13. HANS-JÖRG RHEINBERGER

Experimental Systems, Graphematic Spaces

In recent years, it has become fashionable among historians and philosophers of science to turn their attention to the field of experimentation. We are witnessing, after the Kuhnian move from continuity and verity of scientific knowledge to discontinuity and relativity, another turn—from the Kuhnian predilection for science as theory to post-Kuhnian engagement with science as experiment. A philosophical landmark in this move has been Ian Hacking's *Representing and Intervening*. Hacking reminded philosophers of science that experiments have a "life of their own."[1] Historian of science Peter Galison[2] has taken up this challenge and argued for "a history of experimentation that accords that activity the same depth of structure, quirks, breaks, continuities, and traditions that we have come to expect from theory."[3]

A growing history and philosophy of science industry today is carrying on that move and amalgamating it with what has come to be labeled "Science as Practice and Culture."[4] "Social construction of science" has become a shibboleth for those wishing to be members of the club. Actors, interests, politics, power, and authority have acquired the status of key terms in a "strong program" to treat science on a par with any other cultural activity whatsoever. That Thomas Kuhn is "among those who have found the claims of the strong program absurd: an example of deconstruction gone mad,"[5] might not surprise, and might perhaps be put aside as a matter of taste. From a fundamental epistemological point of view, it is Bruno Latour who most explicitly and most radically has called attention to an impasse of "science and society" studies from which there seems to be no easy escape.[6] To put it crudely: What do we gain by

substituting "social conditions" for what has been taken as "natural conditions" of scientific activity?[7] If, in the perspective of social construction, we have lost the illusion of an ultimate reference called "nature," what do we gain by trying to compensate for this loss with the mirror image of "society" as a new and insurmountable reference? From where do we hope to derive its epistemic legitimacy? With the tetragonic opposition of theory and practice, nature and society, we remain, despite all rotation of competences, within the confines of a conceptual framework that Jacques Derrida without doubt would qualify as the logocentric legacy of occidental metaphysics.[8]

This essay does not claim to transcend these confines with an encompassing gesture. Its purpose is more humble and modest. It sticks to the Derridean program of reworking such oppositions *from within*, of trying to render their limits different/deferent. It starts, therefore, from the more narrowly conceived Hacking and Galison move from theory to experiment within the realm of scientific activity and develops a framework in which experimentation takes on meaning as a set of specific kinds of *epistemic practices*. Nevertheless, this essay is ambitious: it tries to characterize those structures as hybrids that are recalcitrant to classification in either realm, the natural or the social, the theoretical or the practical.

Experimental reasoning, then? Even this expression can easily be misunderstood. Its grammatical structure presupposes reasoning as the *genus proximum*, whose specific difference is to be guided by experiment. What is at stake, however, is just the opposite. It is a kind of movement oriented and reoriented by generating its own boundary conditions, *in* which reasoning is swept off by tracing, a game of material entities. Gaston Bachelard has spoken of instruments as "theories materialized"[9] and has concluded: "Contemporary science thinks with/in its apparatuses."[10] And he has spoken about a "scientific real (*le réel scientifique*) whose noumenal contexture it is to be able to orient the axes of the experimental movement."[11] In analogy to Wittgenstein's well-known expression, we could call this a *tracing-game*. Wittgenstein says: "I shall also call the whole, consisting of language and the actions into which it is woven, the 'language-game.' " And he continues: "Our mistake is to look for an explanation where we ought to look at what happens as a 'protophenomenon.' That is, where we ought to have said: *this language game is played*."[12] We are never able to get behind this weaving. Thus, I am not looking for a "logic" in the relationship *between* theory and experiment, or for a "logic" *behind* experiment. Rather, I am grappling with what must be seen, irre-

ducibly, as the *experimental situation*: in this situation, there are scientific objects and the technical conditions of their existence, differential reproduction of experimental systems, conjunctures of such systems, and graphematic representations. All of these are notions related to the practical process of producing what I shall call "epistemic things."

