dec. 1965. The desired starting date was July 1, 1966 for a period of seven years. Training costs $1,849,817, and research costs $1,133,407. PI Meredith Runner. NSF IDB Folder in MCDB Archives. This document is extensive and detailed.
and biochemistry, and providing graduate training that would prepare students to enter the medical research field. Initially, Runner and Daniel believed that the research center and the new graduate program would be folded into the existing biology department, but Runner met with continual obstructions and anger from both the chair and other members of biology department faculty. In late 1964, Runner and Daniel approached Dick Ham at the medical school in Denver to ask if he would be interested in working in such a research center.\textsuperscript{16} Some of the medical school faculty had been very vocal about the lack of training in modern biology for CU students at Boulder and they often complained that they could not accept CU students into the medical school because they lacked even a basic understanding of developmental biology.\textsuperscript{17} It was clear to the administration that biology at CU needed a drastic overhaul, and they believed that this could be achieved with Runner at the helm.

The administration wasted no time in moving forward with their plans for improving the life sciences programs on campus. Consequently, the creation of a new Institute for Developmental Biology happened very quickly. Over the course of several months, a committee was formed, consisting of Runner, Daniel, Ham, as well as David Prescott and Phyllis Schultz, from the medical school. Many meetings later, and after much discussion with the administration, the DBRC morphed into an Institute for Developmental Biology, which fell under the administration of the graduate school. The Dean of faculties, Thurston Manning, and Dean James Archer of the Graduate School, believed that the establishment of this institute in 1965 gave proof that the university administration was serious about improving the teaching and supporting of life science programs on the university campuses. Indeed, the opinions of the two Deans and Manning’s trust in Runner were not misplaced; several months later, the university was awarded the

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\textit{Joe Daniel (on left)} and Dean James Archer of the Graduate School, believed that the establishment of this institute in 1965 gave proof that the university administration was serious about improving the teaching and supporting of life science programs on the university campuses. Indeed, the opinions of the two Deans and Manning’s trust in Runner were not misplaced; several months later, the university was awarded the
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\textsuperscript{16} Meredith Runner, “The Why and How of MCDB,” seminar transcript, April 3, 1997, at 13.45, held in the archives of the dept. of MCDB.

\textsuperscript{17} Letter from David Talmage, Professor and Chair of the Denver Medical School to Dean Thurston Manning, May 23, 1966. In the letter, Talmage complains bitterly about the existing biology department and the faculty at Boulder. He is especially harsh about the biology education undergraduates receive at Boulder, suggesting that even Denver’s high school students had a better understanding of modern biology than the biology undergraduates did on leaving the Boulder campus. Box 10 College of Arts and Sciences Deans archives, Folder: Biological Sciences
money from the NSF. Perhaps as important, the Foundation recognized the University of Colorado as a potential Center of Excellence – one of only several in the country at the time. Within the proposal to the Science Development Program was a commitment by the University to expand biological sciences as part of its contribution to the Center of Excellence program. The university confirmed its commitment by making new hires in biochemistry and psychology, and with the establishment of both the Institute for Arctic and Alpine Research and the Institute for Developmental Biology.

Shortly after receiving the Center of Excellence award, Runner approached the NSF again. Recognizing the importance of the award and realizing that the time to act was now, if CU was to move into a new era of biology, Runner applied for money to fund research and training in the new institute. The new grant from the NSF was used to equip the new laboratories in the LSRB #1 with modern technological equipment, while a further grant from the National Institute of Health (NIH) was used to fund personnel, consumable supplies, and student stipends. The Institute for Developmental Biology officially opened in July 1966 with a faculty of seven. Shortly thereafter IDB began to accept graduate students for the newly created Ph.D. in developmental biology. This new Ph.D. differed from the existing Ph.D. in Biology in that its main focus was on the experimental aspects of developmental biology, rather than on the descriptive focus of traditional biology. Finally, CU-Boulder had the beginnings of a modern biology degree.

\[18\] History of the Developmental Biology Research Center document, held in the archives of the dept. of MCDB. See also the Graduate Training Grant Proposal, CU# 65.4.233 (NIH# 1 T1 HD 172-01: Title “Differentiation, Morphogenesis and Reproduction”) for $207, 358.00 in Training Grants folder in MCDB archives; NSF IDB Folder, Proposal to the NSF for Graduate Training and Establishment of the Research Institute.

\[19\] All University Life Sciences Committee Report, June 1966, pg. 31. Box 9 College of Arts and Sciences Deans archives, Folder: All University Council. For list of faculty see the proposal to the NSF, # 66.5.222, for “Equipment for Graduate Laboratory Course in Procedures for Investigations on Cell Structure and Function,” dated September 23, 1966, in folder 1966 – 1967 IDB, file 1966 – 1967 IDB Misc. in the Dept. of MCDB archives. Dr. Peter Albersheim, Dr. Joseph Daniel, Jr., Dr. Mancourt Downing, Dr. Lester Goldstein, Dr. Richard Ham, Dr. Alec Kelso, Dr. Gerald McClearn, Dr. Edwin McConkey, Dr. Jacques Pene, Dr. David Prescott, Dr. Meredith Runner, Dr. Bert Tolbert, pg. 9.. This document also provides details of the proposed Ph.D. in Developmental Biology and brief biographical data of faculty, pg. 21 – 55.
The granting of the NSF Science Development Award spurred Deans Manning and Archer to move the university further into the field of modern biology. The graduate program in developmental biology provided students with opportunities for basic research in: biochemistry associated with cell growth and reproduction; synthesis of subcellular components; biochemical virology; cellular ultra-structure; growth and differentiation in cell culture; and embryology. A reading of the prerequisites for entry into the program clearly demonstrates that undergraduates from the existing biology department at CU would not have had the training in mathematics, nor in the physical and chemical sciences, required to transfer into the new graduate program. On completion of the new Ph.D., students would have developed competence in biochemistry as it related to cellular and molecular biology, genetics, cell structure and function, and developmental systems. A glance through the courses available to students in IDB reveals not only the intellectual focus on developmental biology and the intellectual rigor of the new biology degree, but also the attempts made by the CU administration to improve the university’s standing as a science-research focused university capable of competing for scientific funds from federal granting agencies, such as the NIH, the Atomic Energy Commission, National Aeronautics and Space Administration, the Department of Defense, and the NSF.20

Shortly after establishing IDB, Runner, Ham, and Daniel began recruiting new faculty members. The first hires consisted of David Prescott from the medical school in Denver, Lester Goldstein, Ed McConkey, Peter Kuempel, Jacques Pene, and Charles Flickinger – a postdoctoral trainee working on electron microscopy.21 Peter Kuempel worked closely with David Prescott and other scientists, such as Ted Puck and Larry

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20 Roger Harkins, “The CU Graduate School,” *Daily Camera’s Focus*, May 21, 1967, Section D, pg. 3. In this article, an interview with Dean James Archer, the Dean of the Graduate School, Archer notes that: “By the end of next year, we will have added 56 new scientists…under the NSF Science Development Grant. While this grant provides some support for these men during the life of this program, the University is going to need substantially more money for the support of research…for these men when they’re no longer supported by NSF.” Two notes of interest, the fact that the grant substantially increased the number of scientists at the university, and that all the hires were male.

21 Flickinger operated the first electron microscope on the CU-Boulder Campus: Meredith Runner, 1997 talk transcript: 32:30.
Taylor at the Denver Medical School, reflecting the spirit of collegial interaction that was characteristic of that time and place. Kuempel remained at CU throughout his career, though some of the other new hires moved to other research institutions within several years.\textsuperscript{22} During the early years of IDB, collaboration with the medical school was commonplace, and the collaborations helped to alleviate the medical school faculty’s concerns over the biology program on the Boulder campus. 

As IDB grew in the numbers of both its faculty members and graduate students, it became clear that more research and laboratory space was needed.\textsuperscript{23} The original LSRB\#1 housed Dr. Ham and the other original faculty, but the new faculty needed their own space, and fortunately for IDB, the building next door, the Physical Sciences Research Building (PSRB), suddenly became vacant due to the relocation of the National Center for Atmospheric Research (NCAR) to its new building on South Broadway. The extensive re-modeling of the building to create an expansion of available biological-research space and cold rooms on the East Campus in 1967 enabled the arrival of more faculty and students later that year.\textsuperscript{24}

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\textsuperscript{22} Interview conducted with Peter Kuempel, February 2013 deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder. Kuempel worked on the bacteria \textit{Escherichia coli} (\textit{E. coli}) and collaborated with David Prescott, who was effectively his mentor, and other scientists working down at the Denver Medical School (27:00 of Interview \#1 in Karen Lloyd Collection). Kuempel’s intellectual focus concentrated on the cell cycle, but he was also interested in human genetics, which at this time (late 1960s – early 1970s) was still a new science. \\
\textsuperscript{23} By the end of 1967, IDB housed 64 faculty and graduate students. Meredith Runner, 1997 talk transcript:45:16. \\
\textsuperscript{24} Meredith Runner, 1997 talk transcript: 30:46. This refit was supported by a NIH grant, HD 02282, titled “Mechanisms in Developmental Biology” and awarded in 1966 (Also known as the Research Institute Grant – see document in PSR- Facility file in MCDB Archives). In total, Runner and the administration received three grants: two from the NIH and one from the NSF. Meredith Runner, 1997 Talk transcript: 29:35.
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The Ph.D. in developmental biology specifically addressed the shortfall in the university’s commitment to higher education modern biology. The administration had made the decision to retain IDB as an independent institute within the Graduate School - IDB had secured grants that provided funding through 1971 and the administration had agreed to the renovations of the PSRB#1. But there was still a major problem as far as the administration was concerned. While IDB provided a graduate training program in modern biology, undergraduate biology education retained its conservative focus in the existing biology department. The chair of that department gave no indication to the administration that the existing biology faculty members were prepared to make changes to their curricula or to accommodate modern biological techniques and training in their lab-training courses. As far as the administration was concerned this situation could no longer be tolerated. The administration’s decision to create a new Cellular and Molecular Biology Department, which would accommodate both undergraduate and graduate students, had a profound effect both on instruction available on the Boulder campus and on IDB. Its viability as an independent institute with its own Ph.D. in developmental biology became untenable.
Chapter 2  Formation of MCB and its merger with IDB

The establishment of the Department for Molecular, Cellular and Developmental Biology in 1967 was in no small part due to the efforts of the administration and particularly the Dean of the Graduate School, James Archer. Meredith Runner described him as an “activist” who got things done at the university. Archer came from the University of Wisconsin in 1965 to be the Dean of the Graduate School at the University of Colorado Boulder campus and during his short time at CU (he left November, 1967) he effectively changed the direction of biological sciences at the university. He meticulously followed the efforts and findings of the All University Life Sciences (AULS) Committee, and even before it had presented its final conclusions in June 1966 Archer began work on an application for a Health Sciences Advancement Award (HSAA) from the NIH.²⁵

The AULS Committee report offered not only a damning indictment of the university’s biology department, it also criticized the lack of institutional support for the department’s current faculty.²⁶ An extensive review of other biology departments around the country revealed that the salaries of the current biology faculty ranked last (out of 16) for the amount of support received from the state. That department also had the smallest number of faculty members, and ranked 16th, along with Virginia, on the amount of money spent on biological research.²⁷ The State of Colorado might have failed to support the sciences at the University of Colorado, but the university had failed to support its own biology department: Biology education at the university was seriously underfunded, and the situation didn’t bode well for a region that saw itself as the “Front Range of Science” where “science-based industry has contributed to Colorado's present

²⁵ Meredith Runner, “The Why and How of MCDB,” April 3, 1997, seminar transcript, Department of MCDB files, at 20.35. The Health Sciences Advancement Award (HSAA) was specifically designed by the National Institute for Health for universities to improve or advance their Health Sciences Programs.

²⁶ "It is widely recognized that biology is at present undergoing a major revolution which ranks as one of the great intellectual achievements of this century. This revolution has had and will continue to have repercussions throughout human society. At the level of instruction and research the State of Colorado has failed to keep pace with the last decade's rapid and far-reaching advances in the biological sciences.” All University Life Sciences Report, 1966, pg. 1, in the Meredith Runner Collection, Box 8, Folder 4, All Univeristy Life Sciences Report, 1966, located in the Norlin Archives, CU Boulder.

²⁷ All University Life Sciences Committee Report, 1966, pg. 8-14, in the Meredith Runner Collection, Box 8, folder 4 All University Life Sciences Report, 1966, located in the Norlin Archives, CU Boulder.
position of opportunity.” Several medical school faculty members in Denver expressed their disappointment over the education biology students received on the Boulder campus, and even professors not associated with the university shared their sorrow at the state of biology education at the University of Colorado Boulder. Dean Archer immediately understood the implications of the report and proposed to the university administration that a new department of Cellular and Molecular Biology be established. It would be vital to the university’s growth and standing as a national research institute located in the American West. His application for a Health Science Advancement Award (HSAA) then, was certainly not premature.

The existing biology department faculty members continued with their campaign to attempt to block the changes proposed by the report, including the formation of a new biology department, as manifested in their stubborn refusal to acknowledge that molecular biology was here to stay. Robert Pennak, the biology department chair, insisted that with extra money and new research facilities the existing department could easily accommodate any new molecular biologists the university wanted to hire. What he, and others in the department, failed to realize was that the existing department had a less-than stellar reputation with the major granting agencies. It seems likely that any mention of money being used by the university to fund the existing department would have seriously jeopardized CU’s chances of receiving the new funding they sought. The formation of a new department focused entirely on modern biology seemed the most likely way to ensure that CU would receive future funding from the NSF or the NIH. The establishment of a new department in cellular and molecular biology, complemented by the new Institute for Developmental Biology, would be a clear indication of the university’s support of modern biology at CU.

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28 Boulder Daily Camera article, Wednesday June 24, 1964 in Meredith Runner Collection, Box 2, Folder -Biology Department, in Norlin Archives, CU Boulder.
29 Letter dated Dec. 13, 1965 from Dr. A. Eisenstark, prof of bacteriology at Kansas State University, addressed to Dr. Malcolm Correll (a faculty member in the biology department at CU Boulder) in which Dr. Eisenstark stated: "In light of the fact that a good university like Colorado has one of the poorest biology departments in the country, it seems to me that one of your needs is to call in some outside consultants...it is so sad to see a university with great strength in physics and chemistry to have a weakness in a field in which there is great intellectual vigor at the present time." Box 10, College of Arts and Sciences Deans Files, Folder, Biology Department, Norlin Archives, CU Boulder.
30 See letters and memos in packet in College of Arts and Sciences Deans Collection, Box 10, Folder Biology Department, in Norlin Archives, CU Boulder. Memos are between the Robert Pennak, Dean Briggs, and Dean Manning, and various letters from medical school faculty to Deans Briggs and Manning.
The HSAA, an opportunity open to all universities around the country, was a competitive grant from the NIH. The application that Dean Archer put together was detailed, extensive and included information on the establishment of a new department of Cellular and Molecular Biology. CU clearly wanted to expand and strengthen graduate training and associated research in the biomedical sciences, but it also proposed to improve undergraduate biology education. While the exact nature of the undergraduate biology program had not been determined, the administration at CU was adamant that changes to undergraduate training would be undertaken as a result of the establishment of the new department. The support CU sought was needed to advance the training of Ph.D. graduate students both at the University of Colorado, School of Medicine in Denver and at the proposed Department of Cellular and Molecular Biology. The application suggested that the new biomedical programs could communicate via two-way closed-circuit television and a data link between the Medical School and the Boulder campus. The television and data link were seen as opportunity to build stronger links between the two locations, nurturing shared research, and producing a greater opportunity for collegiality among graduate students and scientists.

The administration viewed the HSAA as an opportunity to become the major research institution it was striving to become – a designation, however, that was still in question. A recent survey (1965-1966) of four-year universities by the American Council on Education did little to help the university’s reputation. In the survey, CU ranked 20/46 for graduate training in botany and 21/49 in zoology, and while these ratings weren’t awful, they were less than a ringing endorsement for the current graduate programs in biology education at CU. The awarding of the University Science Development Award by the NSF in 1965, which improved the fields of physics, chemistry, mathematics, engineering, and psychology, and allowed the formation of the Institute for Developmental Biology in 1966, were offered as proof to the NIH that the

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31 See letter from Thurston Manning, Vice President and Dean of the Faculties, to Carl Brewer at the NIH, dated February 27th, 1967. HSAA folder located in MCDB archives.

