Salisburg,DF, Price,A, Collins,RD, Wikswo,JP. Max at Vanderbilt. In: Max
Delbrück and the new perception of biology, 1906-1981, Shropshire,W, Jr., ed.
AuthorHouse, Bloomington, IN, 213-236, 2007

Chapter 22
Max at Vanderbilt

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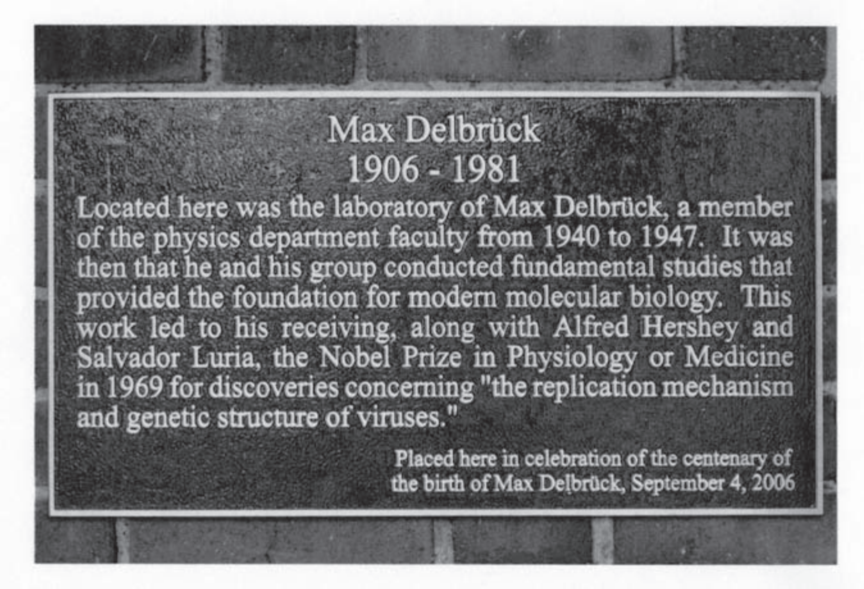
There is a new bronze plaque dedicated to Nobel laureate Max Delbrück on the campus of Vanderbilt University in Nashville, Tennessee. This plaque, on the third floor of Buttrick Hall, reads:

> Located here was the laboratory of Max Delbrück, a member of the physics department faculty from 1940 to 1947. It was then that he and his group conducted fundamental studies that provided the foundation for modern molecular biology. This work led to his receiving, along with Alfred Hershey and Salvador Luria, the Nobel Prize in Physiology or Medicine in 1969 for discoveries concerning "the replication mechanism and genetic structure of viruses."

Max Delbrück had the greatest influence of any physicist on biology in the 20th century, but the fundamental role that Vanderbilt played in his life and career has been largely overlooked by the scientific community. To help rectify this oversight, John Wikswo, the Gordon A. Cain University Professor at Vanderbilt, organized a centenary Delbrück symposium on September 14, 2006, and the university had the plaque created and installed.

Figure 22.1 Buttrick Hall on the Vanderbilt campus, where Max's laboratory in the Biology Department was located in room 330 (Courtesy Vanderbilt University Archives).



Max Delbrück
1906 - 1981

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Placed here in celebration of the centenary of
the birth of Max Delbrück, September 4, 2006

Figure 22.2 Plaque in Buttrick Hall (Courtesy Don Berry).

Around the time that Max got his doctoral degree in theoretical physics, the National Socialist Party came into power. Because university professors were state employees, this gave the Nazis control over university hiring. Although government officials allowed him to do university research they refused to give him the teaching license that he needed to qualify for a faculty position. Following the example of many other German scientists at the time, Max came to America to work. He applied for and received a grant from the Rockefeller Foundation to pursue his interest in biochemistry and genetics and to conduct research on the theory of mutations at the California Institute of Technology for a year, later extended for a second year. There, he completed the transition from theoretical physics to biology. This kept him in the U.S. until 1939 and the outbreak of World War II. Given the situation in Europe, he decided to stay in the U.S., but Caltech didn't have a place for him, so he asked the foundation for help in finding a job.