Briefly, I argue along the following lines: First, *experimental systems*[13] are the working units a scientist or a group of scientists deals with. They are simultaneously local, social, institutional, technical, instrumental, and above all, *epistemic* units. My approach is biased towards this last aspect.[14]

Second, such systems must be capable of *differential reproduction* in order to behave as a device for producing epistemic things whose possibility is beyond our present knowledge, that is, to behave as a "generator of surprises."[15] "Differential reproduction" refers to the allowance, if not to the necessity of shifts and displacements within the investigative process; in order to be productive, an experimental system has to be organized so that the generation of differences becomes the reproductive driving force of the whole experimental machinery.

Third, experimental systems are the units within which the signifiers of science are generated. They display their dynamics in a *space of representation* in which graphemes, material traces, are produced, are articulated and disconnected, and are placed, displaced, and replaced. Science "thinks" within its spaces of representation, within the hybrid context of the available experimental systems. Graphemes are to be understood as the primary, material, significant units of the experimental game, and at the same time, the units of reference. At the bench, the experimental scientist engraves traces into a material space of representation; more precisely, the scientist creates a space of representation through graphematic concatenations that represent the epistemic thing as a kind of "writing." All this is to be understood as a preliminary step toward a history of *epistemic things*.[16] "There is a history of science, not only of scientists, and there is a *history of things*, not only of science."[17]

In order to exemplify my points, I shall draw upon some episodes in the experimental history of the construction of an *in vitro* system for protein biosynthesis.

A Future-Making Machine

What do I mean by the notion of "experimental system"? Traditionally, in philosophy of science, an experiment is seen as a singular instance, as a

dramatized trial (*tribunal en scène*) organized and performed in order to corroborate or refute theories.[18] Quite some time ago, Ludwik Fleck drew our attention to scientific—especially biomedical—research practice and argued that, in contrast to what philosophers of science might assume, the experimentalist does not deal with single experiments. "Every experimental scientist knows just how little a single experiment can prove or convince. To establish proof, an entire system of experiments and controls is needed."[19] According to Fleck, in research we do not have to deal with single experiments in relation to a clearly defined theory, but with a complex experimental arrangement designed to produce knowledge that we do not yet have. Even more important, we deal with systems of experiments that usually do not provide clear answers. "If a research experiment were well defined, it would be altogether unnecessary to perform it. For the experimental arrangements to be well defined, the outcome must be known in advance; otherwise the procedure cannot be limited and purposeful."[20]

Like Fleck, I consider an experimental system to be a unit of research, designed to give answers to questions we are not yet able to ask clearly. In the typical case, it is, as François Jacob has put it, "a machine for making the future."[21] It is a device that not only generates answers; at the same time, and as a prerequisite, it shapes the questions to be answered. An experimental system is a device to materialize questions. It cogenerates, so to speak, the phenomena or material entities and the concepts they come to embody. A single experiment as a sharp test of a properly delineated conception is not the simple, elementary unit of experimental science, but rather the *degeneration* of an elementarily complex situation.[22]

One of the first in vitro systems of protein biosynthesis constructed from components of a rat liver cell sap may provide an illustration for an experimental system. In its outlines, it was established between 1947 and 1952 at the Collis P. Huntington Memorial Hospital of Harvard University at the Massachusetts General Hospital, in the laboratory of Paul Zamecnik. In 1947, the Harvard group had set out to look at growth deregulation in malignant tissue—a classical biomedical research project in a hospital that, under the directorship of Joseph Aub, had long been devoted to cancer research. Because growth could be assumed to be closely related to the making of proteins, protein biosynthesis was one of the possible targets of the neoplastic behavior of cancer cells. Little was known about the factors involved in carcinogenesis at that time. So Zamecnik decided not to consider "a single avenue of biochemical study,"

but rather to start with a "practical" approach and "take advantage of whatever new opportunities became available, in the hope that a definite clue turned up in any corner of the field."[23]

