Chapter 15. Prevention of the Study of Life [1]1917-1975.

FIVE YEARS AFTER HANDLER ENTERED society as a home-schooled, socially retarded child prodigy, he was smitten by the teachings of a college biochemistry professor and a novel he saw as a tale of heroic biochemists. He became convinced biochemistry could transform clinical medicine from a subjective art to an objective science, and constructed a personal mythology that would later underpin his extreme, doctrinaire commitment to biochemistry. At age 21, just before the beginning of World War II, he received a PhD in biochemistry and began teaching first-year medical students that biomedical phenomena were the result of biochemical reactions identifiable by laboratory studies of homogenized tissues. Biology was then undergoing a transformation as biochemists sought to explain life processes through the lens of biochemistry and physics, which themselves had only recently developed and were rapidly undergoing changes. Mechanics and thermodynamics were well established, and electromagnetic theory had emerged as a new and mathematically demanding field. At the same time, vitalist theories — which posited that life required a special, non-physical vital force — were being systematically dismantled by biochemical experiments that synthesized organic compounds. The desire to distance biology from metaphysics led to a strong bias among biochemists in favor of mechanistic, chemical explanations of life processes. This anti-vitalist push made electromagnetism — still not fully understood and associated with mysterious forces — scientifically unattractive for those seeking to build biology into a respected, quantifiable chemical-based science.

In the decade before Handler was born, the term biochemistry was coined to describe studies of fermentation and enzymes; biochemists emphasized molecular transformations in solution, which became their model for reducing the study of life processes to chemical reactions. They did not explore electromagnetic signaling in living systems, but rather concentrated on oxygen utilization and hydrogen transfer reactions. A quantitative, chemical-based approach, not electromagnetism, reflected the norms of acceptable biochemistry, which were reinforced by the discovery of the citric acid cycle, further entrenching a mechanistic view of life. Although electrical gradients were involved in the cycle, biochemists reduced metabolism to stoichiometric and thermodynamic balances, leaving electrodynamic interactions unexamined.

In their pursuit of scientific legitimacy, biochemists aligned themselves with the physics tradition of cause-and-effect determinism, favoring descriptions of biological activity in terms of mechanical and chemical processes that were measurable, repeatable, and discrete. Electromagnetism, especially in its mathematical form, was less intuitive, less observable, and thus less palatable. The first and second laws of thermodynamics were central to the development of biochemistry, but the laws of electromagnetism were not easily incorporated into models of molecular interaction in solution. Even though membrane potentials and ion transport involved electrical forces, the early biochemists largely modeled these as chemical gradients, not field interactions. The laws describing electromagnetism were sophisticated and required an understanding of specialized mathematics that was not taught to biochemists when Handler was in graduate school. He was trained in laboratory chemistry, not models of

[1] This is a preprint of a manuscript that will undergo proof-reading and copy-editing prior to publication.

electromagnetic interactions. The absence of electromagnetism from the biochemical canon meant that electromagnetic signaling in the brain, beyond ionic conduction, remained unconsidered and underexplored. Research into interactions of electromagnetic energy with DNA and proteins was considered fringe or irrelevant.

The exclusion of electromagnetism from biochemistry was not the result of data but of ideological commitments to chemical materialism. Two related forms of resistance to electromagnetism developed within the biochemical community
— institutional conservatism, and rigid articles of faith. The early biochemists upheld the status quo they had developed, and marginalized emerging ideas like electromagnetism in biology because change threatened institutional continuity and control. Additionally, there developed a narrow inflexible conception of what counted as a valid method of inquiry — dogmatic adherence to reductionism. Valid explanations of biophenomena were required to be expressed in terms of chemical reactions and molecular structures. Alternative explanatory frameworks such as electromagnetic interactions or systems-level phenomena were rejected on the grounds they were outside the framework of biochemistry. Pluralism in scientific thinking was resisted, and biochemistry was deemed the only legitimate language of biology and biomedicine. The conceptual foundations of biochemistry were thus locked into one way of thinking — anything that didn't fit that mold was excluded, regardless of empirical merit. Electromagnetic phenomena — characteristically transient, spatial, and often subtle —were deemed too abstract, too speculative, or too metaphysical.

The biochemistry presented to and readily embraced by Handler developed in a molecular straitjacket, with a legacy that prevented exploration of bioelectromagnetic interactions and the processes it mediated, emergent biophenomena. The professional society organized by the biochemists opposed the research results of contemporary scientists who sought to integrate physics with biological systems, particularly Carlo Matteucci, Emil du Bois-Reymond, and Jacques-Arsène d'Arsonval, who discovered bioelectric phenomena. Matteucci systematically extended the earlier work of Luigi Galvani and demonstrated that nerves and muscles generated electrical currents, suggesting electricity was a fundamental aspect of biological processes. The biochemists, however, viewed his electrical findings as side-effects of biochemical reactions occurring in cells, and argued that the actual mechanism of muscle contraction and nerve signaling was chemical, not electrical. They opposed Matteucci's idea that life had an intrinsic electrical essence which mediated functions in the body and that was beyond chemical principles. Du Bois-Reymond discovered that electrical impulses traveled along nerves, but biochemists asserted that nerve transmission was based on a chemical reaction, not an inherent electrical mechanism. He famously declared that certain aspects of physiology, particularly consciousness and the ultimate mechanism of life itself, might forever remain unknowable, further scandalizing the biochemists who speculated that a chemical framework would ultimately explain all biophenomena.

D'Arsonval investigated the interaction between man-made electromagnetic energy and living tissues by studying the effects of man-made electricity on animals, which were employed in an effort to understand how the human body functioned.

He explored the ability of electricity to influence physiological processes and developed electrical therapy techniques, but biochemists considered his work as pseudoscience because it

lacked a chemical foundation. When d'Arsonval suggested living tissue could generate electromagnetic energy, he was accused of implying the existence a life force beyond biochemical reactions, and criticized for not describing a molecular mechanism to explain how electricity influenced processes in the body.
At the time, biochemists were progressing toward explaining metabolic reactions in terms of molecular pathways, and they had little interest in electromagnetic influences on living organisms. Ironically, during the same period, electricity and magnetism were unified in a set of four equations which predicted the existence of electromagnetic waves that moved almost instantaneously, and their existence was discovered. But biochemists remained hostile toward the possibility electromagnetism was the basis of a non-chemical mechanism that mediated and regulated body-wide physiological processes. Instead, they remained focused exclusively on a reductionistic biochemical model of life.

Handler embraced the society's foundational tenet that living organisms were best understood by analyzing their molecular components. He believed reductionistic experimentation would ultimately provide explanations for all biomedical phenomena and ultimately create life by mixing biochemicals in a beaker. The tenet validated the central biochemical dogma that biophenomena can be explained solely in terms of molecular events discovered by reductionistic experimentation. Handler also accepted the corollaries that followed logically. He believed biomedical research should focus exclusively on wet-laboratory biochemical experimentation to discover the causes of diseases while excluding the complications of environmental and social factors and, consequently, federal funding for biomedical research should prioritize biochemistry over holistic or systems-based approaches. Handler regarded electromagnetic energy observed in healthy organisms in the form of voltages or electrical current as only a harmless consequence of normal metabolism, having neither causative or meditative significance nor a role in biochemical endeavor. What had become an established dictum among biochemists was readily accepted as an article of faith by Handler — that the electromagnetic energy observed during disease progression was a secondary effect of biochemical activity that has no influence the course of disease and no biomedical consequences. He also adopted the related dicta that electromagnetic regulation of physiological process in the living body did not occur, and that man-made electromagnetic energy produced no physiological effects except what was immediately obvious — electrical shock and tissue heating.

During the War years, Handler was one of his university's major sources of philanthropic research grant funds, which supported his pointillist research on enzymes and nutrition and reimbursed his university for the time he spent doing research and the overhead costs of the laboratory; in the latter half of the 1940s his research was also funded by the government's atomic energy agency. Although Handler was an excellent grant writer and laboratory manager, he was a mediocre scientist, and after developing an illness that prevented him from working in the laboratory, his interest shifted to science administration and his meteoric rise in the national politics of science began. He secured several grants from the National Institutes of Health for metabolism research and supervised biochemists whom he hired to carry out the work, which he was unable to do because of his health limitations. In 1950, Handler's grantsmanship, management skill, and the money he brought in for his university led to his

appointment — over far more experienced and knowledgeable candidates — as chairman of the biochemistry department.