At about the same time, Vanderbilt wrote the Rockefeller Foundation saying that it would be interested in hiring one of the German scientists stranded in the U.S. The foundation suggested Delbrück, and Francis Slack, chairman of Vanderbilt's physics department, recognized that he would be a valuable addition to the faculty. On December 21, 1939, Slack telegraphed the university's offer of a position as instructor with a salary of $2,500 beginning "January 2 or [as] soon after as you can come," and Max responded via one of his classic postcards that he would arrive on January 1 (Lagemann 2000).

Max's own summary of his time at Vanderbilt, made thirty years later, nicely characterizes the particular circumstances of his position:

> I stayed at Vanderbilt seven and a half years, essentially without change in the arrangement, doing a fair amount of teaching in physics and doing phage research in biology. These were the formative years of the "phage group."

> My relations with Slack were on the whole cordial and peaceful. He tried to draw me over to physics as much as possible and I tried to withdraw to biology as much as possible. We appreciated and respected each other's attitude and got along all right (Delbrück Papers).

One of Max's initial assignments was teaching introductory physics to large numbers of students enrolled in the Army Specialized Training Program, and he was later to write that the U.S. seemed to be making every soldier take a physics course. In 1947, he taught Vanderbilt's first course on quantum mechanics. However, it soon became clear that his real talent lay in designing scientific experiments that produced unequivocal and often landmark results, and even during the height of the war his teaching load was reduced to less than half time.

Figure 22.3 223 Lauderdale Road, where Max and Manny lived from 1943-1947 (Courtesy John Wikswo).

In the small Buttrick lab, he continued the pioneering studies of viruses that attack bacteria (phages or bacteriophages) that he had begun in Pasadena. Max thought of phages as "the atoms of biology" and designed a series of simple experiments that measured the progress of phage attacks on bacteria. He began collaborating with Salvador Luria, who had a Rockefeller fellowship at Columbia University, and they conceived and conducted an experiment that demonstrated that bacteria contain genes. Their 1943 paper, "Mutations of Bacteria from Virus Sensitivity to Virus Resistance," has been cited as signaling the "birth of bacterial genetics" (Stent and Callendar 1971).

In 1943, Max and Luria teamed up with Alfred Hershey, a bacteriologist at Washington University in St. Louis, and began the collaboration that would eventually win them the Nobel Prize. During this time Max also developed the Phage Course, a laboratory course first taught to Vanderbilt students and then for many years as a summer course at Cold Spring Harbor Laboratory. Many of those who took the course became founders of the emerging field of molecular biology.

It was also around this time that Max first learned about Oswald Avery's discovery that DNA is the "transforming principle," or the transmitter of hereditary information, from Roy Avery, a faculty member in the Vanderbilt School of Medicine. Max recalled the occasion in an interview for Caltech's Oral History Project:

> Avery made his great discovery in 1943, but we knew about his working on this problem for at least a couple of years before then, and I think both Luria and I had gone to visit with him. . . . It had been shown that you could use an extract of one bacterium, and expose another bacterial strain to it, and then get some kind of transformation, and the transformation was expressed in producing a particular capsular polysaccharide. The feeling had been that the transforming agent was the polysaccharide itself,

> that somehow that was sort of a crystallization process, or rather, a nucleation process; you add a piece of this polysaccharide, and then more is produced; that was the obvious interpretation at the time. If that was true, then it showed that here you had a genetic property which was not transmitted by genes, but by something more like a whole organism, you might say like every little piece of polysaccharide was a little apple tree that could grow into a big apple tree; however, this little apple tree did not contain genes, but was just a form principle that had made it possible to accrete more in the same form – more like a crystallization process. If you dump into a saturated solution a crystal of a particular substance, then you can get more of that crystal; it's a nucleation process. And if that had been true, it would not have been so overwhelmingly interesting, because it was obvious that this could not be the general principle of genetics. So it came as a total shock and surprise when Avery and his associates discovered that the transforming principle was DNA. He communicated this discovery to his brother Roy Avery at Vanderbilt University, who was in the Department of Microbiology in the Medical School (not where I was, in the Biology Department), in a 17-page-long handwritten letter, which Roy Avery showed me just about the day he received it, and which I read there standing in his office in the spring sunshine, I think it was. It was quite an amazing letter ... (Delbrück 1979).