The "practical approach" consisted in the introduction of radioactive carbon-labeled amino acids as "tracers" for following the incorporation of amino acids into proteins. They were synthesized by Robert Loftfield, who then was a research associate at the Radioactivity Center of MIT.[24] Loftfield had succeeded in producing carbon-labeled alanine and glycine in amounts suitable for biochemical research. What a few years later proved to be one of the most potent technical tools for tracing protein metabolism was itself part of the research program at the beginning. At the outset, it was not at all clear which one of the different amino acids should be used for the incorporation reaction, and what should be done in order to circumvent the possible tracing of metabolic processes other than protein synthesis because of the prior metabolism of amino acids. Workers in the field were confronted with—and indeed constantly haunted by—the possibility that what they observed as "uptake" or "incorporation" of radioactive amino acids might turn out to be a side reaction with respect to the protein synthetic activity within the cell. But how proteins were made there was precisely the unknown process. Because usually no more than 1 percent of the radioactivity added to the system became "incorporated," there was not only a realistic chance of some bonding other than regular alpha-peptide bonding—known to be characteristic for proteins—but also the possibility of a rather unspecific "adsorption." Not only was it unclear what "uptake" or "incorporation" of radioactivity meant, uncertainty also remained for years as to whether the same process was being observed in different experimental systems aiming at protein synthesis and derived from different tissues.[25]

Uncertainty was also a given with respect to the choice of the specific experimental system itself. Should one stick to injecting radioactive amino acids into living animals, thus taking advantage of their regular metabolic turnover? This rendered the measurements difficult, and it required lots of radioactive material. Should one try to avoid these shortcomings and work with liver slices in the test tube? But this could cause metabolic distortions of an unknown order of magnitude. Should one work with so-called "model systems" involving proteolytic enzymes? This implied a theoretical assumption—protein synthesis as a reversal of proteolysis—that was current, but by no means substantiated. Should one try to homogenate the tissue or even take the cell sap apart by means of

differential centrifugation? This promised to identify the components involved in the process, but a cell homogenate was qualified "at present to be a biochemical bog in which much effort is being expended to reach firm ground."[26]

If we take a closer look at the laboratory process between 1947 and 1951, we see that all of these possibilities were explored, that this exploration was centered around the use of radioactive tracing, and that initially it was organized from what could be called a "significant difference." The significant difference was that malignant tissue appeared to take up considerably more radioactivity than did normal tissue. But experimentally this difference turned out to be silent, for it did not tell what to do next. Above all, it did not tell which of the systemic alternatives should be pursued. In this situation, a differential signal, quite surprisingly, came from a control. A particular substance called dinitrophenol (DNP), which Fritz Lipmann had found to inhibit the process of phosphorylation,[27] inhibited the "incorporation" of radioactivity in the rat liver-slice system, too.[28] This could mean that phosphorylated compounds like adenosine triphosphate (ATP) might be involved in protein synthesis. That initiated a change in the research perspective. The medical point of view gradually became replaced by a biochemical perspective. To find out whether a high-energy intermediate was involved in protein synthesis was no longer a question of the differential behavior of normal and malignant tissue. The DNP event also clarified the options. In order to get the system on the biochemical track, the cells had to be homogenized. Conditions had to be found under which the protein synthesis activity could be checked against compounds such as ATP or similar phosphorylated substances. The technical objective at this point became to separate the cellular components in such a way that the cellular compartments *producing* energized compounds could be distinguished from the cellular structures that *used* them.

The "Logic" of the Process

A scientific object or epistemic perspective in the framework of such an experimental system is as inherently open as the system itself with respect to its technical potentials. An epistemic thing may not even be imagined when an experimental arrangement is in the course of being established. But once a surprising result has emerged and has been sufficiently stabilized, it is difficult to avoid the illusion of a logic of thought and even a teleology of the experimental process. "How does one re-create a

thought centered on a tiny fragment of the universe, on a 'system' one turns over and over to view from every angle? How, above all, does one recapture the sense of a maze with no way out, the incessant quest for a solution, without referring to what later proved to be *the* solution in all its dazzling obviousness?"[29] An experimental system can be compared to a labyrinth whose walls, in the course of being erected, simultaneously blind and guide the experimenter. The construction principle of a labyrinth consists in that the existing walls limit the space and the direction of the walls to be added. It cannot be planned. It forces one to move by means of checking out, of groping, of *tâtonnement*.[30]