During the next several years, Handler insinuated himself into the leadership circle of the national biochemistry society, which was financially strapped. He provided financial resources — obtained from his grant funds — needed by the society in return for its recommendation to the National Institutes of Science that he be appointed to its advisory panel that chose what kind of experiments would be done and who would do them. While serving on the panel, Handler implemented the biochemical society's tenets and corollaries. His funding decisions were heavily biassed toward recognition of biochemistry as the canonical science of biomedical research. Handler favored society biochemists, particularly those on the faculty of elite universities, collogues, friends, former students, or those who shared his ideas of what questions to ask of nature, and how to go about answering them. The panel review process Handler shaped became the approved method for retail distribution of federal grant money to biomedical researchers in the U.S. The panel's decisions — always made in secrecy, and unappealable — defined biomedical orthodoxy as identical to biochemical orthodoxy.

Handler appointment as chair of the Institutes' advisory panel provided him an opportunity to establish the reductive enterprise of biochemistry as the sole scientific sub-specialty on which biomedicine was based. He developed into a shrewd strategist and became a powerful force on the panel whose efforts to advance his ideology were rarely opposed. He understood the motivating force of fear biochemists seeking grants had about their future as university employees and exploited the insight, becoming an influential voice in national biomedical research policy. Throughout the 1950s, Handler annually exercised his silver tongue before the Congress, telling it that only biochemists could judge the merits of a research projects, and that the panel review process he directed guaranteed the money budgeted for research would be spent wisely. During the decade, Handler developed into a powerful autocratic leader who had the requisite oratory ability, management skills, and determination to advance his ideology and the interests of the biochemistry endeavor. He largely controlled the panel's composition, procedural practices, decisional process, and its disposition of a large annually increasing budget — the Congress provided the money, but it was Handler who determined how it was spent.

Handler supported funding of grant applications he believed likely to result in pointillist publications that would benefit the biochemistry endeavor, which was the goal of his ideology. Critics argued federal funding should be restricted to applications seeking a result that served a public purpose, not simply biochemical validity. But the operational secrecy of the Institutes' advisory panel coupled with the complexity of biochemical terminology prevented public recognition of whether the funds were used to find the cause and cure of disease — which the public and the Congress believed were the right goals — or the personal interests of biochemists.

HANDLER BELIEVED ALL BIOMEDICAL phenomena — metabolism, growth, healing, health, disease, aging, consciousness — were controlled by interactions among molecules, and that electromagnetic energy was of nil importance for explaining any aspect of human life. Even memory — the capacity to recall the secrets of human individuality. Handler told a congressional committee that memory could eventually be reduced to biochemical reactions.

His reductionist worldview was not a passive inclination but a fervent ideological stance that animated his research when he worked in the laboratory, and his administrative leadership in throughout 1950s and early1960s, when he acquired extraordinary authority within the National Institutes of Health regarding who would receive research grants, and what kind of research they would be allowed to perform. Handler's reductive ideology determined the grant applications he approved for funding. Proposals designed to study the unique regulatory dynamics of organisms were rejected in favor of studying homogenized tissue, literally the biochemical soup of dissected and pulverized life.

Handler encoded his ideology into the funding practices of the Institutes. As its most influential member and then chair of the biochemical advisory panel, Handler exercised sweeping influence over the distribution of research grants. He and his followers functioned as ideological gatekeepers, dispensing federal dollars only if the applicant was willing to follow their rules of for conducting biomedical research.

Historically created to provide unbiased peer review, under Handler's leadership the Institutes' biochemical review panel became a vehicle for promoting orthodoxy and nepotism. Panel members, often selected through personal and professional networks, reviewed only a fraction of submitted applications and deferred to the opinion of designated primary reviewers. This process enabled influential voices like Handler's to unilaterally reject proposals that did not conform to biochemical reductionism and the views of the primary reviewer.

The panel operated in secrecy and its decisions were unappealable, transforming grant allocation into an opaque and insular exercise in ideological conformity. Handler's power extended beyond veto authority: he shaped panel membership, recommended his allies for positions of influence, and used administrative mechanisms to promote those who shared his vision. He obscured the reality that the primary goal of the reviewers was to support research that was intellectually satisfying to biochemists as opposed to foreseeably applicable to biomedicine. As a result, the Institutes' research priorities shifted from investigating the causes, cures, and treatments of disease — as originally mandated by Congress — to elucidating the chemical pathways within cells. This shift went largely unnoticed by legislators and the public, who lacked the technical knowledge to discern whether public funds were supporting societally valuable research or advancing a narrow academic agenda. Handler used his somber demeanor and rhetorical skill — he looked and sounded to laymen like what they imagined a scientist was — to reassure the Congress that biochemists were uniquely qualified to judge applications for biomedical research and determine which investigators would best serve the public interest.

Handler was largely responsible for the policy of the National Institutes of Health to fund only reductionistic research and not support holistic approaches in biomedical research. Consequently, he played a decisive role in shaping the intellectual and administrative direction of biomedical research in the U.S. His stewardship of the Institutes' biochemical advisory panel and formidable influence on the funding policies of the Institutes — particularly after his lobbying the Congress led to the creation of a new Institute — facilitated instantiation and implementation of his ideology in the funding policies of the Institutes. Proposals for biomedical experimentation were expected to be based on reductionistic designs, which excluded hypotheses involving electromagnetic energy, cybernetics, nonlinearity, or any other non-biochemical concept. All fundable research proposals to investigate human health, disease, and life itself were expected to be written in the molecular language of biochemistry.

The Institutes' enforcement of Handler's rigid reductionist biochemical paradigm had a profoundly limiting effect on methodological diversity, leading inexorably to the result that a plethora of pointillist biochemical studies were funded whose results were ignored not only because they had no public utility, but also because they were of no interest to other biochemists. He used his authority and influence while working at the Institutes to enforce his views regarding the experimental designs for biomedical research that were acceptable for funding. He insisted all such research be based on studies of individual molecules — a limitation that prevented direct study of system-wide interactions mediated by the flow of electromagnetic energy, even though it was the only force in nature that had the unique property of acting at a distance and thus could synchronize physiological events occurring simultaneously in different parts of the body. In contrast to holistic approaches to biomedical research based on electromagnetic energy — which travels throughout the body at the speed of light — biochemical reactions occur at a specific location and have a range of influence defined by the relatively slow process of diffusion of molecules. Nevertheless, Handler remained intransigently committed to exclusive reliance on chemical energy as the basis for explaining emergent biophenomena; he refused to accept or even recognize the inherent limits of the reductionistic model on which his opinions were based.
Although biochemistry provided insights into some biophenomena, Handler had no eyes to see the impossibility that it could explain emergent biomedical phenomena.

In Handler's perspective, experimental evidence supporting reductionism came from pointillist laboratory studies like those he once performed. He measured the concentration of a biochemical in homogenized tissues from a group of rats and regarded the average as the true value in an imaginary living rat. In this manner, Handler made biomedical meaning from pointillist results, which he called biochemical facts and believed would sum to biomedical understanding in the Seurat sense of a whole composed of parts. Proposed experiments that did not promise to seek such pointillist evidence invariably failed to gain the approval of his advisory panel for funding.

Handler believed that the points collected by an army of Institutes-funded biochemists would ultimately somehow coalesce into the biomedical knowledge that explained human health and disease. In speeches, newspaper interviews, published opinion pieces, and congressional testimony, Handler argued that the government had a moral responsibility to increase the budget of the Institutes, thereby allowing it to create and sustain an army of biochemists tasked to find biochemical facts. He said producing more PhD biochemists was important and that, while in training, they should be paid at an appropriate level, a point he supported during congressional testimony by telling stories about the privations he experienced as a student.

Handler dismissed biological variability — the fundamental observation that no two living organisms of any species behave identically—as a misapprehension of nature that was remediable by assuming that the average of many independent measurements was the true value. His misapprehension assertion highlighted a core error in his ideology — importation into biomedical science of the model developed by physics for the study of inanimate matter. The model was successful when used in physics because any two samples of a particular kind of inanimate matter —gold, wood, steel, as examples —are essentially identical; consequently,

their thermal, mechanical, chemical or electrical behavior when exposed to the respective forms of energy are essentially identical and can normally be precisely predicted. In contrast, two living individuals in any given species— even though they have essentially the same chemical composition — when exposed to a particular energetic stimulus, normally exhibit different behaviors; consequently, their behavior can not be precisely predicted so there is no such thing as a true value. In other words, in principle and practice, Handlerian reductionism, when used as a model for emergent biophenomena was an historical error.