32 Letter from Robert Pennak (Chair of Biology Department) to Deans’ Briggs, Archer and Manning dated May 27th, 1966. Pennak uses the rankings as justification for NOT forming a new biology department. Pennak believed the rankings showed that biology education at CU was good and that forming a new department would be a waste of money and weaken the existing department. College of Arts and Sciences Deans’ Files collection, box 10, folder, Biology Department, Norlin Archives, CU Boulder.
university was seeking to make changes in its science programs and to become a leading research institution. With the State of Colorado’s reluctance to fund higher education, the support of the federal government was clearly needed if CU was to move from a place of mediocrity to a place where they could compete with Harvard, Yale, UC Berkeley, Stanford, and Caltech for the best students and research dollars.

The administration took a huge gamble on the application, for if they were unsuccessful in receiving the funding, biology education at CU would have continued to languish in mediocrity, and CU would have found it difficult to obtain other awards to support biology education, particularly in light of the earlier comments made by the NSF. Ultimately, CU was successful. It was one of only five universities to get a $3 million award to support the life sciences programs at their Boulder campus and at the medical school in Denver. According to Runner, Archer credited the grant previously awarded to establish IDB as one of the factors used for the NIH decision. The other considerations were the decision by the administration to support modern biology at the Boulder campus through the establishment of the Department for Cellular and Molecular Biology and the award of the Science Development Grant by the NSF in 1965. The award secured CU’s biology department and medical school a place at the table with Harvard, Yale, and Cal Tech.

The 1960s witnessed a rapid growth in the creation of modern biology departments in higher education institutions and medical schools around the United States. When Peter Kuempel finished graduate school he secured a faculty position at Case Western Reserve University in Cleveland, before heading out for post-doctoral work in Copenhagen. Kuempel remembers that Case Western’s new Molecular Biology Department began hiring “like crazy” and had secured 20 new faculty members by 1966, with the promise of a new building to provide research space for everyone. But the money for the new building fell through and the recent hires quickly found themselves looking for new positions elsewhere. Kuempel interviewed at two places: Minnesota,

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33 HSAA application, February 27th, 1967, pg. 2-4. HSAA folder located in the MCDB Archives.
34 The lack of support from the state of Colorado is based upon my observations of the state of science programs at CU: overcrowded lab space; lack of dollars to purchase equipment or modernize existing science departments.
35 Roger Harkins, “The CU Graduate School,” Daily Camera’s Focus, May 21, 1967, Section D; and the All University Life Sciences Committee Report, 1966, pg. 31, in Meredith Runner Archives, Box 8, folder 4 “All University Life Sciences Report, 1966, located in the Norlin Archives, CU Boulder.
which was building a new department in molecular biology and already had a strong biochemistry faculty; and CU-Boulder, which was hiring for its new Institute for Developmental Biology. Kuempel, like so many others before him, was captivated by the vision of the Rocky Mountains on his flight into Denver, and decided that Boulder was where he really wanted to be; despite being offered a faculty position at Minnesota. Of course, the mountains weren’t the only factor for Kuempel. The Denver Medical School faculty, particularly Ted Puck, Larry Taylor, and David Prescott were all concerned with the cell-cycle and genetic mapping – work that was also important to Kuempel.36 The modern biology departments being formed around the country focused either on cellular or molecular or developmental biology; they often formed partnerships with existing departments of chemistry or physics. The new department being formed at CU – one that combined all three disciplines – was, at the time, unique.

With the establishment in 1968 of Cellular and Molecular Biology as a completely separate department, not simply an addition to IDB, the recruiting of faculty to fill the newly created laboratory space in PSRB#1 began in earnest. But one major question remained unanswered: “Who would lead the new department?”37 It was clear to the administration that the chair would have to come from outside of CU. After all, the existing faculty within the biology department was still objecting to the creation of a new biology department, preferring that the old department be “fixed up,” and Runner was in charge of the new IDB.38 During the 1967 – 1968 academic year, the administration and the search committee (of which Meredith Runner, David Prescott, and Peter Albersheim were members) identified several candidates whom they wanted to interview for the position of chair. During various meetings between the search committee and the administration (Dean Briggs), Peter Albersheim, who was a biochemist in the department of chemistry but also had a joint position within IDB,

36 Peter Kuempel Interview, October 2013: 22:47, deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
37 Ibid: It was determined that the new department of Cellular and Molecular Biology would share LSRB#1 with IDB until funds could be secured to build a new building within the Psychology-Biology Complex on the main Boulder campus. The new building would be situated near psychologists, biochemists in the chemistry department, and biophysicists in the physics and astrophysics department. This close proximity to other scientists would permit an easier exchange of ideas.
38 See memo dated January 28, 1967 in the HSAA folder in the MCDB archives. There is no author on this memo, but it would be reasonable to believe that it was authored by Meredith Runner or Dick Ham and addressed to the existing faculty of IDB. It is marked “Confidential.”
suggested that Dr. Keith Porter of Harvard University’s Dept. of Biology might be interested in coming to Boulder. Albersheim had previously worked with Porter while they were both at Harvard, and he spoke highly of Porter’s achievements. The faculty and administration agreed to allow Albersheim to go and talk with Porter.39

In the mid-1960s, as Chair of Harvard’s Biological Laboratories in Cambridge, MA, Porter’s work with the electron microscope was well known, and he had even shown Albersheim how to use this microscope in his own studies. However, according to Runner and Albersheim, it was fairly common knowledge in the biological sciences community that Porter was less than happy with his situation at Harvard. Albersheim flew out to meet Porter for lunch and persuaded him to interview for the position as chair of the new Cellular and Molecular Department at CU. Porter went to Boulder for several visits during 1967 and early 1968, before agreeing to become the new chair.40

While it was considered a great achievement to secure Porter as the new chair, Porter’s conditions for accepting the position represented the death knell of IDB.41

The establishment of a new biology department at CU-Boulder opened up the possibility of new revenue streams for biological research on the campus. While the faculty of IDB welcomed these new revenue streams, they did fear that the new department might become a competitor to IDB. This was not what Runner and his team had anticipated when they suggested that a new biology department was needed.

Runner, Ham, and Prescott envisioned a co-operative relationship between IDB and the new Department of Cellular and Molecular Biology, but it soon became clear that there

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39 According to Peter Kuempel, he remembered that Peter Albersheim, who held a joint position in IDB and Chemistry, was also instrumental in attracting Keith Porter to CU-Boulder. Interview #1 October, 2013: 27:11. Also see the interview with Peter Albersheim deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.

40 Prior to being at Harvard, Porter had spent 22 years at the Rockefeller Institute in New York: Meredith Runner 1997 talk transcript: 24:30. Also see Peter Albersheim Interview, Ibid. See Chapter 3 of this history for a biographical sketch of Keith Porter.

41 See Intra-departmental Memo from Meredith Runner dated October 30, 1967. In this memo he asks for “another consideration of the Institute for Developmental Biology in relation to the Cellular and Molecular Biology,” which he states was brought on by “Porter’s conditions for considering an appointment.” Folder: Briggs Letters C&MB; located in the MCDB Archives.
were concerns about how this would actually play out. In an intra-department memo, the IDB faculty addressed their concerns over the proposed HSAA. These concerns ranged from the loss of funding for IDB faculty (concern that the administration would divert funding from IDB to the new department to cover the cost of hiring new faculty), to the loss of laboratory space in PSRB#1 until a new Life Science Center could be built on the main campus (newly-hired faculty in the new department would be located in space previously assigned to IDB). But the memo also revealed the same pragmatic approach to problem solving that Runner had displayed since his arrival at CU-Boulder in 1962: for example, the new funding would provide money to refurbish PSRB#1 with new laboratory space. Moreover, working in such close proximity with the new department’s faculty would encourage a new period of co-operation and intellectual development for everyone concerned. These aspects were severely lacking with the faculty of the existing biology department. Runner et al. felt that a co-operative relationship would place IDB faculty in a good position to be included in the new teaching and research programs that would be established in the new department. They believed that IDB could be an important asset for Deans Manning and Archer’s attempts to establish a strong biology program at the university, and that the original team’s close proximity to the new faculty and department would give Runner and his group the opportunity to be involved with the planning of the new building and program. The memo closes with: “The potential strengthening of the University and the potential strengthening of IDB on the campus outweighs the risks.”

In January 1967, Runner still believed that IDB would co-exist alongside with the new Department of Cellular and Molecular Biology.

Keith Porter’s acceptance of the offer to become chair of the new Department of Cellular and Molecular Biology contained one important caveat: IDB would be incorporated into the new department and IDB would cease to exist as a separate institute as of July 1st, 1968. The proposal to incorporate IDB into the new department was first made to the IDB faculty in late 1967, and while they approved “in principle”

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42 See memo dated January 28, 1967 in the HSAA folder located in the MCDB archives.
43 See Runner’s transcript, 1997: 25:05-26:10. Runner states that Dean Briggs sent a memo to the IDB faculty in May 1968, after Keith Porter’s final visit before taking over as the new chair, suggesting that IDB might be incorporated into the new department, which would be renamed The Department of Molecular, Cellular, and Developmental Biology. See memo from Meredith Runner to the IDB faculty on May 10, 1968.
that IDB be incorporated into the new department (and move from the Graduate School to the College of Arts and Sciences), they did make some requests of their own: one of which was that the new department name be changed to “reflect and to include the newly established reputation of IDB, e.g., Department of Molecular, Cellular and Developmental Biology.” In effect, all IDB Faculty, including all grant monies awarded, would be transferred to the new department and listed under Molecular, Cellular, and Developmental Biology (MCDB), and all courses currently taught in IDB would also have a new listing under the new department of MCDB. This change would effectively make IDB a precursor to the new department, rather than an independent institute that would co-exist with it. More importantly it stripped Meredith Runner of his directorship of IDB and placed Keith Porter as his superior. Runner had spent the last six years fighting and working to improve the biology program at CU-Boulder, only to see his creation – IDB – scuttled with a stroke of a pen. Runner and the other members of staff suggested to the administration that the merger could happen after Keith Porter had moved to Boulder to take up the chair position full-time in 1969, or after the new building on the main campus in Boulder had been constructed, but their complaints fell on deaf ears. In July 1968, the new Department of Molecular, Cellular and Developmental Biology came into existence. Runner et al. did receive some concessions: they would only have to teach graduate level courses and their teaching load would be light so as to allow them time to focus on their research. Following the establishment of the new department, the administration quickly moved to resubmit

44 See letter from Meredith Runner to Dean William Briggs, December 27, 1967: Folder; Dean Briggs Letters, C&MB. MCDB Archives. All IDB Faculty signed the letter: Joseph Daniel, Charles Flickinger, Lester Goldstein, Richard Ham, Peter Kuempel, Edwin McConkey, Jacque Pène, David Prescott.

45 It is not clear when the new name for the department was adopted. Meredith Runner makes the claim he suggested the new name. See Runner’s transcript, 1997, around 51:10, and indeed in a letter from Meredith Runner to Dean Briggs dated November 22, 1967, Runner does mention the name of Department of Molecular, Cellular, and Developmental Biology: Folder Briggs Letters C&MB, in MCDB Archives.

46 The All University Life Sciences Committee Report, 1966, stated on pg. 31 "Both the Institute and a new department, as well as the current department, will benefit from a great deal of interchange between each other and the biochemistry divisions of the chemistry department." The Committee concluded that the biology program at CU would benefit from having all three departments/institutes in existence, with collaboration between themselves and the biochemists in the Chemistry Department. Meredith Runner Archives, Box 8: folder 4 – All University Life Sciences Report, 1966: Norlin Archives, CU Boulder.

plans to the NSF for a new biology building to be located next to the new psychology building on the main campus.\textsuperscript{48} CU had made the decision to embrace modern science education and research: this decision manifested in the establishment of the new Department of Molecular, Cellular, and Developmental Biology.

\textit{Keith Porter outside PSRB#1}

**MCDB at PSRB#1**

Discussions on the intellectual focus of the new department began very soon after the decision was made to incorporate IDB into it. The first MCDB Faculty meeting was held May 31\textsuperscript{st}, 1968; it consisted of the IDB Faculty and Keith Porter. During the meeting they discussed possible new hires for the new department, but more importantly this meeting was the first tentative discussion by Porter and the IDB Faculty of the intellectual focus of the new department.\textsuperscript{49} Some of the areas of concentration that the faculty considered included animal virology, genetics, cell structure, protein structure, neurobiology, embryology, biochemistry, plant cell structure, and high voltage electron microscopy. All these areas represented new foci for biological sciences at CU-Boulder. The discussions identified several potential faculty candidates who might be interested in moving to Boulder. Among them were Richard McIntosh (biophysical cytology), Lee

\textsuperscript{48} See Runner’s transcript, 1997: 42:39, where he states that plans were resubmitted.  
\textsuperscript{49} Folder: Faculty Meetings, 1968 – 1973. MCDB Archives.
Peachey (electron microscopy), Jeremy Pickett-Heaps (plant cell structure), and Noburu Sueoka (virology), who all eventually came to Boulder during the next several years. This initial discussion helped to shape the department’s intellectual focus and brought in scientists whose research had a tremendous impact on the biological research and teaching conducted at CU – Boulder.

Starting up a new department not only means recruiting faculty members and staff, it also means applying for grant money that can be used to set up new laboratories, run new courses, and pay graduate stipends and faculty salaries. Keith Porter’s reputation, along with that of the IDB Faculty, ensured that grant applications from MCDB would be given careful consideration by the granting agencies, such as the NSF, NIH, the Department of Energy, the National Cancer Institute, and various health-related societies and organizations. One of the first grants that Keith Porter applied for as the Chair of MCDB (1969) was a training grant for cell biology from the NIH.

The training grant, titled “Investigative Procedures in Cell Biology,” represented the fundamental difference between modern and traditional biology; using experimental, rather than observational approaches to understand the structures of organisms at various levels of development and the use of technology in the new disciplines within biology. The grant application, which asked for nearly $800,000 over a period of five years, sought funding to provide broad training for graduate students and postdoctoral fellows in the methods and basic theories of modern experimental cell biology. Undertaking a study in experimental cell biology required the use of modern technologies, such as the Philips 200 electron microscope (but not limited to electron microscopy), to observe and collect information relating to cell structure, fractionation, cytochemistry, and histochemistry. It also involved the use of various isotope tracer techniques to track changes in cell organization or the movement of molecules and other

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50 Lee Peachey came as an adjunct professor. He worked the summers in Porter’s lab and taught a variety of summer courses. Personal communication from Dr. Richard McIntosh to Author, 2013. See also correspondence folders in Porter Collection: Norlin Archives, CU-Boulder. This first faculty meeting can be considered a brain-storming session and does not appear to represent all the faculty that joined early – Michael Yarus, Larry Gold, Charles Yegian, Mary Bonneville, Abe Flexer, and Andrew Staehelin all joined the department in 1969-1970. Sueoka, although mentioned as a possible faculty hire, did not join the department until 1974.
structures within the cell. Understanding the structure, function, and behavior of cells was the key component of the grant application. Students within the department would be able to interact not only with cell biologists within the department, but also with others specializing in biochemistry, biophysics, and molecular genetics. This would allow them to interact with scientists who focused their research on the study of ribosomes, the mechanisms of protein synthesis, and the processes of cell differentiation. Modern experimental biology required money, space, and technology to be effective: the move to modern biology at CU represented a serious investment in science and research both by the CU administration and the funding agencies. The onus to be productive (and successful), both in terms of discoveries and journal publications, fell both on the established faculty members and on the newly-hired faculty members whom Porter identified and recruited to the new department.