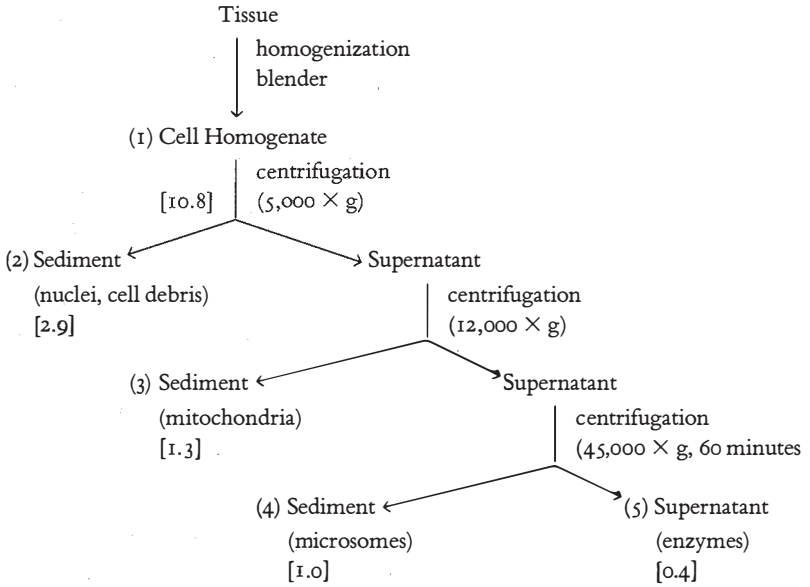
The coherence over time of an experimental system is granted by the reproduction of its components. The development of such a system depends upon eliciting differences without destroying its reproductive coherence. Together, this makes up its differential reproduction. The articulation, dislocation, and reorientation of an experimental system appears to be governed by a kind of movement that has been described as a play of possibilities (*jeu des possibles*).[31] With Derrida, we might also speak of a "game" of difference.[32] It is precisely the characteristic of "fall(ing) prey to its own work" that brings the scientific enterprise to what Derrida calls "the enterprise of deconstruction."[33] On the part of the experimenter, it requires acquired intuition (*Erfahrenheit*) in order to play the game.[34] Experiencedness is not experience. Experience is an intellectual quality; experiencedness is a form of practice.

I would like to add a few remarks with respect to the differential reproduction of experimental systems. The first is that one never knows exactly where it leads. As soon as one knows exactly what it produces, it is no longer a research system. An experimental system in which a scientific object gathers contours and becomes stabilized, at the same time must open windows for the emergence of unprecedented events. While becoming stabilized in a certain respect, it must be destabilized in another. For arriving at new "results," the system *must* be destabilized—and without a previously stabilized system there will be no "results." Stabilization and destabilization imply each other. If a system becomes too rigid, it is no longer a machine for making the future; it becomes a testing device, in the sense of producing standards or replicas. It loses its function as a research tool. It may, however, be integrated as a stable subsystem into another, still growing experimental system, and help to produce unprecedented events within a larger field. This transformation of former research systems into stable, technical subsystems of other research arrangements is

what confers its own kind of material information storage on the process of experimentation. But by the same mechanism, it generates a historical burden. Most new objects, therefore, are first shaped by old tools. On the other hand, scientific objects are continually transformed into technical devices, and in the long run become replaced by devices that embody the current, stabilized knowledge in a more suitable way. The historian of science usually looks at a "museum of abandoned systems."