Handler inherited the attitude of dening a role for electromagnetic energy in the explanation of biomedical phenomena from the previous generation of biochemists. They argued that the possibility electromagnetism had a role in explaining the scientific basis of life or how humans functioned was akin to Descartes' belief that humans were animated by a soul. The early biochemists believed life could be explained as series of chemical reactions fueled by energy extracted from food, and regarded all aspects of life as explainable molecularly as consequences of chemical energy. Handler's teachers ignored the research of numerous investigators who proved that electromagnetic energy of a type not found in nonliving matter was present in all living creatures. Investigators who discovered and documented the existence of electromagnetic energy in living creatures even before biochemists organized into a scientific specialty included Carlo Matteucci, Emil du Bois-Reymond, Jacques-Arsène d'Arsonval, and some biochemists, notably Albert Szent-Györgyi. Nevertheless, the biochemists ignored the work of the electromagnetic investigators because it was perceived as inconsistent with their canon of reductionism, and Handler adopted that view as his own

Neither Handler nor the biochemists in the society he managed in the 1950s received even rudimentary training concerning the four laws of physics that govern electromagnetic energy. He was seemingly unaware that a flow of electromagnetic energy was the only force in nature that could act at a distance and thereby synchronize the emergent behavior of an organ or an entire living individual. Although health, healing, disease, growth, emotion, consciousness and other biomedical phenomena emerge only at higher organizational levels in an individual, Handler mindlessly and baselessly regarded it as an invalid level of scientific enquiry. He believed scientific studies of emergent biophenomena should always be carried out at the molecular level. Under his leadership, this doctrine was systematically implemented by the Institutes despite contemporaneous studies which presented clear evidence his doctrinal beliefs blocked understanding of fundamental biomedical phenomena.

The foundation of Handler's concept of biochemistry was physics, which he praised frequently but understood minimally because he was untrained in its content and language — mathematics. This shallowness denied him an insight into why physics was successful, and why his attempt to capitalize on his influence over national research funding to build biochemistry in the image of reductionistic physics was doomed from the beginning. What he actually helped develop was a sub-specialty that could never master its subject, as did physics.

The authors of the laws of physics assumed each sample of a particular kind of inanimate matter was the same as any other sample of the same kind of matter. Together with the further assumption that every phenomenon exhibited by inanimate matter could be understood by first understanding its parts — the experimental model of reductionism

— physics successfully developed four sets of mathematical laws that govern and describe essentially every phenomenon associated with inanimate matter, ranging in scale from collections of galaxies to the parts that make up the parts of the atoms that make up the parts of matter. A necessary condition for the application of the laws to predict the behavior of any inanimate object was that it existed in a closed system such that it did not exchange matter with other systems. Another necessary condition was that the object under consideration must be identical to every other object of the same type — otherwise, general laws could not exist and the physics endeavor would have failed.

For good reason, physics made no claim that its laws could explain life or any biomedical phenomena that emerged at the level of a cell or any higher degree of organization. Emergent biophenomena — including but not limited to biomedical biophenomena — in stark contrast to physical phenomena, occur only in open systems.

Every living organism is an open system when and only when it is alive; it continually exchanges matter with its environment and ceases doing so only in death. Because no two living individuals of any species are identical, there can be no general laws that can reliably predict behavior of a living individual, at least not in the sense physicists can predict the behavior of inanimate matter. This is not to say that the laws of physics do not apply to animate matter, but rather that they do not apply deductively to emergent biophenomena. Handler wrongly assumed the opposite when he claimed animate matter could be explained at the lifeless molecular level where hydrogen, nitrogen and carbon atoms interact with each other.

Handler was actually wrong thrice when he claimed biochemistry would explain emergent biomedical phenomena. First, although he accepted that physics deductively explained the biochemical reactions that occur in test-tubes, Handler wrongfully rejected a role for the physical laws that govern electromagnetic energy in the process of understanding emergent biomedical phenomena. Only those laws could explain how the results of biochemical reactions propagated instantaneously throughout the body to facilitate and synchronize emergent biophenomena, which occur at the macroscopic not molecular level. Electromagnetic energy was theoretically capable of mediating emergent biophenomena, throughout the body, and the need for such a capability was a condition precedent for every such event. The requirement of some form of electromagnetic energy to explain emergent biomedical phenomena underscored the fact that Handler was wrong when he falsely claimed biochemistry alone was sufficient.

Handler's second error was his contrived invention of the Thought Law to justify his version of reductionism. In a duplicitous attempt to make biochemistry appear more like physics, Handler applied to animate matter the same model physicists used to understand the behavior of inanimate matter. He postulated that animate matter was composed of independent parts whose individual behaviors could be summed to account for observed biomedical phenomena. As applied to animal experiments, Handler contradicted reality by asserting that all animals in a test group actually react identically in a given circumstance, claiming observations of different measurements from different animals were experimental artifacts. To overcome the experimental problem of apparent intrinsic biological variability, which Handler believed was obscuring objective truth, he conjured what he called a Thought Law — that the average response of the group was the true response of each animal. Handler

applied the Thought Law to humans and asserted it was a valid method to determine the true value for each human.

His third error was his dicta that chemical energy, in the absence of electromagnetic energy, was sufficient to predict the creation of life and the function of all living things. He revealed the depth of his blind faith in Handlerian reductionism when he made the absurd prediction that biochemical research would ultimately show how life could be created in a beaker by mixing biochemicals in proper proportions in accordance with the chemical doctrine of mass action. Handler's assertion was no more realistic than the attempts of the 15th century alchemists to convert lead into gold.

The Handlerian reductionist paradigm for biomedical research retarded the development of American biomedicine, paralleling the damage Lysenko caused to Soviet agriculture when he said he could train wheat seeds to grow in Siberia. Handler's demand that biomedical inquiry rely exclusively on reductive experimentation especially devastated the research of scientists who were studying the biological or biomedical role of electromagnetic energy, which was present in the brain, the peripheral nervous system, and in every living cell, but was absent in the blended soup Handler viewed as the source of all biomedical knowledge. Handler believed all biomedical phenomena ultimately could be reduced to parts and explained with physics-like accuracy based on biochemical measurements of cellular detritus. That belief led him to consciously disregard any possible explanatory significance of the unique properties of living systems — complex hierarchical organization, appearance of purpose, and time irreversibility, which does not exist in physics but that invariably results in the death of every living organism. Ignoring these properties enabled Handler to ignore every difficult question in biomedicine.

Handler's ideology provided no starting point to understand the origin of life, the development of a vast number of species, the range of different behaviors of different organisms within the same species, why every organism in each species changes drastically with the passage of time and ultimately dies, the interactions that occur between anatomically distinct living systems within a living individual, and how individuals grow, heal, and develop, and cope with diseases. Handler effectively blocked consideration of the most important questions in biology and medicine that mankind could ask. He saw biochemistry as the sole science of life, and regarded direct study of the properties of living systems as unscientific because, reasoning circularly, they were not describable in biochemical terms. It was as if the child prodigy and PhD at the age of twenty-one had only a walnut-sized brain that could not simultaneously hold the ideas of biochemical and non-biochemical approaches to the elaboration of biomedical knowledge.

In his leadership role on the advisory panel and on the board of the Institutes, Handler systematically advocated funding only those experiments that matched his idea of what biomedical research ought to be. He was hugely antagonistic to non-reductive research proposals designed to explore the explanatory role of electromagnetic, mechanical, kinetic, gravitational, or thermal energy in biomedicine.

He also reflexively opposed a galaxy of types of biomedical studies: cause-effect studies that were not based on a biochemical hypothesis; studies of the role of biological cybernetics in

health and disease; almost all clinical research whose objective was to test a clinical hypotheses such as the safety and efficacy of drugs rather than a biochemical hypothesis; epidemiological studies aimed at providing initial information regarding the determinants of disease; research proposals related to the study of how tissues and organs functioned and reacted to changes in the body's internal environment or to man-made changes in the external environment. He regarded any methodological paradigm or scientific specialty that differed in any material respect from Handlerian reductionism as perforce antiscientific, a category in which he placed a variety of sciences and clinical specialties including psychiatry, psychology, and the social sciences. Instead, Handler exploited his dominant position on the Institutes' advisory panel and governing board, and the Institutes' procedural rules, to chisel in stone his cognitive structure of biomedicine. He approved only purely reductive studies of the biochemical properties of tissue debris, especially studies related to food metabolism, genes, and the biochemical machinery for synthesizing proteins; effectively, he was blind to the limits of a purely biochemical approach to the study of biomedicine. Handler recognized no legal or ethical obligation to create a written record justifying any of his decisions regarding the disposition of grant funds.