At the time of the Training Grant application, MCDB offered a few limited graduate courses in Cell Biology that had been developed by Meredith Runner et al. for their new Ph.D. in Developmental Biology. The process of developing and establishing new courses specifically for the new department did not begin in earnest until new faculty joined the department in 1970. Most of the courses offered a rudimentary understanding of cell structure and function and taught students the various techniques used for studying cell structure in vertebrate organisms. Students who registered for these courses were also required to be registered for, or had already taken, biochemistry. The department also offered graduate courses that were designed for students in the molecular and developmental disciplines. These included courses in genetics, mammalian development, developmental systems, molecular genetics, and teratogenesis and were supported by two training grants: “Embryology and Reproduction” and “Developmental Biology”, both under the directorship of Meredith

51 Some of the equipment needed included: pH meters, balances, glassware, chemicals, radioisotopes and materials, living material, such as animals, feed, cages, diamond knives, centrifuges, and photographic material. Training Grant application, Training Grant Folder – Cell Biology, located in MCDB Archives.
52 Training Grant Folder – Cell Biology, located in MCDB Archives. Abraham Flexer and Andrew Staehelin were already appointed and began their teaching duties in September, 1970. Mary Bonneville (the first woman on faculty) and Jeremy Pickett-Heaps (Plant Cell Biologist) had not yet been officially appointed at the time of the grant application, but they were included on the application. Funding for a technician to run the electron microscopes and a Diener (laboratory helper) was also sought in this grant.
53 During the period 1969-1971, the new department developed many new courses to provide education for both undergraduate and graduate students. This will be discussed in more detail in Chapter 3.
Runner.\textsuperscript{54} In addition the faculty of the Department of MCDB encouraged their graduate students to take courses offered in departments of chemistry, computer science, psychology, and general biology, thus revealing the interdisciplinary nature of modern biology.\textsuperscript{55}

Another important consideration for the establishment of the new Department of MCDB was the availability of laboratory and teaching space. It was clear to the administration that current facilities were no longer adequate for the needs of experimental biology, and that new laboratory and teaching space would be needed if the department and CU-Boulder were to be considered serious research institutes. The granting of the HSAA helped to provide some funds for a new building and equipment, but the rest came from another NIH building grant, from grants to individual Department researchers, which provide funds for equipment, graduate students stipends, and faculty salaries, as well as from the university administration\textsuperscript{56}. The new building, planned on the main campus, would contain 50,000 square feet of laboratory space, of which one half would be dedicated to research in cell biology. In addition to the new work space, Porter, as part of his package for moving to CU-Boulder, also planned to purchase and install a one-million volt electron microscope. This high voltage electron microscope (HVEM) was another serious investment by the university administration and underscores the faith that they had in Porter to establish a first class Department of Molecular, Cellular, and Developmental Biology located in the American West. Porter was certainly determined that he would not fail in this mission. As a consequence, he used his professional standing in the field of cell biology, as well as his many personal connections, to gather around him a group of young, determined, and innovative faculty who would ensure that research in MCDB at CU-Boulder would be some of the best in the field of modern biology.

\textsuperscript{54} These were previously offered within IDB. See IDB course brochure, MCDB Archives. Training grant information can be found on pg. 18 of the Training Grant application – Cell Biology, MCDB Archives.
\textsuperscript{55} These early courses were taught by Dick Ham, David Prescott, Lester Goldstein, and Charles Flickinger. See Training Grant application – Cell Biology, MCDB Archives. Also see pg. 28 of the application for a list of approved courses outside the department.
\textsuperscript{56} See letter from Keith Porter to faculty members of MCDB in MCDB General Folder, AY 1968-1969, located in MCDB Archives.
Chapter 3 New Buildings – New Beginnings

On a chilly September day in 1971, a collection of dignitaries, representing political and scientific institutions from around the country, and the recently appointed faculty of the Department of Molecular, Cellular, and Developmental Biology (MCDB) gathered in front of the brand new biosciences building on the Main Campus to officially declare that “the new biology” had arrived on the Boulder campus. All agreed that the building was an important addition to the university’s plan of improving and expanding science education and scientific research at the university, but the building can also be seen as the beginning of the “formal existence” of MCDB: the department finally had a real home on the main campus. The building, designed and built by the architectural firm Haller and Larson of Denver, included 50,000 square feet of laboratory space (exclusive of administration and teaching space) and was built at a cost of $3.85 million; $2.8 million was received from the NIH (in 1968) in the form of the Health Sciences Advancement Award (HSAA) with the remainder of the money coming from the University of Colorado. As is expected for such gatherings, the rhetoric on the “importance of science for the future of mankind” was high. Funding science for the benefit of society was part of Lyndon Johnson’s Great Society policies, and funding by federal agencies, such as the NSF and NIH, was one of the key components of his policy-making decisions.

William D. McElroy, a biochemist, who headed the NSF at the time, and who was soon to be the chancellor of the University of California at San Diego, was the keynote speaker at the opening events. He explained the importance of "good biology", stating that "for the scientist it is an article of faith that wherever good biology is practiced...benefits will accrue for society.” But he also answered critics who believed that the new biology, and especially biology focused at the molecular and cellular level,

58 Ibid; see also Cell Biology Training Grant application, 1969, Folder – Training Grant Cell Biology, MCDB Archives. At the time the President of the University of Colorado was Frederick P. Thieme and the Dean of the College of Arts and Sciences (which MCDB was included in) was William Briggs.
was just a mere fad by suggesting that "a discipline that appears to have only marginal bearing on the problems of the present may someday, in our rapidly changing society, acquire great importance." 60 The establishment of MCDB at the Boulder campus can be seen as a good example of the relationship that existed between government and academia in the late 1960s and 1970s.

The building completed: view to the North-West

The building completed, view to the South-East
The process of getting to this monumental landmark had been a long and difficult one, but the arrival of Keith Porter, as the new chair of MCDB, and the appointment of Abraham (Abe) Flexer as the administrator to oversee the construction and design of the laboratory and teaching space provided the impetus the university needed. The success of the entire department, however, depended on the faculty Porter inherited from IDB and on those whom Porter had recruited. Porter moved permanently to Colorado sometime during 1970 – until which time he had continued to commute between Boulder and Harvard, where he continued to oversee his graduate students and bring to a close his own research projects. Because of his part-time status at Boulder, the day-to-day running of the department fell to the existing faculty, formally of IDB, and recent hires. While these faculty members focused primarily on designing curricula, developing new courses, and setting up committees concerned with faculty hires and space and facilities, Porter spent his time finding creative ways to raise money to fund the new building the new high voltage electron microscope that was also being installed. Meanwhile, Flexer acted as the “go-between” for the architects and scientists who would eventually take over the new building. The time from when Porter took over the department (when it was still located on East Campus) to moving into the new building was less than three years. Funding for the building was a combination of federal and state support (CU is a higher education institute within the state system) and this type of funding partnership became the model for the next decade or so. By the mid-1980s, federal funding, in the form of grants from the NIH and NSF, began to dry up and universities were forced to look to business partnerships, the filing of patents for scientific discoveries, and wealthy donors for support. But during the late 1960s and 1970s, there was plenty of federal money for everyone: this source of funding was


62 New grants from the NIH and NSF, along with funding from the university helped to pay for the construction of the building and for equipping laboratory and teaching spaces. The Colorado Alumnus, Vol: 62:5, December 1971, Pg. 1 Col. 1. Also see David Prescott’s update report on the department’s progress, June 17, 1975; Folder Faculty Meetings 1968-1975 in MCDB Archives.
responsible, in part, for the establishment of the new department and construction of the new building.63

Abe Flexer knew Porter while they were both at Harvard and moved to take up his faculty position in Boulder during 1969. At the time of his move, Flexer knew that he was moving to Colorado in part to “keep the world away from Keith Porter.” Flexer’s role was to be an administrator, without competition from a research program, who could communicate the needs of scientists to the architects and at the same time deal with the physical limitations of the building, like electricity and gas lines and air removal systems. The building plans already existed when Flexer arrived at MCDB, but one of his first tasks was to explain to the architects that each laboratory space would need water and gas outlets installed for the various pieces of equipment the researchers needed: details that the architects had overlooked. Flexer, as a scientist, knew what the laboratories needed and knew what type of equipment faculty researchers would require for their own research. This attention to detail was vital if the building was to function as a research and teaching space. Porter wanted nothing to do with these mundane tasks and inconveniences such as design specifications; hence, Flexer “kept the world” away from Porter who, unhindered by space and facility meetings, was able to carry out his role as chair of the department more effectively. One of Porter’s most important tasks was searching out new faculty who would help him build a first-class modern biology department.64

Biology was changing rapidly, and Porter had the acumen to recruit faculty members who would situate the department to become one of the leading research departments in the United States. Larry Gold and other early members of the faculty saw Porter as a visionary with the skills to provide structure and focus for the new department. Whereas some of the new faculty hires may have tested his patience, Porter recognized their research skills and scientific potential as beneficial to MCDB.65 While

63 Discussions over funding during this time were conducted with Dick McIntosh, Larry Gold, Abe Flexer, Andrew Staehelin, and Jonathan Van Blerkom either during the oral history interviews deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder or in personal comments. Also see “R & D Budget and Policy Program,” http://www.aaas.org/page/rd-colleges-and-universities accessed December 3, 2014.
64 See Flexer oral history interview, 08052013, 25:20 deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
65 Information gained from personal conservations with Dick McIntosh, Abe Flexer, and Larry Gold. While it is difficult to prove, Porter’s decision to recruit younger and upcoming faculty might have also been an effort to bolster
the Department was hiring junior faculty members, there were differences of opinion on how things should be organized and where the department’s focus of research should be. In the early years of the department, Porter concentrated heavily on cell and molecular biology and recruited faculty from those fields.66

While DNA and its role in inheritance had been discovered in the 1950s, questions about whether this genetic information could define the formation of a cell were still unsolved, and it seemed to the faculty in MCDB that many of those answers would be found at the molecular level.67 Some of the young faculty members joining biology departments around the United States in the early 1970s had been specifically trained in molecular biology rather than coming to the field from another discipline, and MCDB was no different. One of the major changes in biology was the move from the study of the whole organism to the study of organisms at the cellular and molecular level. This meant that the field of study for many young biologists was becoming increasingly focused on the molecules of life. Some of the early hires, like Larry Gold, who studied protein molecules and their synthesis, and Charles Yegian, who studied T4 bacteriophage (a virus that infects bacteria), represented this new discipline within biology. Biology at CU – Boulder now encompassed the study of whole organisms and population biology in the original biology department (known as environmental, population, and organismic biology –EPOB), and the study of the internal organization of cells and organisms in MCDB.68

By the late 1960s, biologists conducting close studies of the fundamental processes of life discovered an explanation of heredity; namely, the transmission of heritable characters and their expression in the building of each cell. This new knowledge was achieved through the study of certain bacteria, such as *E. coli*, and some viruses that parasitize them (bacteriophage). The task of asking analogous questions of the cells in higher organisms (eukaryotes) fell to scientists working in the 1970s and

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66 Faculty from IDB transferred into MCDB so Porter believed that developmental biology was already adequately represented in the department. Meredith Runner and others disagreed with this position. See Faculty Meetings Minutes, 1968-1973, MCDB Archives.


68 Information on areas of study obtained from the MCDB Graduate Program Catalogue, 1971.
1980s. These researchers studied the problems of development at the cellular and molecular level. Fundamental questions about the development of an organism from a fertilized ovum to an adult with cells differentiated into tissues and organs became the focus of much research, including by faculty at MCDB.

During faculty meetings in 1968, one of the many tasks was to anticipate the direction that biology would take, a quite impossible undertaking at the time, and then recruit faculty members who would be at the forefront of these changes and new directions. The faculty meetings considered researchers whose studies ranged from protozoan genetics, to insect development, to protein biochemistry and structure, to neurobiology, plant cell cytology, and animal virology. It seems that Porter, Runner, Ham, Prescott, and scientists from all over the world had recognized that molecular biology was “turning to development and differentiation” at the level of molecular mechanisms, seen within the context of a well-structured cell. Both the senior scientists in the new department and their most recent hires all recognized this issue was of paramount importance. A better understanding and a greater focus on molecular and cellular biology were crucial to solving the problems associated with the development of higher organisms.

A good example of this approach to understanding development was the work conducted by David Hirsh and Bill Wood in the mid-to-late 1970s; their studies concentrated on a small worm, the nematode *Caenorhabditis elegans*, in which they sought to understand how the embryonic cells of eukaryote organisms knew where to end up in the body plan. This problem was perplexing, especially because the cells of eukaryote organisms go through many cell divisions during development.

The move from prokaryotic to eukaryotic organisms brought with it a more defined mechanistic focus on the behavior of certain molecules within the

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69 Ibid, 593.
70 MCDB Faculty Meeting, May 31, 1968. Folder: Faculty Meetings, 1968-1973 located in the MCDB Archives. New faculty hires as of 1970 included Howard Berg, Mary Bonneville, Abe Flexer, Larry Gold, Dick McIntosh, Jeremy Picket-Heaps, Andrew Staehelin, Mike Yarus (joint position with chemistry 1970) and, Charles Yegian.
At the close of the 1970s, the research conducted by members of the MCDB faculty represented this re-focusing in the context of many aspects of molecular, cellular and developmental biology. To get to this stage of intellectual diversity, however, the department had convinced the administration that they needed to invest more money in the department if the university and the department were to keep pace with the ever advancing research in the various fields of experimental biology.

In 1976, it became clear to MCDB faculty that the department needed a new chair to lead them in the next phase of their development. The department wrote a proposal, entitled “Program Plan for Development of the Life Sciences Laboratories,” which they gave to the administration for final approval before submitting it the Colorado Commission on Higher Education and the Office of State Planning and Budgeting. The proposal, which focused on the need for a new chair, but also on the shortfalls of the new building’s infrastructure, was prompted by a number of factors. First, in 1976, the university administration informed the Department that the space they were using on the East Campus (PSRB#1) would have to be vacated and all laboratories (teaching and research laboratories, including Runner who was still located there) that were currently housed on East Campus would have to be relocated to the building on the main campus. The university offered to help the Department find the money that would cover the expense of moving the laboratories and refurbishing and finishing existing and undeveloped space in the biosciences building to accommodate the move. At this time, the biosciences building was still in need of a new chair suite and laboratory and improved teaching laboratories, both projects with low on the university’s lists of priorities at the time. The proposal also laid out various suggestions on how to improve biology education at the university and expand the research focus of the department.

Second, the biosciences building was at about 3/4 capacity for which it was

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71 Taped interview with Bill Wood deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
72 The Life Sciences Laboratories complex consisted of the biosciences building and the Muenzinger building, which housed the department of psychology. See, “Program Plan for Development of the Life Sciences Laboratories,” in Box 23 of the Vice Chancellor of Academic Affairs, Folder Biology – MCD, Norlin Archives, University of Colorado Boulder: about 4000 square feet of space was used for teaching labs; 1200 square feet was used as classroom-seminar; 1100 square feet was used by the teaching assistants; 1100 square feet by teaching assistants in the mathematic department; and 1200 square feet for storage. For discussion on the move from PSRB #1 see faculty meeting notes, 1968-1978, MCDB archives.
designed, both in terms of faculty members and space. Moreover, about 8000 square feet of the building was still not devoted to research and research-related activities for which the federal funding was obtained. This was a major concern for the department’s faculty, some of whom worried that any future federal funding they might seek for research could be delayed if the terms of the original building grants were not carried out in a timely fashion. Faculty argued that the university, by agreeing to accept the NIH grant (new building grant received in 1969), had made a “commitment to finish the building as described in that application.” Finally, it was argued that if MCDB were to recruit a new Department Chair a new suite would have to be built. The proposal to obtain more money for the biosciences building, then, was prompted by a series of events not anticipated by the department.