In order to remain a research system, therefore, such machinery must be operated differentially. If it is organized in a way such that the production of differences becomes the organizing principle of its reproduction, it can be said to be governed by or to create that kind of subversive and displacing movement Jacques Derrida has called the "differance."[35] "Differance" operates at the basis of what has become known as deconstructions, as Derrida prefers to say in the plural: "a certain dislocation which repeats itself regularly . . . in every 'text,' in the general sense I would like to attach to that name, that is, in experience as such, in social, historical, economic; technical, military reality."[36]

How differential reproduction operates on the level of experimental systems can be seen if we pursue the work of the Huntington protein synthesis group. Besides radioactive tracing, a new technique of representation was introduced at the time of the DNP-induced reorientation. After mechanical disintegration of the liver tissue, the resulting cell sap was differentially fractionated by means of a laboratory centrifuge. Differential centrifugation of liver-cell homogenates was not in itself a new endeavor.[37] The problem was that the whole fractionation process only made sense if the "incorporation" activity that had been observed in the experiments with animals and with tissue slices could be preserved while the shape of the system was completely changed from in vivo to in vitro. It does not come as a surprise, therefore, that the first detailed report about such a fractionated incorporation system appeared only in 1952.[38] This report is remarkable in several respects. It reflects how, in the process of the establishment of a cell-free protein synthesis system, the background complexity alluded to as "biochemical bog" was dealt with. At that critical stage, the fractionated incorporation signal still was too "dirty" to be unequivocal, but already sufficiently "clean" to produce some counts that allowed one to regard the fractionated system as a successor to the previous in vivo studies. On the other hand, the experiments yielded no new information with respect to the energy dependence of the process at issue. There was an answer, but again, it was not an answer to the question that



Reconstituted activity:

mitochondria + microsomes	4.2
mitochondria + enzymes	6.6
mitochondria + microsomes + enzymes	9.8
all fractions	10.5

Figure 13.1. Fractionation diagram. The numbers give the activity of the fractions in counts per minute [cpm] per milligram of protein. Reconstructed from Philip Siekevitz, "Uptake of Radioactive Alanine in Vitro into the Proteins of Rat Liver Fractions," *Journal of Biological Chemistry* 195 (1952): 549–65.

had been the driving force for "going in vitro." The essential point was that the crudely structured partition of the cell sap created an interface between two techniques of representation: that of radioactive tracing, and that of differential centrifugation of the cytoplasm, metabolic function, and topology.

In Figure 13.1, we see how representational devices and scientific objects are, to use the words of Michael Lynch and Steve Woolgar, "inextricably interconnected."[39] The content of the liver cells was unpacked into different fractions. The fractions were operationally defined in terms of different centrifugal forces by means of which lighter and heavier components could be separated. Some of the fractions *contained* cellular

components that could be identified by microscopic inspection (nuclei, mitochondria)—yet another layer of representation. This did not mean, however, that the fractions were defined by these components. Rather, the centrifugation velocity determined the fractions, and the partition in turn determined the provisional structure of the scientific object. Soon, the language in which the experimental handling of protein synthesis was captured also came to reflect the intimate packing of technical conditions and scientific object. The laboratory began to speak of protein synthesis in terms of centrifugal velocities and of sedimentation properties. So, "45,000 × g supernatants," and "12,000 × g sediments" appeared. These entities represented a new kind of experimental reasoning.

Another interesting aspect of this early fractionation work is the establishment of meticulous procedures for washing, isolation, and identification of radioactive protein. They were to ensure that the radioactivity that could be recovered from the samples was indeed "incorporated" via peptide bonds. These procedures provided, on the one hand, a framework for sorting out one specific metabolic event: peptide-bond formation. But on the other hand, they did not simply filter this single metabolic event out of a tremendous background of "contamination." They were nontrivial conditions—not merely to be granted in order to obtain "reproducible" results. They interfered with the metabolic signals of the experimental system: they destroyed what was "not wanted," and worse, prevented access to things unknown and beyond the actual scope of investigation. To make the formation of stable peptide bonds a "hard fact" meant to do away with any labile amino acid-bonding to other substances. The rigorous procedures for product analysis deemed necessary in order to ensure the identity of the scientific object in its product form prevented access to the conditions of its formation. The assumption underlying the construction of an in vitro protein synthesis system—namely, that the "incorporation" of amino acids had to be accounted for in terms of alpha-peptide bond formation—took the form of a destruction of everything else that was not alpha-peptide bonding.