The other members of the advisory panel and the bureaucrats in he Institutes, mindful of Handler's clout within the Institutes and the Congress, and his anger when it flared, were no brake on his excesses.

During Handler's time at the Institutes, so-called biochemical-mechanism proposals became the sole experimental design allowed to compete for research funds.

Proposals based on a different scientific approach were more less automatically eliminated from consideration. The effect of the Institutes' adoption of Handlerian reductionism was to instantiate the dogma of biochemistry in biomedical research.

By excluding system-level biomedical studies from possible funding, Handler financially choked off the careers of scientists dedicated to the pursuit of novel paths to understanding the dynamics of processes manifested by living systems.

His antagonism toward any form of biomedical research that differed from that of his biochemical heroes in *Arrowsmith* corrupted the mission of the Institutes and prevented studies of innumerable biomedical phenomena, including but not limited to growth, development, healing, memory, consciousness, health, and the occurrence and prognosis of chronic diseases. Studies of these phenomena could not be supported by the Institutes because Handlerian reductionism recognized no valid method for doing so, and it is axiomatic in science that knowledge is the product of method.

When Handler joined the biochemical advisory panel, most grant applications contained averments of relevance to cancer that were contrived lies told to satisfy the legal requirement of a foreseeable application to disease to merit the use of public funds for biochemical research, whereas in reality the real purpose was to seek knowledge for its own sake. The averments were actually naked baseless claims that served as passwords into the federal bank that dispensed grant funds. Handler told the Congress he lamented the necessity to tell lies, but nevertheless it was in the nations interest to support basic research in biochemistry simply for the knowledge it would produce, irrespective of any foreseeable link to

disease. After the Congress rejected Handler's argument, he fabricated another major path to permit biochemists to seek federal funds for research, one that was based on studies of genes.

The structure of DNA was discovered and some rare defective genes responsible for heritable diseases were identified biochemically. The defects were causal in the sense that every person who had the defective gene developed the disease, and it never developed in someone who lacked the defect. Handler told the Congress that biochemists would eventually find a way to repair gene defects and then show clinicians how to correct the human gene pool, but only if adequate funding were provided. He also testified that cancer was a result of mutated genes in the sense that each kind of cancer was caused by a different defective gene, and only people who had the gene got cancer — a claim that was as baseless as his promise that increased funding would lead to a chemical technology that removed defective genes. Nevertheless, Handler attempted to support his claim by fabricating a principle he said governed the occurrence of cancer,

With the support of the Institutes, Handler asserted that human disease, including cancer, was caused by three types of malevolent biochemicals: special protein molecules that defeated the immune system, allowing infectious agents to enter the body; environmental chemicals that became toxic biochemicals inside the body; defective genes.-Handler promoted his myth, a so-called Universal Biochemical Theory of Disease Causation, in speeches at biochemical society meetings, talks at universities, and congressional testimonies, but never explained it in any scientific publication or otherwise rationalized or supported it — he provided only rhetoric.

He inculcated the myth into the culture of the Institutes, and advocated for pointillist biochemical research to find the so-called biochemical causes for diseases he imagined existed. Handler repeatedly made bold promises to the Congress that, if enough biochemists were produced, and given government grants with the freedom to plan their own experimental objectives, the malevolent biochemical agents responsible for every disease, even aging, would eventually be discovered.

The myth of a causal link between malevolent biochemicals and disease was supported by the leaders of the Institutes during their annual testimony before congressional budget committees. The gist of their message was that disease was a biochemical process caused by specific abnormal or toxic agents, which logically meant there existed chemicals capable of interrupting the process, resulting in treatments and cures. Those salutary objectives could be identified more quickly, the leaders said, if the Institutes' research budget were increased. But although the testimony of the leaders was same as Handler's, his motives differed from theirs. He believed the myth and sought to establish it as reliable truth. The leaders, in contrast, after they were confronted with the issue of a link between smoking and cancer, learned they could use the myth as the basis of a strategic response to an existential problem caused by tobacco issue.

The motives and strategy of the leaders sharpened after the possibility of a relationship between the habit of smoking and the occurrence of cancer was suggested by nonbiochemical scientists, both epidemiologists and medical investigators. In nonreductionistic biomedical research, investigators analyzed clinical and government health data and found that smoking

and cancer were statistically related, suggesting the likelihood of a causal link. Handler, whose home state was the largest producer of tobacco in the country and whose university was founded and funded by the man who started the U.S. cigarette industry, was keenly interested in the issue. Influence by his argument that if smoking caused cancer, there had to be a causative chemical constituent in the inhaled smoke, the Institutes funded pointillist biochemical studies that promised to find the causative chemical. But none was found —not even one of the several thousand chemicals in cigarette smoke was proven to be a biochemical cause of cancer in humans.

Despite the failure of the Institutes to find a biochemical cause, epidemiological and clinical studies continued to yield strong evidence of a correlation between smoking and cancer, particularly lung cancer. The leaders recognized that the inability to identify a putative toxic agent in smoke, despite the persuasive evidence published by epidemiologists and clinicians that smoking caused cancer, had dire political implications for the Institutes. The story the leaders told the Congress — that s few specific malevolent biochemicals directly caused diseases — was not supported by the research the Institutes funded, tobacco-related or otherwise. And even more potentially damaging to the funding honeymoon the Institutes were enjoying, was the possibility that Handler's theory was wrong — that cancer wasn't always the result of a specific malevolent chemical. If so, the situation would be a politically embarrassing limitation on what the Institutes could hope to accomplish. The tobacco issue underlined political problem the leaders faced.

The tobacco companies and their supporters in the Congress criticized the Institutes for funding studies looking for the toxic chemical in smoke that caused cancer. The critics argued that the Institutes should not use taxpayer money to study a possible link between smoking and cancer because the claim that tobacco caused cancer was a hoax, and the studies were a threat to the livelihood of small tobacco farmers. Biochemists employed by the tobacco companies dismissed the epidemiological and medical studies as non-scientific and inconsistent with the opinions of biochemists such as Handler and of physicians the tobacco companies consulted. Biochemical researchers who worked for the tobacco companies interpreted their results as meaning that tobacco was completely safe. The resulting publicity concerning the link between tobacco and cancer threatened the budget of the Institutes and even their existence as government agencies.

Handler remained firmly committed to the myth he created and believed there was no public-health reason for the government to interfere with the tobacco industry because, he said, there was no compelling evidence that smoking caused cancer. His recommended solution to the Institutes' problem was that, on a principled basis, all funding of biochemical studies intended to identify the biochemical cause of cancer immediately cease. He reasoned that "system-level causality" — what most scientists called emergent biomedical phenomena — wasn't a biochemical question and had no meaning at the biochemical level. Consequently, he advised, the Institutes should decline to fund research designed to prevent cancer by discovering its causes, and instead concentrate on treating and curing cancer, objectives that could be achieved by means of biochemical research. The leaders accepted and adopted Handler's advice although they never formally disclosed to the Congress what they had done. This subterfuge was possible then because the Congress had not yet recognized biochemists weren't a special class of humans, but rather were as value-laden, self-interested, and greedy

as any other group of people. After the Institutes ceased funding studies of whether cigarettes cause cancer, the criticism they received abated and shifted to the epidemiologists and medical investigators. The new strategy also immunized the Institutes against adverse publicity generated by future cancer scares associated with other toxic agents because, on principle, the Institutes would not begin to seek finding the cause. The high regard the Institutes' leaders had for Handler increased even further.

Handler was strongly biased against grant proposals involving the biomedical consequences of electromagnetic energy which, in his eyes, had no more credibility as a biomedical hypothesis than the hypothesis of a heavenly spirit. In the mid-1950s, Handler and others at the Institutes were approached by government agents regarding a problem then occurring at the U.S. Embassy building in Moscow. They were told that Russians were aiming a beam of microwave electromagnetic energy at the building, and that Embassy personnel had complained of various nonspecific illness. Handler's advice was that the energy beam was biomedically insignificant because the energy levels he was told were about ten microwatts, which was small, and in his opinion small values of any agent, whether chemical or energy, were harmless.