The most important concern for the department at this time, however, was finding a new chair to replace Keith Porter who proposed to step down as Chair in 1975. Finding someone to replace Porter, with his unwavering focus and strong leadership as well as his national prestige, excellent administrative skills and “political acumen”, would be a difficult endeavor. The department, now a top-class scientific research center, was a result of Porter's drive and vision. On discussing the opening of the new building in 1971, Porter stated: "That's what this department is all about...just fascination: new ideas, new techniques, new concepts, new interests which may open up vast areas to investigate...That's what we are dedicated to - not to filling gaps which have previously been sketched in by someone else. We want be to the original sketchers, not the elaborators." Finding someone with that same passion for innovation and research

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73 See page 1 of the proposal, “Program Plan for Development of the Life Sciences Laboratories,” in Box 23 of the Vice Chancellor of Academic Affairs, Folder Biology – MCD, Norlin Archives, University of Colorado Boulder: about 4000 square feet of space was used for teaching labs; 1200 square feet was used as classroom-seminar; 1100 square feet was used by the teaching assistants; 1100 square feet by teaching assistants in the mathematic department; and 1200 square feet for storage.

74 Ibid. The issue of grants and the terms of their support was an issue right from the beginning of the MCDB Department. In 1970, Meredith Runner was concerned that a NIH grant “Mechanisms in Developmental Biology” received in 1966 by IDB and now up for renewal in MCDB was in jeopardy due to the fact that developmental biology had essentially been usurped by molecular and cellular biology as a result of the HSAA grant. Runner believed that the de-emphasis of developmental biology would negatively impact the renewal of the NIH grant. To get around this problem, Runner suggested that the NIH grant support only those researchers working in mammalian development, as researchers in molecular and cellular biology were supported by other grants (the training grant in cellular biology (pending) and the HSAA grant). Letter to Vice President T.E. Manning, from Joe Daniel, Dick Ham, and Meredith Runner, dated June 8, 1970 in Folder: Future of DVB Program Project, MCDB Archives.

75 Keith Porter quote from the Colorado Alumnus, 1971
would be a tall order. While it was true that some of the younger faculty had the “scientific stature comparable to Porter, they lacked the experience and administrative skills to run a high-ranked biology department.” 76 It was agreed that the search for a new chair would involve going outside the department. Further, it was argued that a new chair of “high stature” would bring their own research dollars; help attract other scientists to the department that would do the same - bring research dollars; and finally, would help and encourage existing faculty members to work together to put together large research grant proposals that would include individuals from MCDB and other departments. The chair, in short, was to be a unifying figure for the department’s faculty who would maintain and further the academic performance of the department. To attract such a person, the department argued, the university would need to develop a new laboratory space and suite appropriate for a newly appointed professor who would also serve as the department chair. 77

It would take another two years to find a new outside and long-term chair, but eventually the Department did identify a new leader. In 1977, William (Bill) Wood agreed to move from the California Institute of Technology to take up the position of Chair beginning in the 1978 academic year. Under Wood’s leadership, the department expanded its research focus within developmental biology and genetics and continued the mission set out by Porter in 1971 to be the “sketchers, not the elaborators.” 78

**Pedagogy**

Creating a new pedagogy in MCDB involved the input of all faculty members; each one with his/her own ideas of what the ideal program would look like. The design of both the undergraduate and graduate programs (and curricula) were important components of the department as the reputation of the department, in terms of education, rested on the success of its undergraduates and graduates in the work place and academia. If the students lacked an education that prepared them to do first-class experimental biology, the department’s reputation, and that of the faculty, would be damaged. The department created two committees that were tasked with researching

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77 Pg. 2 of the proposal in Box 23 of the Vice Chancellor of Academic Affairs, Folder Biology – MCD, Norlin Archives, University of Colorado Boulder
78 Chapter 4 focuses on the scientific research conducted within the department.
and designing the undergraduate and graduate programs in MCDB. The committee
charged with designing the undergraduate program consisted of a few senior faculty
members and newly appointed faculty members. These faculty members received their
biology education at a time when Watson and Crick’s discovery of the structure of DNA
and its significance in the transfer of information was still a relatively new phenomenon;
in other words, everything these new faculty members learned during the time spent in
their graduate programs was new and innovational. When it came to designing the new
undergraduate program, these experiences played a significant role in what they
expected their new students to know about molecular, cellular, and developmental
biology.

One of the major differences between IDB and MCDB was their teaching
programs; whereas IDB had concentrated on graduate students (specifically Ph.D.
students), MCDB developed both undergraduate and graduate programs. Within seven
years of opening the department, the number of undergraduate students studying for a
bachelor’s degree in MCDB had risen to 500 students - each receiving a biology
education that, it was hoped, would prepare them to enter careers as biological research
technicians or teachers, or to compete for places at a medical school or in other health-
related professions. The pedagogical emphasis of the undergraduate program was on the
theoretical basis of modern biology, commonly with the opportunity to gain experience
working in one of the many laboratories in the department. Undergraduate students
were (and are) encouraged to undertake independent study in a laboratory to learn
about techniques, technology, developing scientific hypotheses, and creating their own
experiments under the guidance of professors or post-graduate fellows. As soon as the
department was established, the faculty set about designing the new undergraduate
program with an intellectual focus that was fundamentally different from the program
already in existence in the original biology department.

Developing a new undergraduate curriculum in MCDB required the faculty to
identify the intellectual focus of “modern biology” and to decide what an undergraduate
program in MCDB would look like. The committee tasked with undergraduate
curriculum development included Ed McConkey, Peter Kuempel, Abe Flexer, Peter
Albersheim, and Jeremy Picket-Heaps. Their first assignment was to recognize the
deficiencies of the existing biology program on offer for students wanting to pursue a career in health sciences or research, and then to determine what students would need in an undergraduate biology program if they were to pursue this chosen career path. The resulting two-semester long introductory course in MCDB was quite innovative at the time, as it introduced all the various elements associated with MCDB in a single course. The course was first taught during the academic year 1971-1972 by Peter Albersheim, Mark Dubin, Abe Flexer, and Dick McIntosh who shared the teaching load over the period of two semesters.79 The course was intensive for a 1000 level course and met twice a week 8.15 – 9.50 a.m., with one 2-hour recitation session where students saw and participated in demonstrations. Albersheim, Flexer, and McIntosh had taught introductory-level courses at Harvard in a variety of fields: biology, biochemistry, molecular genetics, microbiology, and cell biology. They all brought their expertise and knowledge to the new course titled “An Introduction to Molecular, Cellular, and Developmental Biology.” After students completed this course, along with introductory courses in general chemistry, mathematics, and physics, plus a second level course in organic chemistry, the department felt that the standard of science education now provided to the students would prepare them for more intensive upper-level courses that focused on more specific aspects of modern biology.80

The rigorous nature and format of the undergraduate program did not abate over the following years, but course content did change in response to new faculty hires, societal issues, and new discoveries in the various fields of study. Keeping abreast with current research and discoveries was essential if the department was to attract the best

79 In his interview, Peter Albersheim describes how he had originally planned an introductory course in the Chemistry Department, but that never went ahead because the department’s faculty was not in favor of a biochemist teaching an introductory course in chemistry. Albersheim goes on to explain that he took the introductory course idea to MCDB where it was better received. In consultation with other MCDB faculty they created the course and Albersheim took his NSF grant funding of $50,000 to teach an introductory course from Chemistry to MCDB. Interview deposited in the Karen Lloyd Collection, Norlins Archives, University of Colorado Boulder. Dick McIntosh and the other teachers designed the syllabus in consultation. Dick McIntosh believes it was the first such undergraduate course of its time. Comments from Dick McIntosh in margins of chapter 3 draft.

80 See leaflet from August 1970 that publicizes the new undergraduate program. Folder: History of MCDB undergraduate program; MCDB Archives.
students to the department. The early curriculum ensured that undergraduates would be educated in cell and tissue biology, genetics, molecular biology, embryology, physiology, developmental mechanisms, and biochemistry, but by the close of the 1980s, students were also expected to learn the connections between science and society. This was in part, I suggest, a reaction to the rise of creationists, demanding that creationism be taught alongside evolution in the classroom. The course “Evolution and Creationism” was still on the course list in 2003.81

Unlike the new undergraduate program that was developed within MCDB, the graduate program (Ph.D. in Developmental Biology), along with several graduate students, was inherited from IDB, which had been running the program since 1966. Initially, it was thought that the program as it existed would be retained, and the department would create new graduate programs in Cellular Biology and Molecular Biology, resulting in three closely-related fields of study to offer graduate students. This situation (having three Ph.D. programs) proved to be unworkable, and instead faculty modified the existing the Ph.D. program’s course content and changed its name to a Ph.D. in Biology.82 As the program had existed in IDB, very few courses dealt with cell biology, but those that had been created, Cell Structure and Function and Culture Techniques, were retained with Drs. Ham, Goldstein, and Prescott continuing to provide support for the Cell Biology Programs. Other courses added to the Ph.D. program included genetics, developmental systems, early mammalian development, nonsexual developmental systems, teratogenesis, and laboratories in molecular genetics.83 The new program, then, came to represent the entire intellectual focus of the department and not that just limited to developmental biology.

81 See 2003 PRP document in MCDB Archives. The course-listing in this document reveals how the department considered its role in educating students about the connections between biology and society. Courses on plagues and society, human diseases, the cancer cell, and fertility represent the importance of science in helping students understanding societal issues.

82 See faculty meeting minutes August 18, 1969 in Folder: Faculty Meetings 1968-1973; MCDB Archives; also Cell Biology Training Grant application, 1969: Folder-Cell Biology Training Grant; MCDB Archives. The official notification of the change of name came from the Colorado Commission on Higher Education had approved the change in name and course content. See the letter from Lawson Crowe, VP for Research and Dean of the Graduate School, to Keith Porter, dated April 2, 1971 in Folder – PhD Program in Molecular Biology; MCDB Archives.

Porter and the new faculty members proposed to add several new courses that specifically dealt with cell biology, including the biophysics of cells and cell products, and computer programming for analysis of data, date storage and data retrieval.\(^8^4\) Perhaps the most innovative course in the Ph.D. program was the introduction of the Core Courses in 1981, assembled by Dick McIntosh, Larry Gold, David Hirsh, Michael Yarus, and Bill Wood.\(^8^5\) This comprised four courses, which ran through fall and spring, lasted for seven weeks each, and provided an “advanced overview of life processes, at the molecular, cellular, and developmental level, as well as an introduction to current research in these areas of biology.”\(^8^6\) Dick McIntosh remembers it as “an amazing effort in which we all came to all of each other’s lectures.”\(^8^7\) The courses encouraged discussion around new research, and McIntosh believes that it was quite experimental in graduate pedagogy and “revolutionized” the graduate program. Previously, discussions had centered on the earlier foundational works of the various disciplines and were more historical in nature than a critical reading and analysis of specific publications. The new approach to modern biology at the Ph.D. level involved learning both the strengths and weaknesses of new techniques, and it encouraged the ability to work in the fields of biology, physics, chemistry, and mathematics. The faculty members of MCDB centered their research and education on interdisciplinary approaches necessary for understanding the mechanisms involved in the development of cells and organisms.

The success of the Ph.D. program can be measured in the number of graduate students studying in the department and the amount of funding received. By the spring semester of 1976, the Graduate program had 45 students studying for the Ph.D. in Biology: an increase from the 38 students in the fall semester of 1969. But more

\(^{8^4}\) Ibid, pg. 21 – 27. Introduction to Cell and Tissue Biology; Cell Growth and Reproduction; Cell Differentiation; Cellular Biology of Eukaryotic Organisms; The Plant Cell; Neurobiology; Techniques for Microscopy; Techniques for Cell Chemistry; Growth, Maintenance, and Manipulation of Cells In Vitro; Nucleo-Cytoplasmic Relationships.  
\(^{8^5}\) Dick McIntosh brought this series of core courses to my attention.  
\(^{8^6}\) Description taken from the University of Colorado – Boulder 1981-1982 course catalogue. This was the first time the course appeared in the catalogue.  
\(^{8^7}\) Notes on margins from Dick McIntosh on Chapter 3 draft.
importantly, the program competed for the best students with "notable success" against the more well-known institutions like Stanford, University of California, Berkeley, Harvard, and the California Institute for Technology.88

The department was, by the mid-1970s, highly regarded by other institutions and professional researchers.89 Because of this high regard for the work being carried out at Boulder, major funding for the Ph.D. program and research (laboratories and equipment) came from outside the university and state, and consisted of a combination of federal money secured from the NIH, NSF, nationally recognized research societies such as the American Cancer Society and Muscular Dystrophy Association, and private foundations. The funding generally supported research programs, salaries for graduate students, post-doctoral fellows, undergraduate student laboratory workers, technical assistants, and faculty members.90

The impact the department’s Ph.D. program had on its graduate students and the study of biology was significant. For example, during an interview with former graduate student Jonathan Van Blerkom, now a renowned embryologist who performed Colorado’s first successful in vitro fertilization (IVF) procedure, in 1982, he reflected on his days as one of the first graduate students in MCDB. He had good memories of David Prescott and Keith Porter, whom he described as being excellent researchers and real gentlemen. They were supportive of graduate students, especially those who had a real passion for learning. But one of the defining moments for Van Blerkom, in retrospect, was being a graduate student with Dick Ham. Jokingly, Van Blerkom remembered graduate students being treated “as unpaid labor” in Ham’s laboratory: Ham created all the cultures for his experiments, and he got the graduate students to do this for him. Consequently, Van Blerkom learned the art of creating cell cultures for his research. With this particular skill in hand Van

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87 A look at the number of letters received by Keith Porter by researchers around the United States and the world bears witness to how highly Porter and the department were regarded. Many of the letters were letters of congratulations or letters enquiring about research opportunities in the department. Keith Porter Collection, Correspondence Boxes, Norlin Archives, University of Colorado – Boulder.
90 Ibid. pg. 5.
Blerkom headed to Cambridge, U.K. to work as a postdoctoral fellow, where he shared these skills with researchers in the laboratory of Robert Edwards, one of the pioneers of IVF in the U.K. On his return to Boulder, he told Dick Ham that he had shared the cell culture procedures with the Cambridge lab, to which Dick Ham replied that he had another technique that would be better suited for the work they were doing in Cambridge. Thinking nothing of it, Dick Ham shared that technique with the Cambridge lab, and a couple of years later the first human IVF child, Louise Joy Brown, was born in 1978.91 The reach of the training received by graduate students in MCDB is far and wide; not only in terms of places visited but in scientific research.92 The example of Van Blerkom’s experiences in MCDB serves to show the willingness of early faculty members to share their knowledge and experiences with the graduate student population. This indeed was Porter’s vision for the department in action.

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91 Interview with Jonathan Van Blerkom, July 9, 2014 deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
92 See Chapter 4 for a discussion on scientific research conducted within the department.
Sound Bites from the *Colorado Alumnus* December 1971 on the Opening of the New Building

*David Prescott*

"In our society the impulse to understand what is not understood has lost some of its importance. Anti-intellectualism, particularly towards science is rampant. A lot of people look upon this activity as purposeless even dangerous straining of the mind."

On education and the importance of combining hard research within a teaching institution, "I can give students information unavailable in a textbook."

*Peter Albersheim*

The recent mid-Western corn blight, for example, was apparently caused by a mutated virus. He stated: "If we could discover the causes, which may be chemically definable, for these mutations, as well as the reason that some varieties of the plant are more susceptible to disease, we might be able to control the disease virus without resorting to the use of pesticides."

*David Hirsh*

"Basic research is the unfettered attempt to gain new knowledge. If society elects to neglect it, it will be electing to neglect a very important thing...its whole future."

*Mary Bonneville*

Mary Bonneville was the department's only female faculty member in 1971. One of her main goals was to increase the quality as well as the quantity of education. She stated: "Research is a creative effort. We should let people have the freedom to come up with new questions, new ideas...they should be able to use their creative imaginations."

"One of the challenges teachers must constantly meet is the elimination of old answers and the substitution of new ones as well as to admit new questions which may open new fields."
Some Notable Achievements in the Early Years of MCDB

1968: Estes Park Conference on The Control of Form in Cells, an innovative meeting organized by Keith Porter that brought together cell and molecular biologists, virologists, and crystallographers to seek a deeper understanding of the cytoskeleton.