These experiments provided a first glimpse of a *reconstituted* amino acid incorporation activity. None of the fractions was fully active per se; but when they were recombined, the initial activity of the homogenate was restored. On the other hand, this was the only unequivocal result. None of the main fractions could definitely be sorted out in order to narrow down the synthetic activity. Especially, there was no hint that the mitochondria might be dispensed with; on the contrary. The fraction in which they were

predominantly gathered did stimulate the incorporation process. Notwithstanding, the whole system worked only if external energy resources were added. However, ATP as such a resource failed to do this job. And finally, the reconstitution signal itself was on the borderline of resolution. What, then, had been achieved? The centrifugal representation did not destroy any essential component required for the incorporation reaction. The promise was nothing else than the further differential reproduction of the system. Two events, one small, one big, became crucial for the next round of affairs: a modified homogenization method,[40] and a higher fractional resolution by the introduction of an ultracentrifuge.[41]

Along the way, the research problem of the first period had silently disappeared from the scene: the work was no longer directed toward the metabolism of cancer cells. The other research problem had become transformed into a powerful technological device: the incorporation of radioactive amino acids into protein was now fairly well established. And although the search for the role of ATP had not led to any appreciable results with respect to that question, it had led to a readily manipulable fractional representation of the liver cell—to chopping it into several components necessary for the amino acid incorporation reaction.

Graphematic Spaces

Given a research system, and given its formal dynamics as a machine for making the future, how does it organize what I have called, preliminarily, the "tracing-game"? This is a question of representation.[42] What does representation mean? If we speak of tracing, are we allowed to speak of representation at all? After all, the term *representation* implies the existence of a reference. But if we conceive of a scientific object investigated through an experimental system as deployed and articulated within a space of material representation—such as radioactive tracing and centrifugal fractionation—the traditional meaning of "representation" is erased.

We certainly miss the specificity of the procedure if we consider representation simply as a "theoretical" reflection of some kind of "reality." In the research process, what goes on *practically* and on a primary level is the articulation of traces with the help of technical devices that can themselves be considered and manipulated as sufficiently stable embodiments of concepts or theories. Trace-articulations are what I call epistemic things. Once stabilized, they can be transformed into technical devices that allow researchers to produce new research objects. They

become implemented into the process of realizing further unprecedented events.

Representation: What goes on when the experimentalist produces a chromatogram, a protein sequence, an array of tubes, to which pieces of filter paper are correlated, on which, in turn, counts per minute of radioactive decay are superimposed? All these epistemic procedures are the objects of an ongoing process of materialized interpretation. They represent certain aspects of the scientific object in a form that is manipulable in the laboratory. The arrangement of these graphematic traces or graphemes and the possibility of their being articulated in a particular space of representation constitute the experimental "writing-game." Out of these units the experimenter composes what he calls his "model."

What is the status of graphematic articulations? A polyacrylamide gel in a biochemical laboratory, for instance, is an analytical tool to separate macromolecules; at the same time, it is a graphematic display of compounds visualized as stained, fluorescent, absorbent, or radioactive spots. The represented scientific object, the embodied model, then is compared to other models, to other representations. Thus, the comparison definitely does not take place between "nature" and its "model," but rather between the different graphematic traces that can be produced within particular spaces of representation. It is *their* matching, not the match between representation and nature, that gives us the sense of "reality" we ascribe to the scientific object under study.[43] The "scientific real" is a world of traces. Bruno Latour and Steve Woolgar have distinguished between machines that "transform matter between one state and another," and apparatuses or "inscription devices" that "transform pieces of matter into written documents."[44] This separation often fails to be drawn in a clearcut manner. What is a polyacrylamide gel? It transforms matter—it separates molecules—and it produces an inscription—blue spots, for instance, on its vertical axis. We have to go a step further and look at the ensemble of the experimental arrangement, including both types of machines, as a graphematic activity. A written table or a printed curve then is only the last step in a series of transformations of a previous graphematic disposition of pieces of matter, which is given by the experimental arrangement itself.