At the same time, the U.S. military funded a theoretical analysis of the heating effect of microwaves by a physicist, Herman Schwan, who had worked in a Nazi laboratory during World War II and studied the potential use of microwaves for cooking the food of the crews on German U-boats. After the War, the military sponsored Schwan for U.S. citizenship because of his experience with the effect of microwaves, and hired him to find the safe level for servicemen exposed to electromagnetic energy while operating radars and communications systems. In his reports to the military, Schwan employed the most reductionistic model conceivable of a human — a copper ball — and, based on the laws governing the interaction of electromagnetic energy with inanimate matter, he calculated the temperature rise expected in the copper ball as a function of the level of the applied energy. He arbitrarily defined the safe level for human exposure to be the level at which the applied energy could no longer elevate the temperature of the reductive human copper-ball model above room temperature, which he found was ten thousand microwatts. Soviet scientists, however, based on animal and human experimentation rather than phony models and simplistic calculations, arrived at a safety level of one microwatt which became a Soviet national standard. Handler discounted the Soviet safety level because, he told the government agents, Soviet biological research was far inferior to that in the U.S. He supported Schwan's calculated safety level because it was based on what Handler called "general biological principles," by which he meant that a very small amount of anything is presumably safe unless conclusively proven otherwise.

Handler's opinion didn't pass the laugh test, and the U.S. government began a series of secret animal and human studies in various government and university laboratories, including those at the University of Rochester and Veterans Administration Hospitals in California and Kansas, but the results were classified, and ultimately destroyed. Throughout the duration of the secret program, and thereafter, Handler and the Institutes maintained a strict ban on funding biomedical studies of the health and safety aspects of exposure to electromagnetic energy —there were no exceptions. Because of government secrecy policies and the absence of any source of funding, progress in the area was significantly impeded.

Handler's simplistic reductive model for biomedical research was intended to generate disjoint points of biochemical knowledge that, he claimed, would coalesce one day and explain the specific causes of diseases. His silent assumption was that all diseases have a specifically identifiable cause, which he arrived at by arbitrarily excluding consideration of interactions between environmental agents and systemic regulation. His arbitrarily restricted model of human health and disease coalesced into his universal biochemical theory of disease, which ignored real human problems — chronic diseases, the effects of anthropogenic pollution, and role of societal factors.

Under his influence, the Institutes adopted his policy, which delayed regulatory efforts for years. Handler invoked the same simplistic model when advising the government on reports of Russian microwave energy on U.S. embassy staff in Moscow. He relied not on empirical data but on an a priori belief in the harmlessness of any potentially causative factor, whether chemical or electromagnetic, if the dose of the factor were what he judged too small. Handler's refusal to accept system-level energetic models of disease causation, subordinated national health to his dogma, and overrode attempts to launch serious investigations of the link between anthropogenic factors and human disease.

The promise of Handlerian reductionism was that reducing living systems to chemical reactions would result in scientific certainty, but in practice it led to scientific paralysis. Despite more than a decade of the reductionist biochemistry sanctioned by the Institutes and Handler, they failed to provide meaningful explanations for diseases beyond those caused by vitamin deficiencies, single-gene mutations, or infectious agents. The research approach they approved had nothing to say about what caused chronic disease, controlled healing and growth, governed the dynamic interactions among tissues and organs, or explained human life and its fundamental processes such as consciousness and memory. Handler not only mandated reliance on a reductive model that could not explain the causes of chronic disease or why emotional trauma could manifest as physical illness, he also forbade scientists from utilizing models that had the potential to provide the explanations.

Handler's administrative influence became a tool for intellectual repression, and he wielded it with precision against those who explored alternative frameworks. Among his targets was René Dubos, a biochemist who transitioned to system-level research and proposed that infectious disease resulted from complex interactions between host and environment—not merely from microbial agents. Dubos' theory challenged Handler's belief in biochemical determinism and was supported by elegant animal studies, yet Dubos' grant proposals were systematically denied by Handler's panel. Handler never publicly criticized Dubos, which was a wise strategy for Handler because he communicated mostly in short, interview-length rhetorical flourishes, unsupported by evidence or rational analysis, whereas Dubos communicated in thoughtful analyses published in prestigious scientific journals, and in an impressive series of books. Harold Wolff, who pioneered research linking stress to somatic disease, similarly found himself excluded. Wolff viewed the body as a cybernetic system reacting to environmental inputs — an approach fundamentally different from Handler's biochemical lens, and was decidedly opposed by him.

Handler's rejection of nonlinear systems, feedback loops, and information regulation deprived biomedicine of essential conceptual tools. His suppression of biomedical research extended to Norbert Wiener's cybernetics and Ilya Prigogine's work on self-organization. Both scientists represented a vision of life as regulated, adaptive, and driven by information, which Handler viewed as a rhetorical concept except when he needed to employ the word to describe whatever it was that genes contained, enabling them to specify the chemical composition of proteins and to convey heritable traits. Even after Shannon showed how information could be quantified, and Lorenz showed immeasurably small informational changes could have dramatic effects on a nonlinear system, of which life was an example, Handler refused to allow development of relevant biomedical initiatives. He responded not with debate but with funding embargoes, cutting off avenues of discovery that might transform medicine. Wiener's cybernetics offered a model of the body as a system governed by communication and control, not just molecular machinery. Claude Shannon's information theory demonstrated that information was not metaphorical, but a measurable scientific entity. Ilya Prigogine showed that order could emerge from thermodynamic chaos in open systems, a breakthrough that explained biological complexity. Everywhere Handler looked there were competing ideas to reductionism, but he learned that if he strongly opposed an idea shortly after its birth, it was likely to disappear permanently.

Even the Nobel Prize-winning Albert Szent-Györgyi found himself marginalized when he attempted to explore bioenergetics. He made clear that biochemistry alone could not explain life or any of its myriad system-level behaviors, and proposed that the absence electromagnetic signaling was a fatal flaw in Handlerian reductionism.

Handler approved funding only for Szent-Györgyi's conventional biochemical studies while pointedly rejecting support for any inquiry involving electromagnetic energy.

Harold Burr proved electromagnetic energy was continuously flowing between any two points on the surface or in the interior of any living organism but in no inanimate material, indicating Handler was foolish to ignore the energy flow when trying to understand biomedical phenomena. Burr studied the role of the energy in embryogenesis and provided evidence it guided growth and organ formation; he published his experimental results many times over several decades, but his work was dismissed by Handler as pseudoscience. No federal funds were ever granted to Burr during Handler's reign. Frank Brown showed that animals had evolutionary-created sensory detection systems that allowed them to detect geomagnetic energy, thereby gaining information about the environment which was important for their survival.

Handler's opposition to Brown beggared belief. He disapproved of Brown's work without providing any specific rationale, and used his authority to undercut its acceptance by approving research grants for J. Woodland Hastings, who misleadingly discredited Brown's work on the basis that his research was not reductionistic.

Robert Becker asked the question why salamanders can regenerate a missing limb but no other animal higher on the evolutionary scale can do so. He discovered that not only could electromagnetic energy be detected at every point on the skin of a salamander, but also that the pattern of the measurements reflected the anatomical pattern of the peripheral nervous system, suggesting that the energy had physiological relevance. He doubted that a special biochemical was responsible. Instead, he hypothesized that salamanders were organized in

such a way that they could generate an electromagnetic signal that triggered appropriate cells to initiate the regeneration process. Becker began animal experimentation to identify the nature of the putative electromagnetic signal, with the ultimate goal of reproducing it to stimulate regeneration in higher animals. During the 1960s, Becker's. research was highly successful and he published the results of many experiments in the prestigious journals. But Handler disapproved of Becker's experimental approach, and was instrumental in preventing Becker from receiving funding from the Institutes.

According to Handler's dicta, models of biomedical phenomena should be built solely from pointillist biochemical data collected from homogenized tissues.

He maintained that destroying issue structure — thus rendering it devoid of electromagnetic signaling — facilitated understanding its biochemical properties.
Handler's blindness and bias persisted even though his reductionistic approach failed to identify the causes of chronic diseases, predict disease progression, explain systemic healing, or guide clinical treatment. The approach did little more than create a data-rich but insight-poor biomedical science. Instead of catalyzing clinical breakthroughs, as Handler repeatedly promised, Handlerian-based biomedicine became an expensive exercise in molecular cataloguing, increasingly detached from the suffering of patients and the realities of disease.