1968: Keith Porter wins Teaching Recognition Award in his first year at CU Boulder

1970: Mary Bonneville appointed first female faculty member of MCDB, she remained in MCDB throughout her career

1973: Dick McIntosh wins Teaching Recognition Award

1975: Kathleen Danna and Rose Litman become the second and third appointed female faculty

1977: Keith Porter receives National Medal of Science from President Carter

1978: Keith Porter receives one of the first two “Distinguished Professor” titles at CU

1980: David Prescott named Distinguished Professor at CU

1982: Porterfest Symposium held in honor of Keith Porter’s retirement and 70th birthday. The papers given by scientists from both CU and other institutions were published in Spatial Organization of Eukaryotic Cells (a symposium in honor of K.R. Porter) (1983) ed. by J. R. McIntosh Modern Cell Biology vol 2, pp.365.

1982: Porter Biosciences Building is dedicated

1982: Keith Porter is awarded honorary CU degree

“Porter-Fest”, 1984 A scientific party in honor of Porter’s Retirement
Some of the Key Members of Staff and their Importance in Developing the Strengths of MCDB

Evelyn Krohn, Admin. Assist. for Student Affairs

Doris DeFalco Secretary to the Chair

Wendell Stewart, Superv. of the Stock Room
Chapter 4  Delving into the Cell: a historical perspective on the research undertaken in MCDB

In the late 1960s, the state of biology, particularly in the newly established Department of Molecular, Cellular, and Developmental Biology, was one of newness and discovery. Larry Gold stated: “We couldn’t fail to discover something new...everything was new!”93 In many ways he was right; when MCDB was established in 1968 the structure of DNA, determined by Watson and Crick, had been known for only some fifteen years. This structure contained an abundance of new information and implications for the study of life. It formed the basis for understanding the nature of a gene, how cells could replicate their genes in preparation for cell division, and how genetic information could be interpreted by the cell. The discovery changed the study of many aspects of biology, encouraging a change from a largely descriptive discipline to one that sought to uncover the mechanisms that controlled the fundamental processes of life. It is true that experimental biology had a long tradition, but until the structures of DNA and of several proteins were established it was impossible to relate the macroscopic properties of organisms to the properties of the molecules from which they were built. Discoveries at a molecular level then, enabled a new kind of biology that worked to link the properties of organisms to the properties and behavior of their constituent parts.

It was during this time of change that the young, recently appointed faculty in MCDB received their training. New technologies also played an important role in the emerging new discipline in experimental biology - helping to reveal how cells and molecules behaved under certain conditions and at certain times of an organism’s development. Learning how to use these technologies was crucial for those early researchers if they were to gain insight into how macromolecules worked, how cells functioned, and how organisms developed over time.94

93 Larry Gold, Interview -17.45, deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
94 During a conversation with Dick McIntosh, he recalled that during his time as Chair of MCDB he had made a comment that basically united the three disciplines around a common notion of understanding how cells developed. A molecular biologist in the department stated he didn’t actually care at all about cells or development; he was only interested in molecules. The comment is revealing – for while the department appeared to be united around a
Technology, equipment, and laboratory space were an important part of the new biology with its focus on the molecular and cellular levels of organismal development. Indeed, one of the major reasons that the University of Colorado decided to establish a new biology department was the existing biology department’s lack of laboratory space, equipment, technology, and technological skill that were necessary to study organisms at a micro-level. The new building constructed on the main campus was designed to accommodate the tools necessary for new kinds of experiments, and with funding received from federal agencies, such as the National Science Foundation and the National Institutes for Health, the building was fitted out with up-to-date laboratories and equipment. Cold rooms, dark rooms, clean rooms for cell culture, animal rooms, and laboratories all contained equipment that ranged from simple glass test tubes to centrifuges and machines for measuring the amounts of radioactive materials that were used as tracers (or labels) to map molecules during their transport through biochemical reactions within cells, or during an organism’s development. The new building was described as the best designed and equipped biosciences building “between California and the Mid-West.”

The physical resources provided in the new building meant that researchers in MCDB were now positioned to study many aspects of biology. To do so they employed a range of organisms: bacteria and the viruses that could infect them, slime molds, cultured mammalian cells, and embryos of various organisms (fruit flies, frogs, chickens), and small rodents such as mice and hamsters. Scientists interested in development sought to understand the molecular processes that allowed the specialization of cells during the formation of the tissues and organs in an organism. But, this type of work required familiarity with a wide range of techniques and equipment whose proper use depended on knowledge that spanned several sciences (biology, physics, and chemistry). Such experimental complexity required MCDB researchers to collaborate with each other so each could learn new techniques.

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necessary to complete their research. It also led them to “sit in” on each other’s lectures to learn more about a particular sub-discipline that might be useful to their own research. This was particularly true for some molecular biologists who lacked the knowledge to deal with higher organisms (like a mouse) – for this they had to retrain and “plunge into the complexity of development, to learn the techniques of experimental embryology and cell biology.”

Researchers in MCDB often collaborated and engaged in lively discussions about their common interests: having a space where they could come together to share mutual interests and engage in intellectual discourse was important to the success of their research. Sharing techniques, equipment, and knowledge increased their research power through the grouping of skills, talents, and expertise; it helped in finding solutions to research problems. For example, just one year after the establishment of IDB, David M. Prescott and Lester Goldstein discovered protein transport into and out of the nucleus and proved that the cytoplasm had an important influence on nuclear DNA synthesis. Prescott and Goldstein’s research proved that the cytoplasm played a role in nuclear phenomena: prior to their research and findings there was only a presumption that it did.

Howard Berg and his bacterium tracking microscope

In 1973, Peter Kuempel and Prescott discovered bidirectional replication of DNA in Escherichia coli. (This work began in IDB, but both researchers were in MCDB at the time the work was

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97 Michel Morange, *A History of Molecular Biology* (Cambridge, Mass.: Harvard University Press, 2000), 177. This is a generalization on the part of Morange; as noted above some molecular biologists didn’t care about development or cellular biology and were only interested in researching macromolecules.


published). Kuempel and Jonathan Van Blerkom, a graduate student in IDB, appreciated and valued this form of collaboration with older and more established scientists, such as Prescott, Richard Ham, and Meredith Runner, all of whom were all willing to share their knowledge and time with younger researchers. Such collaborations proved particularly effective when the younger scientist was trained in some new techniques of molecular biology. The knowledge gained from this type of collaboration, however, benefited everyone, as the older researchers learned new techniques and methods required for modern biology. The proximity of the laboratories may have played some role in developing these collaborations, but whatever the reason, the early years in IDB and MCDB saw a flourishing of collaborative research and journal articles with authors from multiple laboratories.

**Cell Biology**

Modern biology research, which focused on the mechanisms of the process under study, required the use of high-powered microscopes to gain a better view of the various structures within a cell, but obtaining new images of the cell required the development of new techniques by which the cell could be prepared. One of the leaders in this new way to study cells was Keith Porter, who is credited with introducing the electron microscope into the study of the cell structure. Porter began this work in the early 1940s while working at the Rockefeller Institute in New York. In collaboration with Ernest Fullam, a microscopist at Interchemicals Research Laboratories in New York, Porter developed techniques with which to prepare cancerous cells for view under the electron microscope. These methods included new modes of cell cultures and of

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100 See interviews with Peter Kuempel and Jonathan Van Blerkom, deposited in the Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder. It is unclear from the archives that I have visited whether this type of collaboration continued. Certainly, professors collaborated with their graduate students and published articles together, but whether collaboration between professors in an academic setting continued past the mid-1970s is unclear. Dick Ham worked extensively with the Chinese hamster and developed many cultures and procedures for developing cultures, which were used around the United States. Kuempel worked primarily with *E. coli*, and Van Blerkom became a pioneer in in vitro fertilization and embryology. David Prescott was a cell biologist working in developmental biology and who, according to Kuempel was a good microscopist and used radioactive compounds to create micrographs, and Meredith Runner worked with mice in the field of developmental biology.

101 See timeline of major research conducted by researchers and faculty at MCDB at the website (Paul Muhlrad).

chemical fixation. Soon thereafter, Porter was also involved in the design of a microtome capable of cutting very thin slices of cells (the Porter-Blum microtome), which was useful for the type of new research Porter was conducting. The images that resulted from these collaborations became the standard for all future journal article images, but more importantly, the collaborations revealed miniscule features of intact cells that had not been previously seen.

From these beginnings, it became evident that much more work would be needed to gain a deep knowledge of a cell’s internal structures. Dogged determination for a better understanding of the cell’s organization led Porter and others to concentrate on developing ever better techniques for culturing cells and fixing them in media that would preserve the cell’s architecture. It was hoped that these new techniques would produce clearer and more reliable images that would be free of altered structures, which were considered artifacts of the various processes and techniques used in the preparation of the cells. Conventional methods of fixing and staining tended to alter the cell structures, but to what extent the structures were altered was hard to determine. In Boulder, several scientists developed different approaches to fixation, albeit, each with its own limitations. Jeremy Pickett-Heaps explored rapid chemical fixation of algae growing in their natural habitat; Andrew Staehelin worked with rapid freezing; Porter and his Boulder laboratory concentrated on chemical fixation followed by a variety of methods to dry the cells and make them useful for study in the electron microscope. All of these approaches contributed to a better understanding of cell structure, but in spite of significant progress the results were never the “last word.”

Porter’s confidence in the abilities of the electron microscope to provide a better understanding of the cell structure led him to convince the University of Colorado at Boulder to invest in a high-voltage electron microscope (HVEM) made by the Japanese

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104 At CU, Mircea Fotino, Richard McIntosh, Jeremy Pickett-Heaps, and Andrew Staehelin have spent many years perfecting fixation techniques and imagery of cell structures. As the use of the electron microscope became more standard throughout the discipline, cell structures that were assumed to be part of the original cell were later determined to be artifacts of the processes used in staining and fixing the cells. See interview with Andrew Staehelin in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
Electron Optical Laboratories (JEOL); it was one of only three HVEMs dedicated to biological research in the United States. Porter hoped that this instrument would open a new window on the fine structure of cells. Such progress would only come, however, at considerable cost. The HVEM was expensive to purchase and demanded a large space within the new building. Funded by a grant from the NIH, the HVEM was installed in 1972. It stood 32 feet high and weighed approximately 22 tons and was located at the west end of the new building in a space constructed with separate foundations so as to reduce the effects of vibrations caused during the operation of the microscope. The maintenance and usage of such a machine demanded a highly trained staff, which included physicist Mircea Fotino who was recruited specifically to be the Director of the high voltage EM lab and design the installation, and George Wray, who came from the U.S. Steel Corporation to be the manager of the microscope and to maintain it. A high level of technical expertise was required to keep the HVEM running, but because of Wray’s skills and attention to detail cell biologists could focus on their samples, leaving the maintenance of the microscope to others. Porter believed that the instrument would allow the exploration of a cell’s three-dimensional organization because the high energy of its electron beam permitted the imaging of comparatively thick samples, slices that were several micrometers thick, or even whole cells. The microscope could take stereo electron micrographs, which provided the researcher with a 3D image of a cell at a resolution better than could be achieved by light microscopy.

The success of the HVEM, in terms of new scientific discoveries was limited, despite the beautiful images produced by the machine. Porter’s laboratory used the HVEM to examine cells that performed physiological tasks, such as the motion of cytoplasmic

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106 Porter and Tucker, “The Ground Substance of the Living Cell.” pg. 58
107 Cell Biology Training Grant Application, pg. 31.
pigment granules. He believed that a network of slender fibrils within the cytoplasm defined the position and behavior of all the cell’s constituents: the nucleus, mitochondria, endoplasmic reticulum, the Golgi complex, and even the cytoskeleton.\textsuperscript{109} He called these structures the “micro-trabecular lattice” and found evidence for this interconnecting network in several cell types, all prepared in several ways. Unfortunately, further work in other laboratories suggested that this network was an artifact of the various preparative methods used, rather than a novel cytoplasmic component.\textsuperscript{110}

Porter, his students, and his colleagues used the penetrating power of the HVEM’s megavolt electrons to image whole cells, as he did with a conventional microscope during his time at the Rockefeller Institute. They produced extremely detailed images, but in reality they showed very little that had not previously been described. Others, such as Lee Peachey from the University of Pennsylvania (and a summer adjunct professor in MCDB for many years) and Pierre Favard from Paris, devised ways of staining specific compartments in the cells they studied. The samples they produced were then imaged with the HVEM, but again, while the images produced were striking they did not create any new knowledge about the cell.

\textit{Column and console of the HVEM}

\textsuperscript{109} Porter and Tucker, “The Ground Substance of the Living Cell.”

\textsuperscript{110} Pawley, J and H. Ris (1987) Journal of Microscopy 145(3): 319-32. However, Porter’s concept of interconnectedness between the elements in the cell’s structure has been borne out by the discovery of structural proteins that link the elements of the cytoskeleton to one another and to the cyto-membrane compartments, forming some kind of unified mechanical system. Richard McIntosh, personal communication and Heuser, “Whatever Happened to the Microtrabecular Concept?”
Throughout the 1970s, the HVEM helped to provide the department with a greater presence in the field of cell biology, helping to make MCDB a renowned electron microscope structural research center. The resolution of the HVEM was excellent, but the images of thick samples proved to be less useful than had been hoped, largely because so much cellular material was projected onto a single 2D image. Even with stereo viewing, observers struggled to decipher the HVEM image of a mitotic spindle intricacies of the cell. The utility of the microscope for biological studies appeared to be limited. After Porter retired from the department in the early 1980s, enthusiasm for the HVEM declined, both in the department and in biology more generally. Porter had been the driving force for the HVEM in MCDB, but the research that could be achieved with the microscope at that time was severely restricted. Dick McIntosh took over as the director of the HVEM laboratory in the early 1980s, but he and his colleagues regarded the continued use of the microscope with skepticism. Andrew Staehelin described the HVEM as a “microscope in search of a purpose,” rather than a solution for solving problems in structural biology. The microscope represented a huge monetary investment by the NIH and subsequent grants had been secured to ensure its continued usage by the department and visiting researchers from other institutes.

During the 1990s, however, the fortunes of the microscope were reinvigorated with the introduction of electron tomography by Dick McIntosh, David Mastronarde, and others in the department. The use of tomography to generate 3D images of cells was first developed effectively in the laboratories of Joachim Frank in Albany, NY and

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111 Andrew Staehelin, 23:00 to 25:00 of Interview No. 2, deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
112 Per comments received from Dick McIntosh
113 Andrew Staehelin, 29:00 of interview No. 2 deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
114 Andrew Staehelin quote – 28:00 of Interview No. 2, Ibid.
Wolfgang Baumeister in Germany. The method permitted the use of relatively thick samples, e.g., slices of a cell as much as a micrometer thick. The sample is placed in a tilting sample holder and imaged at a wide range of tilts. The images are aligned and combined by any of a variety of algorithms, thus generating a true 3D representation of the original sample. Implementing this approach at MCDB required an up-grade to the HVEM with a side-entry stage and an electronic camera for the rapid image recording and digitization. The NIH, once again, provided funding to support these changes to the microscope, allowing McIntosh and Mastronarde to produce 3D images of cells that really did provide new information.115

During this same period of renewed activity in the HVEM laboratory, Andrew Staehelin and his colleagues explored the value of different methods for the rapid freezing of samples big enough to include the complexity of important biological systems, such as root tips, embryos, and small samples of tissue. Conventional methods of chemical staining and fixing tend to alter cell structures, but it was believed that if the temperature of a sample could be lowered fast enough, molecular motion would simply slow down, thereby minimizing cell distortion and preserving cell structure for examination in the electron microscope.116

The key to making this approach work was to solve a problem caused by cooling water and crystal formation. As crystals grow, they deform the biological structure and damage the sample. To avoid ice crystal damage, earlier workers introduced chemicals that inhibited crystal formation, but their effect on cell structure made the resulting images suspect. From his previous work in the late 1970s, Staehelin knew that if he could freeze samples fast enough, the ice crystals either would not form at all, or if they did they would be too small to damage cell structure at the resolution available with the electron microscope. Staehelin’s laboratory was aided by the development of an instrument by Hans Moore in Switzerland. Moore’s device applied a very high hydrostatic pressure to a sample within milliseconds just prior to a rapid lowering of its temperature. The high pressure inhibited the formation of ice crystals, so making the

116 Clark, “Research Highlights.” Pg. 11
use of chemical additives unnecessary. Experiments in Moore’s laboratory showed that cells frozen in this way could be thawed, and a significant number of them would live to grow and divide again. This appeared to be a promising method for sample preparation.