Max published twenty-five papers while at Vanderbilt and the value of his research was recognized at the time. For example, the university's 1942-43 annual report contains the statement "Another research of great importance is that conducted by Dr. Delbrück and his associates in the field of bacteriophage. This is probably the most important piece of research that has been carried on at Vanderbilt for some time. It has attracted national attention" (Lagemann 2000).

Max also gave a series of lectures at Vanderbilt's School of Medicine in April and May of 1944, called "Problems of Modern Biology in Relation to Atomic Physics." In the first lecture, he analyzed complementarity with wonderful clarity:

> On the other hand, chemistry and physics were able to retain a hold over biology by virtue of two great generalizations. Chemistry showed that living material is made up of the same elements as the materials of the inanimate world, and physics showed that conservation of energy is valid for processes occurring in living material just as it is for all processes in the inanimate world.
>
> . . . the distinction between the observing tool and the object of observation which we have to make at some arbitrary point necessitates a certain latitude in our description of the object. This situation, the analysis of which is due chiefly to Bohr and Heisenberg, has been termed "the principle of indeterminacy" by Heisenberg, and "the principle of complementariness" by Bohr (Delbrück 1944).

Much has been made of Delbrück's search for complementarity in biology, and some have wondered whether he was looking for new forces in physics. The Vanderbilt lectures put such speculations in an interesting perspective.

On the other hand, in the living cell we know that a great deal depends on very fine features of "structure". By "structure" we mean relevant inhomogeneities in the makeup of the cells. These relevant inhomogeneities go right down to the atomic scale. In order to gain knowledge of these details, sufficient to allow optimal quantum mechanical calculations, observations of such finesse as to blow the living cell to pieces would have to be made, just as, in order to locate the electron in an atom, we blow it out of its stationary state. According to this idea we may expect certain features of the living cell to be complementary to its description in terms of atomic physics. *To put it very crudely, we may find out where the atoms in a cell are, but in doing so we will kill the cell* [emphasis added]. We should be prepared, then, to find features of the living cell which are not reducible to atomic physics, just as we find features of the atom, viz., its stability, which are not reducible to mechanics.

This idea puts the relation between physics and biology on a new footing. Instead of aiming at the whole of the phenomena exhibited by the living cell we now expect to find natural limits and, thereby, implicitly, new virgin territories, on which laws may hold which are independent of those of physics, by virtue of the fact that they relate to phenomena whose appearance is conditioned on not making observations of the type needed for applying atomic physics.

Quantum mechanics, presumably, is self-limiting in its range of application to living cells due to a characteristic incompatibility feature. *Specifically it may be presumed that the maintenance of the living state is inherently incompatible with physical observations of*

> *a finesse requisite for complete application of quantum mechanics* [emphasis added] (Delbrück 1944).

The two sentences we have emphasized provide an important perspective for the interpretation of Max's search for complementarity – it was more closely related to the indeterminacy of measurement than the search for new forces. Hence the indeterminacy might result in phenomena that appear to defy explanation in terms of fundamental laws of physics, but largely in the sense that history cannot be described by the laws of physics. In the concluding lecture, Max summarized the state of biological research:

> The status of biology may be likened to that of physics around 1890. The separate branches of classical physics, i.e., mechanics, optics-electromagnetism, thermodynamics, seemed to have reached their final formulation. There seemed to be no hope of progressing further to an understanding of the structure of the atom. The discoveries of radioactivity, of X-rays, and of the electron, all in the 1890's, completely changed the situation. The partition between these branches, as well as that between physics and chemistry, was broken down, and the common basis of all, atomic physics, was rapidly constructed.
>
> Perhaps we are approaching a similar phase in biology. Genetics, embryology, biochemistry, and physiology may find a common root in a fundamental theory of the organization of the cell. It would seem that the principles of atomic physics will have a large share in the construction of this "modern biology" (Delbrück 1944).

The role of history in biology is clearly stated in his famous 1949 lecture “A physicist looks at biology”:

> . . . every biological phenomenon is essentially an historical one, one unique situation in the infinite total complex of life.
>
> If it be true that the essence of life is the accumulation of experience through the generations, then one may perhaps suspect that the key problem of biology, from the physicist’s point of view, is how living matter manages to record and perpetuate its experiences.
>
> . . . any living cell carries with it the experiences of a billion years of experimentation by its ancestors. You cannot expect to explain so wise an old bird in a few simple words.