Handler turned a blind eye toward the extensive research regarding the biological effects of electromagnetic energy conducted in Russia, an insight into which was provided by A. S. Presman, who reviewed and evaluated extensive Russian literature dealing with biological influences of electromagnetic energy. Presman described a substantial, rapidly increasing number of studies, mostly Russian, that showed the effects of the energy were unrelated to the theoretically predictable thermal effects; based on the evidence, he concluded electromagnetic energy conveyed information from the environment to the organism, and between points within the organism. He proposed that in the course of evolution, living organisms developed sensory systems for detecting geomagnetic and cosmic electromagnetic energy that functioned in conjunction with the well-known sensory, nervous, and endocrine systems in effecting coordination and integration of physiological functions and providing information about the environment which aided survival. Presman made a good case for the thesis that the coordination and information occur in the organism as a whole, and was not present at the molecular level. Handler, however, rejected Russian biological and biomedical results without assessing the research on its merits, choosing instead to dismiss them based on his ideological commitments —a preemptive dismissal, not a thoughtful or evidence-based refutation.

Handler's leadership in biomedical science was not one of scientific advancement, but of intellectual repression. He misused his administrative authority to enforce his narrow ideological agenda and undermined the principles of open inquiry and critical evaluation that science was meant to uphold. The biomedical establishment he helped build was deeply flawed. His ideologically-driven policies fragmented the scientific disciplines, neglected health research, and greatly impeded integration of electromagnetic energy into biomedicine which, as a direct consequence, did not embrace methodological pluralism. Instead, Handler led the nation into a future governed by the toxic myth that biochemistry alone can explain everything

about life, health, and disease. He effectively pigeonholed biomedical research as a second-rate endeavor because, being self-limited to the study of the effects of chemical energy, it could not possibly explain life or its activities, or develop general theories expressed in mathematical laws that could do so. Handler's commitment to molecular biochemistry as the exclusive lens for biomedical research profoundly mis-shaped federal research funding, suppressing alternative models including electromagnetic regulation, systems theory, and cybernetics. His policies prevented progress in understanding emergent biomedical phenomena and caused a lasting fragmentation of biomedical science.

THE PILLAR OF HANDLER'S REDUCTIONIST creed was that life and all its manifestations were nothing more than the sum of biochemical reactions duplicatable in test-tubes —duplicating complex biophenomena would simply require more test-tubes. His ideology gave him jurisdiction over defining what was a real biomedical question and a proper method of study, and he decided only experiments for which there was a molecular hypothesis should be funded, and that causal, system-level, or teleological studies should be dismissed as unscientific. Under Handler's leadership, the biochemical advisory panel at the Institutes — and other grant-gatekeeping panels for which it served as a model —steered U.S. biomedicine toward ever-finer molecular detail and away from other experimental approaches. Handler's model for causality was a linear, one-way chains of cause-effect chemical reactions governed by the simplistic law of mass action — perfectly suited to siloed laboratory research but ill-suited to studies of nonlinear causality, the process that yielded emergent order.

Handler framed reductionistic biochemical experiments as ultimately capable of explaining living systems, constructing them from parts, and curing all diseases. He became a biochemist at a moment when amino-acid sequencing, isotope tracers, and spectrophotometry were identifying every biochemical in a cell. In his own research on nicotinic-acid metabolism during World War II, he epitomized the reductionist creed: break a physiological phenomenon into discrete enzymatic steps, purify each enzyme, and observe its function in a beaker. He believed every biomedical question was ultimately solvable by extending this molecular approach. When he rose to national leadership, he translated that conviction into administrative practice, favoring grant proposals anchored in an a priori molecular hypothesis and dismissing system-level inquiries as what he called "premature" or "unscientific."

Handler's creed retarded but did not arrest the occurrence of new scientific insights into the growth of a practical and useful biomedicine, or the development of methods other than Handlerian reductionism for conducting research applicable to biomedicine. Advancement occurred in diverse areas, although at a muted level and outside the domain of biomedical orthodoxy established by Handler and the Institutes.

Scientists who ignored their dictates had no or, at most, sparse access to federal funding, a limitation that slowed the progress of their research. Despite being intentionally discouraged and seriously underfunded, the hetrodoxers were active in diverse area of scientific research. The common aspect of their work was its promise to revolutionize biomedical research, and transform it into an endeavor intended to benefit the public rather than edify Handler and university biochemists. The heterodoxers showed ways the limitations on biomedicine embodied in Handlerian reductionism could be overcome, and poignantly demonstrated the methodological impossibility for biochemistry alone to explain emergent biophenomena. The

unit of analysis in the view of the heterodoxers was the whole organism, in Handler's method it was the molecule. According to the hetrodoxers, causality was circular, networked, non-linear, foundational, and irreducible, whereas for Handler it was a linear additive process,

Norbert Wiener and Claude Shannon, who studied cybernetics and developed information theory, introduced information as a third measurable element in nature — adding to mass and energy. But the only aspect of biomedical information Handler accepted was that contained in the structural organization of DNA; he blocked federal funding for the study of biomedical cybernetics. Ilya Prigogine, a Nobel physicist, proved ordered patterns emerged in energy-driven open systems, and offered a thermodynamic basis for evolution, but the Institutes followed Handler's lead and clung to a deterministic molecular scheme, and denied funding to Prigogine and those who sought to follow his path in the new area of work and thought he opened.

Edward Lorenz demonstrated the inherent unpredictability of even simple physical systems — an observation that virtually guaranteed unpredictability existed in the far more complex living systems. In so doing, he showed that Handler's goal of total predictability based on biochemical facts was impossible. But Handler ignored Lorenz's work and continued to maintain that biomedical research funded by the Institutes must pass the test of proposing to find answers to biomedical problems that were built on discrete, causally-connected parts.

Harold Wolff, a neurologist, studied the role of the nervous system as the master organizer of the complex reactions in the human body that occur in connection with changes in the internal and external environments. He presented extensive clinical evidence showing that an unidentified but indubitably real regulatory system protected the individual despite continuous changes occurring inside the body and the presence of diverse factors in the environment. The external stimuli consisted of infectious agents, man-made chemicals in the environment, and neurogenic reactions resulting from involvement with other people that resulted in fear, anger, or threat.

When the limits of the normal adaptive reaction pattern controlled by the regulatory systems were exceeded, the body responded with a self-destructive reaction that could not be simulated in beakers, hence could not be studied using Handler's method. The resulting manifestations included common maladies as peptic ulcer, hypertension, colitis, and migraine headaches. René Dubos, whose interest was experimental medicine, showed that infection depended on host–environment interactions, and characterized disease as a breakdown in the body's defensive mechanisms. He regarded Handlerian reductionism as "dream of reason." Handler, however deemed grant requests intended to follow the trail Dubos blazed as the pursuit of nothing.

Hans Selye, arguably the most prominent and successful biochemist-physician in the twentieth century, further advanced the idea that somatic and neurogenic stresses routinely encountered in daily life can contribute to the onset and intensity of numerous human diseases. His lifetime of work in the laboratory and the clinic — described in his many scientific publications and books — showed that human pathologies were caused or influenced by mental processes such as goals, purposes, aspirations, and values, as well as by physical agents. Selye was the direct opposite of Handler in matters related to laboratory and clinical research,

scientific publications that rationalized and supported his ideas and hypotheses, and human empathy.

Handler saw Selye as a persistent intellectual adversary and ideological antagonist who represented a worldview and scientific approach Handler deeply opposed. He regarded Selye as a threat to reductionist biochemistry because he was scientifically and clinically successful even though he did not seek to explain life in terms of molecular mechanisms. Selye championed holistic, systemic concepts such as stress and a general adaptation syndrome, which emphasized the body's integrated responses to environmental challenges — ideas that could not be reduced to the linear biochemical pathways extolled by Handler. Handler's opposition to Selye was ideological and strategic — he viewed Selye as a persistent challenge to the dominance of the reductionist paradigm and a symbol of what biomedical science should not be.