Staehelin obtained the first high-pressure freezer to arrive in the United States, and with this tool he developed method for cryo-immobilizing a wide range of biological samples without the formation of visible ice crystals. These samples were then treated at low temperature with organic solvents to dissolve the solidified water. In the 1990s the process was perfected in collaboration with Kent McDonald, then Associate Director of the HVEM laboratory, and Thomas Giddings, the supervisor of the department’s conventional electron microscopes. The quality of the resulting images led to this process of “freeze-substitution” being accepted in the cell biology community as the method of choice for preparing cellular samples for electron microscopy. The research carried out by this group built on work done at other laboratories around the world. They were able to show that, at around a temperature of -80°C, acetone dissolved the frozen water from the sample, which allowed for the introduction of chemicals that cross-linked the biological molecules allowing them to be fixed in place. These samples were then embedded in plastic and sliced into thick sections before imaging in an intermediate voltage electron microscope (IVEM).

Using the well-preserved samples and the imaging methods of tomography, the HVEM produced some quite dramatic images. In 1996, David Mastronarde (a computer expert trained in physics), Jim Kremer, and Dick McIntosh published a new user-friendly program package reconstruction by electron tomography.117

3D model of the Golgi complex from an insulin-secreting cell prepared by rapid freezing, then electron tomography and computer-based modeling for 3D

According to Staehelin, the new images produced at MCDB pushed electron microscopy to a new level and CU-Boulder was again at the forefront of new developments in microscopy. Through these efforts, MCDB made a real contribution to the way people studied cell structure. The 1990s and early part of the new millennium, then, saw a renewed impact of the department and the HVEM on the ways cell structure was studied.

The study of cell biology at MCDB was not limited to just structural studies and the HVEM. David Prescott, for example, was an experimentalist cell biologist. Prescott and others were more interested in understanding the cell cycle and mapping growth and division. They sought to uncover the processes that determined when a cell divided and where in the cell cycle DNA was made. In other words, while Porter was interested in discovering how cells were built, Prescott and others wanted to know how cells worked. It was these two fundamental research approaches that represented the early focus of cell biology at Boulder. Work undertaken by Jeremy Pickett-Heaps brought these two approaches together. Using both light and electron microscopy, Pickett-Heaps’ laboratory examined not only the cycles of growth and division in unicellular plants, they also examined the complete life cycles of diatoms and desmids, revealing the ways these organisms could reproduce by vegetative growth in some conditions yet turn to sexual reproduction in others.

**Molecular Biology**

At the time of the department’s establishment, the nature of a gene was just coming to be understood. Both the details of DNA replication and the mechanisms by which gene expression was regulated were issues for active research. Current research of the time, then focused on phage and bacteria, indicated that DNA replication might occur at specialized sites on the bacterial membrane, but the genetic and biochemical requirements for attaching DNA to these sites were still mysteries. Determining the mechanisms of regulating gene expression was one of the challenges taken up by the

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118 Andrew Staehelin, 44:00 to 1:8:20, interview No.2, deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.

119 The HVEM was finally taken out of commission in the early 2000s.
molecular biologists in MCDB. However, before they could approach an understanding of these processes in higher organisms, biologists worked with model systems that could be used to determine how cellular and molecular mechanisms worked in simpler organisms; these were easier and cheaper to use for experimentation than higher order organisms. Once this knowledge had been gained, researchers hoped that it could be applied to the understanding of more complex organisms. *Escherichia coli* (*E. coli*), a bacterium that lives in the digestive tracts of humans and animals, is an example of a popular model organism used by all biology researchers in MCDB, molecular biologists, however, used biochemical techniques to study the regulatory systems of phage-infected bacteria and virus-infected mammalian cells.

The study of ribonucleic acid (RNA) became a major focus for molecular biologists in MCDB who developed techniques and model systems to aid in their understanding of the nature of RNA. Questions focused on understanding how protein synthesis worked and the processes involved in the regulation of gene expression were at the root of much of the research undertaken in MCDB, where, more specifically, researchers looked at the structure, role, and function of macromolecules involved in the cell. Macromolecules are complex and undertake multiple functions within a cell – for example, they play roles in DNA synthesis, transcription and translation, and the catalytic activities that underlie metabolism. The mechanisms by which these processes are controlled, so that specific genes are transcribed, or specific mRNAs are translated at precisely defined times during the life cycle of the organism, represent a fundamental expression of differentiation at the molecular level. Molecular biologists, then, were less interested in the structure and mechanisms of the cell and more interested in how nucleic acids, both DNA and RNA, and proteins functioned within the cell.

Early faculty involved in the function of RNA included Edwin McConkey, who focused on protein synthesis in eukaryotes, ribosome synthesis, and nucleolar functions.

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120 Andrew Staehelin claimed that, during the 1980s and 1990s, MCDB and Biochemistry could be considered the RNA Capital of the World. Interview #2 - 1:13:50. Interview deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder. Michael Yarus, one of the early molecular biologists and biochemists at MCDB, agreed with this statement. Personal comment to author. Dick McIntosh, in margin comments to author, stated that the work being carried out in MCDB and biochemistry was some of the best research on RNA anywhere in the then current scientific world.
Charles Yegian studied the regulation of phage development, and the regulatory functions of bacterial transfer RNA. Larry Gold’s laboratory worked on the regulation of gene expression in T4 phage through the study of gene32 and this phage’s bacterial host, *E. coli*. Gold and his lab hoped that these specific studies would help them to understand the mechanisms that controlled the transcription and translation of genes in general. Two graduate students in the Gold lab made discoveries that are widely used and acknowledged today. The first discovery, in the 1970s, was made by Patrick O’Farrell, who worked out a method for two-dimensional separation of the proteins from complex mixtures, like the cytoplasm of a phage-infected bacterium. This method, called 2D gel electrophoresis, could reveal both the molecular weight and isoelectric point of about 1000 proteins in a single process, and the method became widely used. The second major discovery was made by Craig Tuerk in the late 1980s. He invented a process for the systematic evolution of specific RNA ligands, molecules that could recognize and bind to a molecule of interest, by sequential enrichment *in vitro*. This method, published in *Science* in 1990, subsequently led to a process called SELEX, which became the cornerstone of two biotechnology companies founded by Larry Gold.\(^1\) SELEX identifies single-stranded oligonucleotides (aptamers) that bind tightly to a protein of choice. The fact that RNA molecules could form strong bonds with specific proteins contributed to scientists no longer thinking of single-stranded nucleic acids as “wiggly lines,” but instead as objects with a defined structure, much like proteins. This knowledge is today utilized in both diagnostic procedures and in delivering therapeutic medicines to combat diseases. Other work coming out of the Gold laboratory focused on the identification of nucleotide sequences that defined binding sites for proteins, such as those that regulate gene expression.\(^2\)

Mike Yarus and his laboratory focused on the biochemical and biophysical properties of transfer RNA molecules (tRNAs), which interpret mRNA sequences at the ribosomes. His studies helped to build an understanding of how subtly tRNAs function

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2. See work by Gary Stormo, Tom Schneider working in the Gold lab in the late 1980s.
within the ribosome during translation. Much of Yarus’ research has built on this initial research to focus on protein synthesis (proofreading of amino acid incorporation) and binding sites (RNAs that bind amino acids) and the development of protein synthesis inhibitors. One such inhibitor was crucial to later the identification, by structural studies at Yale, of the ribozyme’s active site, and to proof of the mechanism by which amino acids are joined together in all organisms.

It was in this context that researchers in Boulder began to realize that RNA molecules can also serve as catalysts – that is, they can speed up specific chemical reactions in a way that had previously been thought to be exclusively carried out by proteins. Tom Cech in the Dept. of Chemistry and Biochemistry studied the splicing of RNA in a unicellular organism called *Tetrahymena thermophila*. He discovered that a particular RNA molecule would splice itself without the help of any protein. In other words, the RNA molecule could cut itself into pieces and join the genetically important RNA fragments together again. Through the discovery of this chemically complex, self-splicing reaction, Cech in 1982 became the first to show that RNA molecules can have a catalytic function. Subsequent development has been rapid and today close to a hundred RNA enzymes (called ribozymes) are known. In 1989, Cech shared the Nobel Prize in Chemistry in recognition of this work.

The discovery of these new “ribozymes” in Tom Cech’s lab created immense interest in RNA molecules, their structures and functions. For examples, the discovery supported an earlier hypothesis put forward by Carl Woese, Francis Crick, and Leslie Orgel in the 1960s that the earliest forms of life may have relied solely on RNA both to store genetic information and to catalyze chemical reactions. Discussion of this and related ideas led to a period of innovation and discovery, helping to make RNA

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research a major intellectual focus at CU. Because RNA research involved many disciplines, such as biochemistry and biophysics, the researchers in MCDB formed a bond with researchers from these disciplines whose interests overlapped their own. In the mid-late 1980s, these researchers came together to form the “RNA Club”, which led to a creative and stimulating atmosphere that inspired intellectual debate on many aspects of the structure and function of RNAs. Cech and his lab also profited from interactions with David Prescott, who was working both on mammalian cell cycle control and on the process by which micro-organisms, called ciliates, generated a special nucleus that contains highly processed DNA that it used for making all the mRNA, which is necessary for the cell to grow and divide. One of the nuclei in these ciliates (Oxytricha and Euplotes), the “macronucleus,” contains many small pieces of DNA that are about one gene long and include a telomere at each end. It was this abundance of telomeres that allowed the Cech lab to clone the first genes for proteins that cap off the ends of chromosomes and to clone the gene for the protein subunit of telomerase, the enzyme that extends telomeric DNA. In short, telomerase is not a ribozyme, because it contains an essential catalytic protein subunit as well as the templating RNA subunit.

Prescott went on to work out the complexities of the processes by which these special pieces of macronuclear DNA are made. This work has shown that ciliates are in some sense a model system for understanding the DNA processing events that occur in the immune system when we make genes that produce specific antibodies to combat bacteria and diseases.

These developments in molecular biology occurred, at least in part, because of the nature of the department where intellectual discourse was made possible as a result of the close proximity of researchers focused on different disciplines within biology. While Mike Yarus suggests that the recruitment of faculty was less contrived than it appears, there is no doubt that researchers collaborated with each other over the years, even if that only meant sharing ideas or participating in intellectual discourse.

The discoveries in molecular biology during the 1970s, more generally, led to the creation of a new type of industry – biotechnology. While “recombinant DNA” (rDNA) was becoming a reality, based on discoveries in molecular biology and genetics, the idea that these methods and discoveries could be turned into an industry was not on the
minds of many of the scientists working in the field. To be sure, the medical applications were attractive as they offered perhaps another source of funding, but to many molecular biologists, rDNA represented another tool for understanding their scientific research work and problems. The methods and procedures associated with rDNA were the subject of an Asilomar conference in 1975. The participants at this conference addressed what we now call bio-ethics and regulations for research. At the conference several prominent biologists proposed protocols, which became established and adopted by the National Institutes of Health (NIH). At CU for example, Rose Litman, vice chancellor for research and a faculty member of MCDB, suggested in April 1976 that MCDB faculty members working in this field of research should adopt their own regulations based on those developed at Asilomar and the NIH. rDNA research was also grabbing the headlines in the *Daily Camera*, and Litman, perhaps knowing of the problems that other universities faced with their research programs in rDNA, wanted to show that CU was “on top of” the issues and concerns of the local people.

Biotechnology, however, did become an important industry in Boulder. In 1981, MCDB faculty members, Larry Gold, David Hirsh, Larry Soll, and Mike Yarus set up one of the first biotechnology firms in Boulder, Synergen, a pharmaceutical protein manufacturing company.

**Developmental Biology**

The experiments and discoveries in the field of molecular biology at CU were made in parallel with those in the related field of developmental biology. As mentioned in an earlier chapter, new biology first came to CU in the form of developmental biology, and while the original members of IDB and some of the early hires in MCDB continued to work on developmental biology, the appointment of Bill Wood as the department chair in 1978 moved the study of developmental biology into a more active and incisive form.

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127 See faculty minutes, May 5 1976, where Rose Litman reported that she was setting up a committee responsible for monitoring procedures in experiments dealing with rDNA. On February 1, 1977 Litman responding to a *Daily Camera* article and “internal campus concerns” about the rDNA experiments in MCDB, suggested that those involved got together to make a coordinated response to the concerns.

of research. Wood first came to CU in 1975 as a visiting professor working in the laboratory of David Hirsh.\textsuperscript{129} He had originally worked on the morphogenesis of bacteriophage T4, but he took a deep interest in the work that Hirsh was doing with the nematode worm, \textit{Caenorhabditis elegans} (\textit{C. elegans}). Hirsh had learned the study of \textit{C. elegans} from Sydney Brenner at the Laboratory for Molecular Biology in Cambridge, England. The approach of making mutant animals whose defects included failures in particular processes of development appealed to Wood, given his experience with the power of genetics to elucidate morphogenetic pathways in T4 phage. A genetic analysis of animal development became the focus of Wood’s subsequent work. \textit{C. elegans} is a small, soil-dwelling nematode that is now widely used as a model system by those who study development in higher organisms. Its popularity resulted from the confluence of several factors: it can be cultivated rapidly and cheaply in the laboratory; its developmental program has been described at the cellular level though definition of the lineage for every cell in the adult animal; it is highly amenable to both “forward” genetic manipulation by mutation and “reverse” genetics by RNA interference (RNAi) and other techniques; and its genome was one of the first animal genomes to be completely sequenced.\textsuperscript{130}

As in molecular biology, biologists working on the genetics of development used model systems for their experimental research. David Hirsh and Bill Wood centered their research on embryonic development and sex determination in \textit{C. elegans}.\textsuperscript{131} Some important discoveries relating to worm development came from their labs: especially the importance of regulated gene expression in the worm’s early development and the location of specific mRNA’s. Later, Wood and his co-workers showed that both the animal’s sex (through action of the \textit{her-1} gene) and the handedness of its left-right asymmetry were established early in embryonic development. His postdoc, Susan Strome, discovered “P-granules,” which segregated specifically into embryonic germline

\begin{itemize}
\item \textsuperscript{129} It is my understanding that Hirsh used molecular biology, and more specifically genetics, to understand development.
\item \textsuperscript{130} J. Sulston, “\textit{C. elegans}: The Cell Lineage and Beyond,” Nobel Lecture, December 8, 2002.
\item \textsuperscript{131} Although Bill Wood refocused his attention to the worm, he still conducted research with bacteriophage T4 until the late 1980s, when his attention was completely on the worm. See Bill Wood CV.
\end{itemize}
cells and subsequently proved to play a role in germline determination.\textsuperscript{132} In 1987, Michael Krause, working with David Hirsh, found that mRNA made from two different genes could be spliced together, in a process called “trans-splicing.” Other \textit{C. elegans} researchers who came later to MCDB included Min Han, who discovered many signaling pathways that help to control the development of various organs of the worm, and Ding Xue, who elucidated the pathways by which the worm uses programmed cell death in accomplishing its development.

When Wood became department chair, some of the new hires he made included Robert (Bob) Poyton, Matthew (Matt) Scott, Margaret (Minx) Fuller, Susan Dutcher, and Michael Klymkowsky. Their appointments expanded the department’s variety of model systems used for cell and developmental biology to include budding yeast, the alga \textit{Chlamydomonas}, the frog \textit{Xenopus}, and the fruit fly \textit{Drosophila}.\textsuperscript{133}

Wood’s choice to expand the number of geneticists was less about attempting to create departmental unity between molecular and developmental biologists and more about advancing the use of genetics as a tool for the study of cell and developmental cell biology. While developmental biology had long been an intellectual focus of the department, few faculty members used genetics as a tool to further their understanding of how organisms grew from zygote to adult. Meredith Runner, for example, while an experienced and well-respected developmental biologist, still focused on describing the action of chemicals that inhibited development, rather than the study of genes that controlled the relevant processes. Runner built on the classic traditions of his own training by describing how embryos changed over time. Using teratogens, chemicals that disrupt development, Runner observed that the normal developmental changes were altered, but he was unable to understand the processes that caused these changes; indeed, no one really knew exactly what these drugs were doing, so it was hard to interpret the results. In an attempt to better understand why and how the disruptions in development occurred, biologists turned their focus to genetics.