The relationship between history, biology, and physics is worthy of intellectual exploration, as has already been done for physics and history (Porter 2004). From this perspective, it is interesting to note that observational astrophysics involves history in many of the same ways that biology does, although biology allows active experimentation with the historical record that is not possible at the galactic scale. The laws governing biology, however, are harder to discern and the history is richer, if only by the difference in the size of the vocabularies in which the history is transcribed. Max, with his early interests in astronomy, would have been intrigued by modern cosmology and astrophysics (J. Delbrück, personal communication), and at the least it would have been fascinating to argue these points with him.

This lecture provides an additional view into the historical tensions between the physical sciences and biology. While physics and chemistry provide the foundation for biology, they do not necessarily provide the best-suited vocabularies or grammars to describe biological phenomena. In Max's words,

> . . . physics and chemistry have a firm hold over biology by virtue of two great generalizations: living matter is made up of the same elements as those of the inanimate world, and conservation of energy is valid for processes occurring in living matter, just as it is for all processes in the inanimate world.
>
> The habits of animals and plants, their reproduction and development, their relations to their symbionts and to their enemies, can all be described and analysed with very little reference to the concepts of physics and chemistry.
>
> The root of this science lies in the existence of natural units of observation, the individual living organisms, which in genetics play somewhat the same role as the atoms and molecules in chemistry.
>
> Each process of observation has an individuality which cannot be broken down beyond a certain limit and different types of observation stand to each other in a mutually exclusive, complementary relationship (Delbrück 1949).

In many ways, the dichotomy between biology and the physical sciences can be resolved by viewing biological complexity as an emergent phenomenon that arises out of chemistry and physics, *i.e.,* biological systems exhibit properties not readily apparent in the laws and principles that describe the constituent components (Huang and Wikswo 2006). There are similarities with the historical evolution of chemistry out of physics – rather than await the first-principles understanding of molecular interactions based upon the quantum mechanics of many-body systems, chemists devised a vocabulary and grammar that allowed them to develop the field without a full description of the underlying physics. While chemistry can ultimately be reduced to fundamental physical interactions, it is often neither convenient nor efficient to do so, and a higher level of description provides the central insights to the field.

Max recognized this clearly. The view of Hermann von Helmholtz in the 1870s was that "the behavior of living cells should be accountable in terms of motions of molecules acting under certain fixed force laws." Delbrück's perspective:

> . . . if we tried to adhere to this ideal we could not even account for the behavior of a single hydrogen atom.
>
> Just as we find features of the atom, its stability, for instance, which are not reducible to mechanics, we may find features of the living cell which are not reducible to atomic physics but whose appearance stands in a complementary relationship to those of atomic physics.
>
> . . . the vista of the biochemist is one with an infinite horizon. And yet, this program of explaining the simple through the complex smacks suspiciously of the program of explaining atoms in terms of complex mechanical models (Delbrück 1949).

It would be fascinating to hear Max's views on the role of mathematical modeling in the attempt to devise a first-principles understanding of systems biology – models that might become so complex as to require a Leibnitz of partial differential equations (Huang and Wikswo 2006).

Of Max's performance as a teacher of physics at Vanderbilt there are few (and widely varying, from "indifferent" to "brilliant") reports (Lagemann 2000), but we get a glimpse of the sort of students he encountered and his relationships with them – not to mention excellent examples of his characteristic candor – from two letters of recommendation. The first was written on behalf of Joseph M. Reynolds, who in the spring of 1946 was applying for a position as graduate assistant in the Department of Physics at the University of Illinois:

> I have known Mr. Reynolds for two years. He took an advanced physics laboratory course and a course on selected problems in modern physics with me. These were very small classes permitting me to become well acquainted with his ability and personality. I also took him with me last summer to Cold Spring Harbor, Long Island, as technical assistant in research work on bacterial viruses.
>
> I would rank Mr. Reynolds second highest among the physics majors at Vanderbilt during the last six years. He is a slow but thorough and imaginative thinker. His weakness is an untidy and disorganized working habit. This derives from poor early training. He comes from a family with very narrow religious views, from which he has emancipated himself. I am confident that he will overcome this habit eventually.
>
> Mr. Reynolds' interest in physics is genuine, almost fanatic, but has not prevented him from becoming acquainted with other branches of learning. He has worked as technical assistant in chemical, biochemical, and bacteriological research. His mind is quite open to the interesting aspects of these and other lines

> of research but physics holds a special fascination for him, and I believe that it will continue to hold him for many years.
>
> I have not had an opportunity to judge his ability as a teacher, but I would assume that he will do well. He expresses himself clearly and interestingly and I think he will be very helpful to students because he loves to explain physics to any comer, willing or not (Delbrück Papers).