Albert Szent-Györgyi's Nobel-winning discoveries aligned with the molecular narrative of biochemistry, but his later embrace of electromagnetic energy and holistic models of biomedical organization directly challenged the reductionist paradigm Handler vigorously championed and institutionalized. Szent-Györgyi argued that biochemistry failed to explain life because its reductionistic model of living systems was wholly inadequate. He emphasized the need to allow a causal role for electromagnetic energy in the explanation of emergent biophenomena, which placed Szent-Györgyi outside the boundaries of what Handler defined as legitimate biochemistry, and activated his animus. The irony of the conflict was not lost on many observers; Handler, who was a mediocre laboratory biochemist, at best, and retired from laboratory research very early in his career because of chronic illness had the audacity to criticize the quality of the research of Szent- Györgyi who won a Nobel Prize for his research. And if what Szent-Györgyi told me is true, he should have won a second Nobel Prize for the discovery of the citric acid cycle, because the discovery for which Hans Krebs won the Prize was done in Szent-Györgyi's laboratory, under his supervision

Handler, wary of undermining the authority of reductionist biochemistry, distanced himself from Szent-Györgyi in public forums, disassociated himself from Szent-Györgyi's ideas, and successfully influenced the Institutes to deny research grants to Szent-Györgyi that would allow him to pursue his novel ideas. Consequently, Szent-Györgyi's research concerning the biomedical role of electromagnetism was unfunded by the Institutes. Handler's treatment of Szent-Györgyi was emblematic of a broader ideological policing within postwar American biomedicine, in which institutional legitimacy was secured by marginalizing heterodox approaches and consolidating the authority of molecular reductionism under the banner of scientific objectivity.

Frank Brown was a biology professor who studied the behavioral rhythms of aquatic animals and proved they had the ability to detect changes in the electromagnetic energy of the geomagnetic field. Brown showed the rhythms were a result of complex interactions among multiple levels of organization in animals. His discovery provide the first evidence that animals had a sensory system — in addition to the eye — for detecting natural electromagnetic energy and transferring information in the detected signal to the brain,

permitting it to orchestrate appropriate behavioral responses. Subsequently, many investigators showed birds, insects, fish, bacteria, and mammals were sensitive to natural environmental electromagnetic energy, and employed the information in the detected signal for purposes of migration, orientation, and prey-location. Brown's work was pregnant with the implication that humans also had the capability to detect electromagnetic energy, and Rutger Wever, a German scientist, proved it was so; in subjects voluntarily exposed to anthropogenic electromagnetic energy, he observed changes in their circadian rhythms.

Handler and his friend, Woodland Hastings, a prominent biochemist, denied the validity of Brown's research simply because of their dogmatic beliefs experimental designs should be reductive rather than integrative, and that electromagnetic energy had no role in the regulation of emergent biophenomena. The altered rhythms Brown observed were inherently unexplainable at the molecular level because they were emergent properties resulting from complex interactions among multiple levels of organization in the animals. Nevertheless, Handler and Hastings opposed Brown's work not because of any identified or even suspected inconspicuous experimental defect, but rather because they believed nothing worthwhile could come from a non-mechanistic study regarding biological effects of electromagnetic energy. Neither Handler nor Hastings realized Brown's research proved the existence of a previously unrecognized animal sensory system for detecting low-level environmental electromagnetic energy — one of the fundamental biological discoveries of the last half of the twentieth century. Instead, Handler adhered to his career-long behavior of subverting types of scientific research which he disapproved on ideological grounds, and limiting federal funding to investigators whose proposed research was consistent with his ideology. Handler used his influence to secure Hastings' appointment to the Institutes' advisory committee and, predictably, Brown's grant applications were rejected. Handler did the same thing to Harold Burr, a biology professor for many years at Yale University, who published results of electromagnetic measurements in animals and humans that appeared to be guiding growth. Handler labelled Burr a charlatan and successfully denied him research funding.

Robert O. Becker arrived as the head of orthopedic surgery at the Syracuse Veterans Administration Hospital in 1958, determined to probe the mystery of how the body heals itself. He regarded the reigning reductionist creed — that growth and healing were explainable by biochemistry — as insufficient because it said nothing about how they were controlled and regulated. Becker asked how the body learned a fracture occurred, initiated and controlled the complex healing process, and then stopped it when the repair was complete, questions then not considered in textbooks.

His desire to ask these questions and pursue answers experimentally put Becker outside the biochemical mainstream several years before he encountered Philip Handler personally.

Inspired by René Dubos, Harold Burr, Hans Selye, and Albert Szent-Györgyi, Frank Brown, and A. S. Presman, Becker looked beyond isolated molecules and viewed healing as a whole-organism process. Beginning in the late 1950s, Becker mapped electrical signals on the skin of laboratory animals and observed a pattern that mimicked the architecture of the peripheral nervous system. Based on his results, Becker envisioned a cybernetic control system in which the brain sent and received information-rich electromagnetic energy through nerves, a closed-loop feedback control system — entirely distinct from the well understood neuronal

sensory system — that regulated the formation of new bone and throttled growth as healing neared completion, one of the very few examples of true tissue regeneration that occurs in the human body. Under Becker's hypothesis, biochemistry supplied the building blocks but control resided in electromagnetically encoded information—an idea Handler deemed metaphysical. After Becker published supporting evidence in preeminent scientific journals and described the results of his research at national science meetings, the Veterans Administration's central office in Washington significantly supplemented the Syracuse hospital's support for his research. He expanded his research regarding the idea that disease and healing were system-level phenomena rather than determinates of isolated molecules.

For Becker, what he observed daily in the clinic — that the body was a self-organizing entity whose injured bones automatically dissolved their damaged parts, grew new bone of the appropriate size and shape at the correct location, ceased growing when felicitous, and remodeled the new growth to create a perfect copy of the uninjured bone — was an orchestration of healing that pointed to a controller invisible to reductionist biochemistry. Handler's explanation for healing was only a sermon to the effect that physicians didn't understand healing because they didn't yet know the responsible biochemical reactions, which only biochemical research could provide. Becker asked why salamanders regenerated lost limbs while humans did not, even though the limbs in both species were anatomically identical. Handler warned such global questions were non-biochemical and therefore unscientific. He believed they belonged in medicine's future, but Becker thought the questions he asked were central to clinical progress and merited immediate attention.

When Becker showed the electrical changes on the skin of salamanders following limb amputation differed from the corresponding changes in frogs, a species only slightly higher on the evolutionary scale but that did not normally regenerate limbs, the conflict with Handler sharpened. Becker interpreted his observations as suggesting the possibility that limb regeneration could be restored in frogs, and possibly even in more phylogenetically animals, if the information in the cybernetic loop guiding limb regeneration that was lost during evolution were identified and then simulated using appropriate technology. Handler, who was a biochemical consultant to the Veterans Administration at the time, disapproved of Becker's research, but was not formally consulted as a reviewer because Becker's financial support came from the rehabilitation rather than biochemical division of the Veterans Administration research program. Nevertheless, even though the first dozen of Becker's scientific publications appeared in prestigious scientific journals, Handler regarded the electrical signals Becker observed as electrical noise and derided his research as voodoo science fit for mesmerists not scientists. Becker's application to the National Institutes of Health to widen his research program was rejected by the Institutes' biochemical advisory panel because the proposed experimental design was non-reductive, reinforcing his sense that biochemical reductionism policed the gateways of Institutes science. Becker's findings suggested that limb regeneration might one day be engineered by manipulating man-made electromagnetic signals—a prospect that threatened the Institutes' biochemical-centric research hierarchy, which was failing to produce beneficial practical results, despite Handler's promises to the contrary. His version of reductionism, to which the Institutes were married, produced no biochemical solutions to biomedical problems and no practical information save for the areas of genetics and metabolism.

Handler and Becker spoke past one another. He unveiled his physics-based program at national scientific meetings and published his results; Handler extolled the virtues of biochemistry before the Congress but published nothing substantive. Each development hardened their positions: Becker as the insurgent who used physics to probe life's organizing signals, Handler as guardian of reductionism. In Becker's emergent cybernetics model, the brain monitored healing through a negative-feedback loop of information-rich electromagnetic signals coursing along nerves. Handler, convinced that every biomedical problem reduced to biochemistry, dismissed the very framing of Becker's hypotheses as unscientific, setting the stage for a clash of paradigms and personalities. The power differential became obvious when Becker, after publishing promising data in leading journals, again sought Institutes funds to increase the size of his laboratory, and again was denied due to Handler's influence. Handler perceived Becker not merely as a dissenter, but as a well-funded rival operating outside the gatekeeping reach of the Institutes.