In “forward” developmental genetics, as employed by Hirsh, Wood, Han, and Xue,

\begin{itemize}
  \item \textsuperscript{133} For an excellent history on the fruit fly as the material culture of geneticists and experimental biologists see Robert E. Kohler, \textit{Lords of the Fly: Drosophila Genetics and the Experimental Life} (Chicago: University of Chicago Press, 1994).
\end{itemize}
a culture of healthy worms is treated with chemicals to induce mutations in their DNA. Likewise, those that studied *Drosophila* (Scott, Fuller, Bob Boswell, and later Tin Tin Su and Ravinder Singh) applied the same logic to the complex, multistage development of this insect. These scientists then screened for atypical or irregular developmental events, selecting individuals that deviated from the norm in the particular process under study. Since these deviations came from changes in their DNA (mutations), individual organisms would produce offspring that showed the same or similar deviations, so one had a strain with a permanent property in which to study the relationship between the altered DNA and the altered developmental behavior. For example, this approach led to the discovery of how an organism develops a head–to–tail axis, and how it defines where the differentiation of sex organs will take place. Researchers using this approach focus their attention on the product of the mutant gene, usually a protein, to determine how the gene contributes to the particular developmental process under study.

Robert Poyton’s work focused, and still focuses on, the expression of yeast genes, whose products are the enzymes that make mitochondria work. Through Poyton’s research we have a better understanding of the location of the genes before their products unite in the mitochondria to make the enzymes needed to make ATP at optimal rates. His work is an example of using the combination of genetics and biochemistry to study a basic cellular process. The similarities between his approaches and those mentioned above show that the distinctions between cellular and developmental biology were eroding as researchers learned how to use multiple disciplines to understand fundamental biological mechanisms.

During his time at CU Matt Scott discovered a relationship between genetic and positional information in the embryonic development of fruit flies. A pioneer in the cloning of animal genes, he was able to isolate and characterize one of the genes encoding the master transcription factors that control the overall organization of the body plan in *Drosophila* and, as it later turned out, in all animals. Mutations or translocations of this Antennapedia gene produced flies that had legs growing where their antennae should be or produced other severe disruptions of anterior development. In these studies, Scott co-discovered the DNA “homeobox” DNA sequence encoding the “homeodomain” of the Antennapedia transcription factor protein, which allows it to
bind to specific promoter sequences of other genes that elaborate the body plan as the animal develops. Margaret (Minx) Fuller focused her work at CU on fruit fly spermatogenesis, leading to her studies on mechanisms used to regulate stem cell behavior (she and Matt Scott are now both at Stanford). Other contributions to Drosophila studies included Bob Boswell’s work on cytoplasmic determinants of development, Ravinder Singh’s work on the molecular processes involved in sex determination, and Tin Tin Su’s work on the regulation of the cell cycle. Identifying a relevant gene and learning its sequence allowed all these investigators to make predictions about the gene product’s function. Work of this kind, carried out in Boulder and by developmental geneticist all over the world, has identified many of the key genes and proteins involved in organismal development for a significant range of organisms.

Wood’s mentor R. S. Edgar, a pioneer in the genetic approach to understanding development, once described genetics as the “shock troops” of biology. The analogy is an interesting and useful one. Shock troops are sent first into a battle to establish a beach-head or assault an enemy position, allowing subsequent conquering of additional territory. Geneticists attack complex and unknown processes by looking for mutations that disrupt them, allowing identification of the mutated genes. From the resulting defective phenotypes, how loss of gene function affects the process of interest, researchers can infer the normal functions of mutated genes and in this way “genetically dissect” the developmental process by further study of the phenotypic defects. This use of genetics created a paradigm shift in how organismal development was studied. It was contingent on knowing the role of DNA and RNA in gene expression, but more importantly it was greatly aided by the ability to clone the DNA for a mutant gene. Molecular biologists vigorously pursued techniques such as gene splicing, genetic sequencing, and predicting the structure of proteins at the same time that developmental geneticists were researching mutant genes and the disruptions they caused in development. The new developmental biology combined the tools of molecular biology and genetics to solve the complex problems of development.

Comment by Bill Wood during the review process of this history.
Research on the worm has been prolific and it is still an important model system for the study of genetics today. Tom Blumenthal, who came to MCDB as Department Chair in 2007, Han, and Xue have made important strides in developmental genetics: RNA editing and the discovery of signaling pathways that help control development and the roles of programmed cell death in development. But it was not until the mid-1990s with the arrival of Leslie Leinwand as department chair that MCDB’s molecular approaches to developmental biology expanded to include research on mammalian systems. Leinwand’s addition to the department also added the dimension of work on issues of immediate medical relevance - heart disease. These changes in department focus are described in the next chapter.

Conclusion

The boundaries between molecular, cellular, and developmental biology became decidedly blurry during the 1980s and 1990s as both developmental and cellular biologists began to use the tools of molecular biology and genetics to address their own scientific questions; that is, they applied the knowledge created by the understanding of the function and structure of DNA, enzymes, ribozymes, structural proteins, and RNA to work on a cellular or developmental problem. These tools were an important addition to the study of cellular and developmental biology. But cell biology also featured in the work of molecular biologists, especially work on the location of genes in the cell nucleus, cytoplasm, and mitochondria. The cell was also fundamental to research carried out by developmental biologists. The parallel emergence of developmental genetics (worms and flies), and the emphasis on RNA, gradually supplanted cell structure studies as the principal intellectual thrust of the department, but what emerged from all of this activity was that all the organisms studied (bacteria, yeast, worms, flies, and mice) appeared to be

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135 See interview with Leslie Leinwand, July 3rd 2014 deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
dependent on genes so similar that they had to have evolved from a common ancestor in the distant past. The basic mechanisms by which all organisms function are essentially the same and the concept of a “model organism” has proven to be very useful. As biology has moved into the twenty-first century, the boundaries between molecular, cellular, and developmental biology have blurred, perhaps even disappeared, and the new biology of the 1950s -- out of which these specialized disciplines emerged -- is now just biology.

136 I would like to acknowledge Dick McIntosh, Andrew Staehelin, Bill Wood, Mike Yarus, Norman Pace and Tom Blumenthal for the assistance given and time spent helping me navigate the complexities of the scientific research undertaken in the department. This chapter could not have been written without their help. Thank you.

Main Image: Isolated cytoskeleton from a Giardia lamblia cell. Inset: 3View reconstruction of an intact Giardia cell. The 30 nm thick tomographic slice in the main image shows the front of the cell as outlined by the red frame in the inset. Four pairs of flagella, one anterior (purple in inset) and three posterior pairs (pink, blue and cyan) originate from the basal bodies visible towards the left. They overlay the ventral disc, a highly ordered structure of microtubules and microribbons that form a flat spiral (green structure in inset). The regular, almost crystalline structure on the right is called the marginal plate. (Pictures by Cindi Schwartz and Joanna Brown, kindness of Andreas Hoenger.)
Fluorescence light micrograph of a section cut from the skin of a mouse showing the infoldings that occur at the sites of hair follicles. Nuclei are stained blue and proteins of the basal lamina are red. Green shows the localization of microRNA-205, a small, non-coding RNA. This microRNA is highly expressed in neonatal progenitor and stem cells of the skin where it functions to expand the stem cell population of the skin during early development. At the molecular level, microRNA-205 enhances the production of phosphorylated protein kinase B, also known as Akt, which plays a key role in cell proliferation and migration. Micrograph kindness of Rui Yi.

Neurula stage embryos of the frog, *Xenopus levis*. Control embryos are clear, but the embryos stained with antibody to the transcription factor Sox3-C identify neural precursor cells within the developing neural tube and central nervous system. Image kindness of Joe Dent and Michael Klymkowsky.
Light micrographs of the nematode, *C. elegans*. The upper worm is wild type (normal), the lower one is mutated to the phenotype, "multivulva". This condition results from abnormal activation of the RTK/Ras signaling pathway that regulates the formation of the vulva. Image courtesy of Min Han.

Lateral and ventral views of 3-D reconstructions of the fluorescence pattern a GFP fusion protein that delineates the borders between the vulval toroid cells in *C. elegans* hermaphrodites. Images courtesy of Min Han.
Happily, not all moments were serious, and members of MCDB sometimes had a lot of fun!

Christmas parties brought out a wide range of attitudes and behaviors
Chapter 5 The Gold Building and New Frontiers – 1990s to the Present (ish)

The 1980s can be seen as a decade of transition and new directions for MCDB, not only in terms of leadership - Bill Wood stepped down as chair in 1983 and was followed by Mark Dubin (1983-1988) then Larry Gold (1988-1992) - but also in building on earlier successes in research and teaching. In the early 1980s, the university administration introduced the Program Review Panel – an institution-wide self-assessment study. The study provided MCDB with the opportunity to take a critical look at the needs of its undergraduate and graduate programs and the department’s research portfolio as it moved into a new decade.\(^{137}\) The review process solicited responses from faculty members and graduate students, as well as external reviewers, to determine where the department’s programs fell short of their goals and where they excelled. The 1988 review is particularly telling, for it raised some important issues that lingered from the first review in 1982. The most notable were long-standing problems with the design of the building and its limited research space, which, the report claimed, hindered the department’s ability to continue its high level of research and teaching activities.\(^{138}\)

Although the building was built in 1971, the problems, it seems, related to the amount of research activity conducted in the department by faculty, researchers, and students and the availability of useable research space. As of 1988, the department had twenty-one regular faculty members, nine adjunct, joint or attendant rank professors, fifty-three research associates, sixty-three graduate students, forty-five technical staff, and four hundred and seventy undergraduate students – all housed in the newly-named Porter Biosciences Building and all requiring research and teaching space.\(^{139}\) Laboratory research took up the “majority of the department’s physical and intellectual efforts, space, and expenditure” with twenty four independent laboratories carrying out research in the building. But the amount of research that could be undertaken was seriously limited by the space available. Likewise, the number of students in research

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\(^{137}\) “Findings and Recommendations of the Internal Review Committee of the Department of Molecular, Cellular, and Developmental Biology,” 1988, pg. 5, (herein cited as the Internal Review) in the Internal Review Memo Folder, located in MCDB archives, Cabinet 1, top drawer.

\(^{138}\) Ibid, pg. 2.

\(^{139}\) The building was named the Porter Biosciences Building in 1982 to honor the first MCDB chair, Keith Porter. The department held a symposium, Porter Fest, to commemorate and honor Keith Porter on his retirement from MCDB and his commitment to science.
apprenticeships with a professor or technical staff was dependent on how much space was available to carry out experiments and training. Many of the laboratories, designed to accommodate four researchers, now housed at least six working on projects, and many of the common rooms had been converted into offices or equipment rooms. The department had simply outgrown the building.

The success of the department can be measured by both the number of scientific publications, the discoveries made, and by the high number of grant awards received by individual faculty members and other research associates within the department. MCDB researchers received, on average, $250,000 for each research grant submitted to a variety of federal granting agencies and private institutions with the total net of the grants received by MCDB totaling approximately $7.5 million, which corresponded to one of every nine dollars awarded to the CU Boulder campus. The prolific research efforts of MCDB faculty and research associates made considerable contributions to the national scientific effort and consequently raised the profile and visibility of the department and the university more generally. The success of MCDB, therefore, led to overcrowding within the building and as a consequence a stress on the resources available (both space and equipment). In an attempt to alleviate the problems, the university administration agreed to the modernization and re-distribution of some of the spaces in the existing building. The department, with Larry Gold as the recently appointed chair, re-hired Abe Flexer to act as the project manager to coordinate the modernization of the building, particularly its air-handling system, and to act as a buffer between the architects and the department, much as he did when the building was originally built.

What the department really needed, however, was a new building. The internal review and especially the comments made by the external reviewers made it clear that if MCDB was to continue to be an innovative and important contributor to national science, a new building with new technology and equipment was needed. Only then

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140 Internal Review, 1988, pg. 4.
141 See the timeline currently in progress and chapter 4 of this history.
142 Internal Review, 1988, pg. 4: this would be equivalent to nearly $485,000 per year in today’s terms [http://www.westegg.com/inflation/infl.cgi](http://www.westegg.com/inflation/infl.cgi) accessed December 30, 2014
143 Interview with Leslie Leinwand conducted in July 2014, deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
could MCDB provide proper training for its future graduates, who would gain positions in prestigious universities, medical schools, and in non-academic institutions. Only then would the MCDB faculty be able to continue educational innovations, like the graduate core course that became a model for other universities. The reviewers feared that if a new building was not secured, MCDB would stagnate and lose its place in the scientific hierarchy (national rankings). Flexer worked with the administration, the department, and the architects to come up with workable designs, both for renovating the existing building and constructing a new one. The latter plans would effectively double the existing space, but securing funding for the new building was a major undertaking for both the department and the administration.

Funding the New Building

Larry Gold took over as chair of the department just as the Internal Review was coming to an end, and he embraced the reviewers’ comments that called for a new building. Gold believed a new building would allow the department to expand and attract new faculty members who would bring to the university new research projects, reflecting areas of biology not currently represented in the department. But finding new funding for the building was a difficult task. By the late 1980s, Colorado’s state legislature’s budget support for higher education had dropped by 25% from 1970 levels. Moreover, the state was unwilling to support such an expansion of the department – despite the department’s success at bringing grant dollars to the university. As a result it was left to the department and the university’s administration to come up with enough money to get

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145 Abe Flexer interview, no. 1, 08/05/2013: 52 – 59:00, deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.

It is interesting to note, that Flexer also helped Gold, Hirsh, Yarus, and Soll design the labs for their new biotech company in the early 1980s: Gold recognized Flexer’s strengths and abilities at project/design management of science labs and buildings. Flexer resigned before construction on the new building began.
the project started.146 Gold remembers having extensive discussions with then Vice Chancellor for Academic Affairs, Bruce Eckstrand, about finding creative solutions to the funding problem. Both came away from those discussions agreeing that the expansion of the department was crucial for its continued success, and determined to find the money.147

By this time, Gold had created and sold a profitable biotechnology firm and was familiar with various methods for raising capital; one such method was venture capitalism. Gold knew several venture capitalists and approached them to determine if they would be interested in partially funding the new building. Gold was informed enough to know that what he was proposing was permitted by university rules and was a legitimate solution for the funding problem. The proposal was essentially that the venture capitalist would provide partial funding of the new building in return for having the “right of first refusal” on all patents and inventions that came out of the research labs at MCDB. Gold presented this solution to Eckstrand, who rejected it outright; he was especially negative about giving venture capitalist the right of first refusal on any new patents. No more discussions took place, either with the venture capitalist or with Eckstrand, and the only funding for new building construction came from a bond issue between the university administration and state.148

Shortly after the building construction began in 1992, Gold resigned as Department Chair and as a regular member of the faculty to start another biotech firm, NeXagen. Securing the additional funding needed to complete the building project was left in limbo: Gold and Eckstrand failed to reach a consensus on how to accomplish that essential goal.149

146 Support for higher education in Colorado has been on the decline – dropping by nearly 70% from 1970 to 2011. The American Council of Education project that, at this rate of decline, Colorado’s support for higher education could be at zero by 2019. http://www.acenet.edu/the-presidency/columns-and-features/Pages/state-funding-a-race-to-the-bottom.aspx accessed December 31, 2014
147 Interview with Larry Gold, February, 2014: 48:00 onwards, deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
148 Ibid; Interview with Leslie Leinwand, July 2014, deposited in Karen Lloyd Collection, Norlin Archives, University of Colorado Boulder.
149 Interview with Gold, 50:00. Gold stated that after he had left CU Eckstrand called him back to discuss the funding. At that meeting, Gold was asked about how much money he had raised to match the bond money, to which he replied “nothing.” Gold told them that the plan he came up with was the only one he’d had and they didn’t like that one. Gold remembers the administrators looked at him “dumb-struck.”
In 1995, Leslie Leinwand arrived at CU as the new Department Chair just as the new building opened. Her appointment represented the first of the new faculty hires recommended by the internal review committee in 1988. But even before she could move her lab and staff from the Einstein Medical School in New York, her plans encountered a challenge. She received a call from the Chancellor inviting her to join him and other administration officials for a meeting in his office. The meeting was to discuss the debt owed by the department to the University for the new building – a debt that Leinwand had no knowledge of when she accepted the position as the MCDB Chair. Leinwand’s initial impulse was to pack up her things and move back to New York, but after talking with the administration about a variety of options, she decided to stay. Subsequently, she came up with some innovative ways of paying back the $5 million the department owed to the university. These included using patent payments on processes and other research developed in MCDB and renting out unused office space to other departments on campus.