Here Max clearly captured the spirit as well as the academic talent of a young man who would fulfill his early promise. Mr. Reynolds went on to earn a doctorate in physics from Yale University in 1950 and served as a professor of physics at Louisiana State University until 1965, when he became Vice President for Graduate Studies and Research, the first of several positions of increasing responsibility, culminating in his term as Vice President for Academic Affairs from 1981-85. His research interests included low temperature physics, measuring gravitational waves, and superconductors (because of which one of us, JPW, had the pleasure of several conversations circa 1970 at Stanford long before JPW knew of Max or Vanderbilt). Among Reynolds's recognitions and honors were a Guggenheim Fellowship as a physics professor at the University of Leiden (1958-59), membership in Phi Kappa Phi and Omicron Delta Kappa, a post at Stanford University as visiting scholar (1969-70), appointment as a Boyd Professor in 1965 (LSU's highest honor for teaching faculty), and two consecutive presidential appointments to the National Science Board (1968-76). Max called this one correctly.

The second letter from Max is brief but equally candid, written for a medical school applicant:

> I have slight personal acquaintance with the candidate and had him as a student for a short time in an elementary physics class.
>
> Despite the fact that Mr. [X] seems endowed with great desire and enthusiasm to become a physician, I think that he will make only a mediocre medical student and doctor. His health and endurance may be good, but he is lacking in intellectual ability, leadership, and independence, and his use of English is poor. I am sorry that I cannot say more for him. Perhaps he would make a good veterinarian (Delbrück Papers).

We can only hope that Max's assessment of this student was mistaken, as he was accepted into medical school and practiced medicine (on human beings) for many years.

While living in Nashville, Max applied for naturalization. His first attempt failed (putting the university's Board of Trust in the awkward position of having to table an action for promotion to assistant professor). On his second appearance before the federal district court, he was accompanied by the head of the physics department and an attorney and in 1945 he was granted both American citizenship and promotion in faculty rank. In a letter of February 8, 1945 to Vanderbilt Chancellor Oliver C. Carmichael regarding the latter action Max wrote, "I also wish to thank you for your kind congratulations on my attainment of American Citizenship. Permit me to say that I count the years during which I have been connected with Vanderbilt University among my happiest and most fruitful. The liberal attitude of my chiefs, particularly of the late Dr. Reinke [head of the Department of Biology], has permitted me to devote a great deal of energy to the work in which I am interested. I realize that I was fortunate indeed to be able to continue my work during the war, notwithstanding my status as an alien" (Delbrück Papers).

Figure 22.4 Max in Nashville in 1940 (Courtesy Jonathan Delbrück).

As appreciation of his accomplishments spread, Max began getting offers from other universities, including Carnegie Institution of Washington and the University of Manchester, both of which had started active phage research programs. As late as 1945, Max told colleagues that he was happy at Vanderbilt and had no desire to leave as long as he could continue his research. To do so, however, he felt that he needed upgraded lab facilities and additional assistants and faculty colleagues. So he approached the administration with the proposal to establish a separate institute for studying phage at the cost of $500,000. According to a rough calculation of the comparable buying power of this sum sixty years later (in the neighborhood of $5 million), Max's request was not unreasonable and came very close to the start-up costs for a senior research scientist. But for a cash-strapped university in the post-war period, raising such funds would have been next to impossible. As a result, when Caltech offered him a professorship in biology in December 1946, Max resigned from his tenured position as an associate professor of physics at Vanderbilt and returned to Pasadena where, just 10 years before, he had embarked on the research direction that had proven so successful. After moving to Caltech, where he remained until he retired, his research interests quickly moved away from the phage studies that he perfected while at Vanderbilt and for which he received the Nobel Prize.