Further resources provided by the Veterans Administration, both money and clinical manpower that allowed him to reduce his clinical responsibilities and increase his time doing research, allowed Becker to test progressively bolder ideas. He extended electromagnetic-control theory to myocardial regeneration and discovered that salamanders can regenerate heart muscle — and quickly. The results, which amazed everyone in our laboratory, were published in what was then the most popular and respected international scientific journal. Becker theorized, limb and heart regeneration were self-organizing electromagnetic-governed phenomena akin to but distinct from the negative-feedback circuitry of fracture repair he described which itself, by definition, was an example of regeneration because the process replaced injured tissue with tissue that was identical to the original uninjured tissue, as opposed to scar tissue.

Methodologically, philosophically, and ethically the schism between Becker and Handle was stark. Becker's experiments tracked electromagnetic signals over time in intact tissues, correlated signal levels with tissue growth, and manipulated the signals to alter healing trajectories in bone. His metrics were holistic, temporal, and feedback-oriented — features that conventional biochemistry neither measured nor valued.

Handler favored experiments that dissected biochemical pathways into linear independent molecular steps involving genes and enzymes. Thus, each man saw the other's methods as incomplete, at best, and illegitimate at worst. In personal terms, Becker viewed Handler as an ideologue wielding institutional power to stifle innovative, potentially lifesaving paradigms. Handler interpreted Becker's work as a threat to the hard-won authority of molecular biology. Becker was a well-published research scientist and a surgeon who genuinely cared for his patients and among whom he was exceedingly popular. Handler was a mediocre biochemist but a world-class talker on science policy who always made money for his biochemical constituents, among whom his popularity was unsurpassed. He scorned physicians because their therapies were unscientific, and refused to be treated by them for his chronic diseases

The conflict between Becker and Handler was an instantiation of the broad battle regarding what biomedical science was —systems thinking versus reductionism, participatory science versus centralized expert control, emergent bioelectromagnetics versus the dominance of biochemistry, an enterprise that sought to benefit the patient versus the scientist.

Under Handler's leadership, the Institutes became a monoculture of entrenched reductionism, with a closed funding door for diversified research in biomedicine. Study of emergent biophenomena and the complexity of life was habitually avoided on ideological grounds. New concepts such as cybernetics, positive and negative feedback loops, nonlinearity and deterministic chaos remained in limbo. Exclusive reliance on Handlerian reductionism created a blind spot in biomedicine by removing the explicit consideration of values and by blocking gold-standard animal and human studies of the effects of anthropogenic chemical and electromagnetic factors. Even after Handler left the Institutes, his intellectual lineage shaped peer-review norms, perpetuating funding hurdles for emergent-level research. Handler's biochemical reductionism offered early triumphs involving enzyme kinetics and DNA structure. Yet by wielding institutional power to declare system-level questions illegitimate, he inadvertently galvanized a diverse set of hetrodoxers scientists whose work forecasted integrative biology. Their collective message was that matter, energy, and information co-govern living systems, all biophenomena emerge from dynamic relationships, and that Handlerian reductionism was a historical error.

THE 1950S WAS A RIPE PERIOD for Handler's aggressively narrow vision of biomedicine. The metabolism and protein paradigms of biochemistry were successful and the concept of DNA as a master molecule was rapidly developing. Handler believed he was on the cusp of establishing biochemistry as a free-standing science whose mission was the production of pointillist facts that, he believed, would ultimately coalesce and govern clinical medicine. The Congress had tasked the National Institutes of Science to develop a comprehensive science of biomedicine as a rational basis for clinical medicine, and Handler worked diligently to make his goals and objectives the definition and methods of that science. He established the cognitive priorities of the Institutes and was instrumental in its creation of a formidable political alliance with a group of biochemical societies that — with his help and guidance — had formed a federation to best further their mutual interests. The framework of the Institutes' research agenda was not governed by democratic processes but rather was determined by consensus among the leaders of the Institutes and the biochemical establishment — the heads of the biochemical societies and the chairmen of the biochemical departments in the elite universities where much of the research took place.

Handler's biochemical vision of biomedicine had dramatic intellectual and social consequences. He effectively created a national industry dedicated to biochemical research that was financed by grants from the Institutes and housed in university laboratories, especially those at prestigious universities, which benefited greatly from the influx of federal research money. The biochemical research business created a strong demand for expensive scientific equipment, which helped the emergence of a scientific-equipment industry. Handler had a key role in choosing and promoting the biomedical issues and problems that merited consideration, and therefore were fundable by the Institutes. The injurious aspect of his program was the absence of financial support for biomedical research that wasn't strictly biochemical in design.

The Institutes targeted their resources at select areas that were politically popular, thereby accelerating their development and creating a congressional sense of progress which elevated the prestige and budget of the Institutes. They purposely avoided funding research into

numerous critical problems that required novel methodological approaches, with the result that workers in the neglected areas faced enormous financial obstacles trying to establish those areas as sources of true biomedical knowledge. Study of the role of electromagnetic energy and the cybernetic processes of regulation and control was especially marginalized, despite their intellectual validity.

Measured against his objectives, Handler was successful during the 1950s and 1960s because he was able to define what questions were important in biomedicine, establish Handlerian reductionism as the monochromatic method of biomedicine, and gain prodigious support within the biochemical community by virtue of his ability to generate the government support it needed to thrive. From the beginning, however, the exclusive reliance on reductionism mandated by the Institutes effectively forbade experimental approaches far more appropriate for studying emergent biomedical phenomena. There were many questions that went unexplored because the Institutes aimed their money only at the narrowest targets, those amenable to study by resort to reductive biochemistry. Many possible representations of life that merited consideration — alternative visions of nature and nurture — were baselessly and harmfully forbidden

The projects funded by the Institutes exclusively favored upward causation by biochemical mechanisms, and regarded them as the only path to understanding health and disease. Handler successfully established the false belief among the leaders of the Institutes that health and disease could be understood within the same framework that resulted in the understanding of metabolism, proteins, and genetic determinism. His success in persuading the Institutes' bureaucrats seriously impeded recognition of the need for non-reductionistic explanations and secured the Institutes' neglect of all perspectives of biomedicine except his — he was like a lion that kills the cubs of other males so his progeny will survive. The faith of the Institutes in the power of reductive biochemistry led to enormous investments in drugs designed to block unwanted biochemical mechanisms — a dialectical process in which reductive biochemistry and the drug industry justified each other.

During his time on the biochemical advisory panel, Handler became a fully-fledged autocrat, imperious and domineering, someone people didn't argue with unless they were courageous. He achieved wide-spread support among biochemically orientated researchers, who benefited significantly from his success. Handle said he recognized "biochemistry was an old-fashioned word that was in the process of passing away," and used a plethora of synonyms during his speeches to characterize its practitioners — molecular biologists, physiologists, pharmacologists, microbiologists, immunologists, embryologists, geneticists, among others. In that way he broadened his base of political support to include the numerous groups of biochemical subspecialties that had arisen. Handler became their hero because they were competitive for the additional research money he secured from the Congress, and their professional societies lobbied Congress incessantly in favor of whatever Handler favored, like the followers of a cult leader. There was no one in American science who was even remotely as successful as Handler at raising federal support for scientific research. He shaped biomedical research, as if it were wet concrete and he were the mold into which it was poured and hardened.

By the time Handler's tenure as chairman of the advisory panel ended in the 1960s Handlerian reductionism was firmly established at the Institutes and dominated the funding

marketplace. He had successfully blocked or impeded development of many new alternative ideas concerning biomedical research that deserved consideration but were anathema to him. Handler's only disappointment was the Pyrrhic victory he won after a four-year effort of lobbying the Congress to create a new Institute specifically intended to support basic biochemical research that was free of the ordinary requirement that public money should be spent only for a public purpose. Shortly after the new Institute was created, the Congress suddenly awoke from its slumber in scientific matters and recognized that — under the influence of Handler's silver tongue — it had created an agency for an illegal purpose, the expenditure of public funds for a private purpose, the personal edification of biochemists. Strong political pressure resulted in a requirement all Institutes promulgate an official policy that every grant funded by any Institute must serve an identifiable public purpose or state a foreseeable public benefit. Although Handler's achievement was transient, his disappointment was cushioned by the reality that the new policy was easily undercut by skilled grant writers who told transparently contrived lies which satisfied the legal requirement of a foreseeable application to human health.