In 2013, Leinwand, the department, and the administration recognized Gold for his continued support of MCDB and science at CU, plus his contributions to the biosciences more generally by naming the new building the Gold Biosciences Building. The redesign of the Porter building and the construction of the Gold building allowed the department to recruit new faculty and expand the department’s intellectual focus to include researchers working in mammalian development biology and human health and disease (immunology and virology).

**New Frontiers**

Leinwand’s appointment brought to the department a new focus on mammalian developmental biology, expanding the interdisciplinary nature of biology at CU. Outreach to other departments, including some at the medical school, was another important part of her mission as the new MCDB Chair. Leinwand also recognized the intellectual challenges facing the department and worked to create better relations with other departments on campus. She reached out to the other biology departments on campus.

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campus, EPOB (the original biology department) and Integrated Physiology, but these attempts to bridge the enduring rift between Boulder’s biology departments failed, in part, Leinwand suggests, because the methods and content of each department’s introductory courses differed too much; it would have been difficult to devise a series of courses that could satisfy each curriculum. Leinwand was, however, successful in building stronger relations with the Department of Physics, College of Engineering, and the Anschutz Medical Campus in Denver, where she held a joint appointment.151 Interestingly, while the department’s original mandate was to strengthen its ties with the medical school, this had not been sustained through the 1980s and early 1990s, in part due to the physical distance that separated the two campuses and in part to the limits of communications technology. The technology simply did not exist during this period to enable convenient access to remote lectures; today, video-conferencing, live-streaming, and Skype allow students and faculty to communicate and participate in lectures and presentations off campus.

One of the other major challenges for the department, and indeed all science departments, involved teaching science to undergraduates. In the early years of the department, science education was an important focus for many faculty members - new course offerings and new ways of presenting material in the classroom quickly established MCDB as a premier science department in the American West. In subsequent years many of the department’s faculty have continued to introduce new courses, but the manner in which these courses were presented remained largely unchanged. By the late 1990s, however, science educators around the United States researching how students learned science in the classroom demonstrated that active learning achieved better results for the retention of new material than the more passive listening to lectures. This new approach to teaching science to undergraduates was quickly adopted on the CU-Boulder campus.

151 Interview with Leinwand; The relationship with chemistry was already strong since the establishment of the department, and even more so with the establishment of the RNA club in the 1980s.
Carl Wieman, a CU physics professor and Nobel Laureate, led the charge on campus to introduce the Science Education Initiative (SEI), but it was Bill Wood and Jennifer Knight who promoted active learning in MCDB courses and who were most involved with these new approaches to science education during the early years of the SEI. Wood and Knight demonstrated that substituting about a third of the lecture time with student-centered active learning exercises, formative assessment, and peer discussion significantly increased students learning gains in a large biology course. Other MCDB faculty members soon adopted these approaches to their undergraduate courses, and they have since adapted old course material or created new courses based on the new educational research - in many cases faculty members have conducted their own research in science education.

Michael Klymkowsky was interested in two novel aspects of teaching biology: the use of computers as instructional tools, and the identification of concepts that could be used to organize the huge maze of biological facts, thus making pedagogy more effective. His computer-based projects included serving as a co-editor and author on The Dynamic Cell: A New Concept for Teaching Molecular Biology, a CD-ROM based virtual tour of the cell, and assisting with the design and content for the “Working with Literature” web-site for the 4th edition of Molecular Cell Biology. Klymkowsky’s interest in identifying the important concepts of biology led to a National Science Foundation-funded project that brought Klymkowsky together with Kathy Garvin-Doxas, an expert in human communications, and Ed Svirsky, a computer programmer. The team developed “Ed’s Tools,” a web-based software toolset that enables teachers to capture and analyze student’s responses to open ended questions and essays focused on molecular biology. Several observations have emerged from this work, for example,

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154 K. Garvin-Doxas., Isidoros Doxas, and M.W. Klymkowsky, “Ed’s Tools: A Web-based Software Toolset for Accelerated Concept Inventory Construction, 2006. Developed for the Biology Concept Inventory Project then
students uniformly fail to understand the implications of stochastic processes, and they show interesting differences in their understanding of intra-molecular interactions. In addition to these web-based tools, Klymkowsky has also developed an alternative introductory molecular biology course, Biofundamentals, and a set of “Flash-based” virtual laboratories to accompany the original version of that course. Klymkowsky has also led the way in adopting the “fully-flipped” approach to teaching in his Biofundamentals course, in which class time is devoted entirely to students working through and talking about the implications of various observations in specific biologic scenarios. Improving biology education was important for the establishment of the department in the 1960s, and over forty years later, faculty members are again not only working to improve the content of courses, but also are striving to develop innovative ways of delivering biological concepts to students.

Two examples of new courses aimed at improving undergraduate science education are “From Bench to Bedside: The role of science in medicine” and the “python project,” both implemented by Leslie Leinwand in 2006 while she was a Teaching Professor of the Howard Hughes Medical Institute (HHMI). “From Bench to Bedside” helps undergraduates understand the role of research in the creation of devices and therapies to improve human health. It also challenges them to think about the ethics of their research, such as the ethics involved in genesequencing. The python project – a lab-based course – provides undergraduates with a real experience in the processes involved in developing and carrying out a research project, with post-doctoral fellows acting as their advisors.

housed in MCDB. The software is available for free download from edstools.colorado.edu. The design of the program is now being adapted to work with math and calculus and space physics.

http://virtuallaboratory.colorado.edu/Biofundamentals-2012/
http://virtuallaboratory.colorado.edu/BioFun-Support/virtuallabs.htm

New discoveries in biology elicit changes in how biology is taught and presented, for example, in the 1960s teaching cell and molecular biology was the “new” biology at CU, and in the late 1990s/early 2000s, mammalian developmental biology and the search for finding cures or treatments for human diseases has become the focus. This is a larger national trend in part driven by the National Institutes for Health and other private institutions looking to improve human health.

These two courses are used as examples of the commitment of the MCDB faculty to improving biosciences education and are by no means singled out as being more worthy than the work done by other faculty members. In her interview Professor Leinwand used her own courses as examples to show how the department is continually updating and modernizing the teaching of biology.
In 2009 the freshmen MCDB laboratory experience was enhanced by the addition of a course in phage genomics, sponsored by the HHMI Science Education Alliance and implemented by members of the department’s teaching faculty, Nancy Guild and Christy Fillman. This course was designed to provide an authentic research experience for a small group of MCDB freshmen who expressed an interest in research and a genuine passion for biology. Coursework included the isolation of a novel bacteriophage from the environment, characterization of that phage using current molecular biology techniques, purification of the phage DNA for sequencing, and once sequenced, annotation of the phage genome using current bioinformatics programs. The course was taught for six to nine hours per week and allowed students time to trouble shoot their experiments, design different experimental approaches, and develop their skills as experimentalists. It was so successful that in the fall of 2011 Fillman modified the existing course so students taking the department’s introductory genetics labs (the more traditional two hour per week laboratory course) would also have an opportunity to isolate and characterize a novel bacteriophage.

This change exposed even more undergraduates to the scientific process at an earlier stage of their science education.

In 2012 Guild continued this trend to incorporate more research-oriented projects into introductory courses by modifying the introductory molecular and cellular biology laboratory course. In the revised course, students spent the semester characterizing microbial communities from municipal water samples they had gathered (modeled after the work of Dr. Norm Pace in MCDB) using current molecular biology techniques and bioinformatics programs. As a result of these new introductory laboratory courses, MCDB freshmen have developed a deeper interest in the experimental outcomes of their work and a greater understanding of the scientific process. Some of the department’s upper division laboratory courses, such as the Cell
Biology laboratory designed and run by Joy Power, have also been modified to include laboratory experiences that are real investigations, rather than the rote activity of following instructions, as has been so common in teaching labs world-wide.

MCDB has also been committed to improving biosciences education throughout the local community. In the mid-1980s, the HHMI put out a call to major biological research universities around the country for proposals to improve both the education of their enrolled students and biological education in the community more generally. Dick McIntosh and Todd Gleeson (a faculty member of EPOB) secured financial matching from the university administration, put together a grant proposal, and applied for one of these grants. The proposal was successful, and in 1989 MCDB began such a program with Mark Dubin, then Chair of MCDB, as the principal investigator and Julie Graf as Program Manager. This grant led to the formation of the Biological Science Initiative (BSI) - a program designed to improve biological education at the undergraduate level and scientific literacy in K-12 schools from the local community. BSI has worked effectively to improve the community’s understanding of the relevance of science to their lives through a variety of programs, such as hosting summer schools for educators from the local school districts and developing lesson plans and laboratory demonstrations that can be used in the classrooms. Faculty members from MCDB, Chemistry, Integrated Physiology, and Ecology and Evolutionary Biology (EEB, renamed from EPOB) have lectured at these summer schools and at local community events, while graduate students who joined the “Science Squad” have designed lessons and trained K-12 educators in how to present them in the classroom. CU has successfully applied for funding to run these programs for the last twenty-five years; in 2014 it received another $1.5 million to run the program for another four years.158 The HHMI has awarded CU at total of $11.5 million to support the BSI, which has been matched by the University by providing facilities, equipment, and funding for undergraduate research projects.159 The success of this program demonstrates MCDB’s

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158 http://bsi.colorado.edu/about/ accessed January 5, 2015. The recent funding cycle saw the HHMI change their focus from improving K-12 education and undergraduate education to just the first two years of college. This means that the programs such as the “Science Squad” are no longer funded; although the professional development programs for educators will continue to be hosted at CU.

commitment to improving undergraduate science education and other STEM programs at CU – Boulder.

The commitment to breaking down barriers between science and society was taken a step further with the establishment of the Colorado Initiative in Molecular Biotechnology (CIMB) in 2003. The CIMB, renamed the BioFrontiers Institute in 2011, was seen as a collaboration of CU scientists, including faculty from MCDB, to work across disciplines on challenges in biosciences to create new knowledge and new solutions for improving the well-being and health of humanity. During her time as MCDB Chair (1995 - 2007) Leinwand also acted as the Director of the CIMB (2003 - 2009) before becoming the Chief Scientific Officer, a position she still holds today. Leinwand sees the new institute as an opportunity for MCDB to continue to be an intellectual home for scientists who are interdisciplinary in their approach to their research. Many of the more recent hires associated with the institute have chosen MCDB to be their home department, which Leinwand sees as a testament to MCDB’s long tradition of interdisciplinary approaches to the biosciences. While the new hires might not “look like biologists” – their Ph.D’s gained perhaps in disciplines other than biology – their research focus is rooted in the biosciences: not unlike the first hires when MCDB was established in the 1960s. Using new approaches to finding solutions for human diseases has been the hallmark of MCDB and continues to be so in collaboration with BioFrontiers and its focus on developing quantitative methods, such as math and computer-programming, for use in the biosciences.

The future of biosciences at CU has been nurtured by the establishment of the BioFrontiers Institute, but funding continues to be a major cause of concern for everyone in MCDB – a far different scenario than when MCDB was established during the Cold War period of American history. Today federal and state governments appear to be reluctant to fund the sciences, and the grants that do exist are focused on health-related problems; private foundations and donors continue to be a source of funding to support research, education, and department expansions. This funding model is showing some evidence of success, but donor relations take time and effort to cultivate. The scientists in MCDB and elsewhere need to be able communicate the value of their

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160 Leinwand Interview, 2014.
research and the significance of their financial needs to potential donors – a skill that many are quickly learning. Indeed, potential faculty hires are considered not only for their research focus but also on their ability to bring in money to fund their research and the graduate assistants employed in their labs. It is clear that funding will continue to be a major source of headaches for faculty members in MCDB and the BioFrontiers Institute. What lies in the future for MCDB and BioFrontiers is hard to predict, but what is certain is that the department will continue to be innovative in its research focus and undergraduate education and in its efforts to secure funding for its programs and research.

**Conclusion**

The history of the department offers us a model for understanding the growth of science and biotechnology in the Rocky Mountain West, beginning with the time of the Cold War when the American West became a center of U.S. Cold War activities. But the department also provides us with an opportunity to understand how biology has moved from a more traditional approach, focused on systematics and taxonomy, to one that included a molecular and cellular understanding of how organisms function today and how they might have evolved. The schisms that emerged in biology at CU were similar to those experienced in other universities around the country, but the history presented here provides us with a better understanding of what those differences were.

I have mapped the establishment and growth of MCDB, both in terms of the physical space the department now occupies and in the intellectual focus of the faculty, from 1968 to the turn of the twenty-first century. This account reveals how the department has remained focused on its commitment to undergraduate education and research.\textsuperscript{161} While the journey has not always been smooth or easy, the efforts of the faculty members to keep these goals in their sights cannot be underestimated. Under the guidance of Keith Porter, the department gained a national and international reputation for its contributions to biology; this stature was based on its research activities, its interdisciplinary approaches to finding solutions to research questions, undergraduate education and the significance of their financial needs to potential donors – a skill that many are quickly learning. Indeed, potential faculty hires are considered not only for their research focus but also on their ability to bring in money to fund their research and the graduate assistants employed in their labs. It is clear that funding will continue to be a major source of headaches for faculty members in MCDB and the BioFrontiers Institute. What lies in the future for MCDB and BioFrontiers is hard to predict, but what is certain is that the department will continue to be innovative in its research focus and undergraduate education and in its efforts to secure funding for its programs and research.

\textsuperscript{161} Chapter four provides an in depth history and description of the type of research conducted in the department.
training, and graduate program. Happily, this reputation has been sustained ever since.\footnote{Chairs: Keith Porter (1968-1974); David Prescott (1974-75); Lester Goldstein (1975-76); Howard Berg (1976-1977); Dick McIntosh (1977-78); Bill Wood (1978-1983); Mark Dubin (1983-88); Larry Gold (1988-1992); Mike Yarus (1992-95); Leslie Leinwand (1995-2007); Tom Blumenthal (2007-2013); Mark Winey (2013-present).}

The establishment of a new biology department was seen as essential in the 1960s, given that the existing facilities and structure were not meeting the needs of students wanting to move into biomedical fields. The university and Meredith Runner, the director of the Institute for Developmental Biology, met this challenge through the formation of the Institute for Developmental Biology, the program that eventually morphed into MCDB. From its inception, then, the department has been committed to undergraduate and graduate education and to training students for research in the biomedical fields. These were some of the core missions of the department at its inception and they persist today. Bioscience research in MCDB played a large role in the creation of the local biotechnology industry, which is an active part of both scientific progress and economic development for the State of Colorado. Moreover, between the department’s inception and May, 2015 the members of MCDB have contributed more than 4,000 original articles to the research literature, an average of about 85 papers per year for 47 years. While we cannot predict the future, it is clear that with the continued collaboration of MCDB, BioFrontiers, and the Anschutz Medical Campus, bioscience research and education will continue to play a large role in the university’s efforts to retain its place as a first-class center of science and research.
Appendix on research productivity of the MCDB labs.

**Number of Publications from MCDB per Annum**

**Number of Citations of MCDB Papers per Annum**