In the book *To Quarks and Quasars: A History of Physics and Astronomy at Vanderbilt University*, Robert Lagemann raises the issue of Vanderbilt's loss:

Both inside and outside the university, one occasionally hears the question: "Why did Vanderbilt not do more to keep this future Nobel Prize winner?" No regular faculty position existed at Vanderbilt that could accommodate Delbrück in 1947. The Physics-Astronomy Department was about to initiate its new Ph.D. program, and Max would not have cared to direct student thesis research in physics. In the Biology Department he could direct theses with consummate success, but he could not be expected to teach undergraduate classes in botany, zoology, or bacteriology, fields in which he possessed no formal credentials or comprehensive knowledge. He might have found a niche in the Medical School, but those were before the days of extensive federal support of research in medicine, and considerable teaching was required of every faculty member. In the face of the financial constraints of the postwar period, Vanderbilt could not go all out to create a suitable position for him or provide a laboratory and supporting staff that would allow a full use of his recognized talents. And of course no one at that time could have predicted that he would be awarded a Nobel Prize twenty-two years later (Lagemann 2000).

And assuredly the faculty of the Physics Department felt that Max's departure was lamentable. Entered in the department's annual report of 1946-47 is an item headed "RESIGNATION OF DR. MAX DELBRUCK":

We are very regretful that Dr. Max Delbruck has decided to accept a position as professor of Biology at California Institute of Technology. Dr. Delbruck will terminate his connection with Vanderbilt University at the end of this present quarter and he plans to spend a portion of the summer in travel in Europe and return to California in September. We feel that Vanderbilt University will suffer a very great loss and that this loss will be felt not only by the Physics Department, but by all of the Science Division. Dr. Delbruck's successful researches at Vanderbilt University are attested by his large number of publications and by the wide recognition that he has received throughout this country and abroad.

It is certain that we will not be able to replace Dr. Delbruck at this time by a man as capable as he. We should hold open the possibility of employing at any time it may become possible any scientist who shows promise of work such as that which Dr. Delbruck has performed (Vanderbilt Physics Department Report 1947).

Thirty years after leaving Vanderbilt Max recalled this period of his life in a letter quoted in T*hinking About Science:* "Here I had the opportunity to develop my talents quietly while others were concerned with the war." And, as Fischer and Lipson add, "With Luria's participation, molecular genetics was spawned in the secluded American South" (Fischer and Lipson 1988). All in all, a worthy role for Vanderbilt to have played, and one that it is proud to acknowledge at the centenary of Max's birth.

We can now bring the history of Max at Vanderbilt full circle. The Department of Physics became the Department of Physics and Astronomy. After Max's departure, the department maintained a faculty line in biophysics and another in medical physics, albeit without Max's notable impact on the field. The university continued to grow its research and teaching programs in what has since become known nationally as "biological physics" and has built an outstanding medical enterprise with excellent connections to the department.

While the department was aware of Max's contributions at Vanderbilt through the writings of Robert Lagemann (2000), it was Erwin Schrödinger's book *What is Life?,* first published in 1946, that reinstituted Max into the Vanderbilt curriculum. Every year or two from 1998 to the present, one of us (JPW) has taught an honors seminar entitled *What is Life?* to undergraduates in the College of Arts and Science and the School of Engineering. The seminar begins with a critical reading of Schrödinger's book, followed by Gunther Stent's and R. Callendar's *Molecular Genetics,* and the 1970 edition of Jim Watson's *The Double Helix,* and finally Freeman Dyson's *Origins of Life* (1990), accompanied throughout by the relevant literature and commentaries on these works. Students in the seminar, many of whom are humanities majors, have the thrill of discovering on their own errors by Schrödinger, such as the number of human chromosomes (46 not 48) and "negative entropy," and observing the role of creativity and genius in science. Max's role is summarized succinctly by Max Perutz:

> . . . a close study of his [Schrödinger's] book *[What is Life?]* and of the related literature has shown me that what was true in his book was not original, and most of what was original was known not to be true even when it was written (Perutz 1987).

As always, Max provided the truth, and continues to inspire another generation of students in the sciences and humanities.

Acknowledgements

We are indebted to Jonathan Delbrück for his friendship and guidance, Gunther Stent for his writings and conversations, and the many people who made possible Vanderbilt's celebration of Max's centennial.

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