The production of "inscriptions" is neither an arbitrary process in which anything goes, nor is it completely determined by the technical conditions and the instrumental equipment of the respective system. In the differential reproduction of experimental systems there is a permanent

"game of presentation/absentation" going on. For every grapheme is the suppression of another one. Trying to show or enhance a particular trace inevitably means trying to suppress another one. It is as in a game with wedges. If you drive in one, you drive out the other. In an ongoing research endeavor one usually does not know which of the possible traces should be suppressed and which should be made more prominent. So, at least for shorter spans of time, the game of presentation/absentation has to be conducted as reversibly as possible. In other words, the epistemic thing must be allowed to oscillate between different interpretations/realizations.

Experimental systems create spaces of representation for things that otherwise cannot be grasped as scientific objects. A biochemical representation in particular creates an extracellular space for processes assumed to run in the cell under regular conditions. The laboratory language speaks of model reactions here. Models of what? Models of what is going on "out there in nature." Thus, "in vitro systems" would be models for "in vivo situations." But what goes on "within the cell"? The only way to know it is to have a model for it. Thus, "nature itself" only becomes "real," in scientific and technical perspective, as a model. And so in vivo experiments, too, are model systems. In an in vitro system, any intact cell behaves, as Zamecnik once said, as a "whole cell artifact."[45] Paradoxically we are faced with the notion of a natural artifact. There is no external and final point of reference for anything that becomes involved in the game of scientific representation. The necessity of representation *as* intervention implies that any possibility of immediate evidence is foreclosed.

What, then, do scientists do *practically* when engaged in the production of epistemic things? They continuously subvert the opposition between representation in the traditional sense of the word and reality, between model and nature. They treat their scientific objects not as representations *of* something behind, but *as* epistemic things within their system. Thus, they treat representation not as something of another order, not as the condition of the possibility of knowing things, but as the condition of the possibility of things becoming epistemic things. Furthermore, they practice representation as repeated bringing forth; and they represent in the sense of a repetition, an iterative act. Any intervention in the sense of a scientific representation is a reproduction. Nature cannot be an external reference for this activity. It is experimental nature only insofar as it is *always already* representation, insofar as it is always already an element, however marginal, of the game. With that representation is

always already the representation of a representation. As Hacking puts it, the real, as a problem, comes into existence "as an attribute of representations."[46] The same goes for the model. The model is part of what is modeled, and what is modeled itself is always already a model. Jean Baudrillard speaks of a "precession of the model": "Facts no longer have any trajectory of their own, they arise at the intersection of the models."[47] Instead of conceiving the epistemic activity of representing or modeling as an asymmetric relation, we should consider it to be symmetric: both terms of the relation are representations or models of each other.[48]

I will try to exemplify this with another episode from the history of the in vitro protein synthesis system. The episode refers to the "microsomal fraction" of that system. In 1952, it was considered to stimulate the incorporation reaction. Two years later, it had acquired the status of one of the essential fractions. In order to sediment this material quantitatively, the cell homogenate had to be centrifuged at high speed and for a longer time. This could not be done until an ultracentifuge had become available at the Huntington Laboratories in 1953, and it would have made no sense to do before it had become possible to obtain more active homogenates.[49]

In order to examine this high-speed sediment with respect to its particulate appearance, another technique of representation had to be introduced into the system: the electron microscope. The untreated cytoplasmic fraction looked heterogeneous and appeared to be composed of large, irregular chunks of intracellular membrane vesicles, and small electron-dense particles of a somewhat more regular size. Using deoxycholate as a detergent,[50] the membrane vesicles obviously dissolved and the electron-dense particles could be recovered from a 105,000 × g sedimentation run (see Fig. 13.2). These particles, although still varying in size, exhibited an average diameter of about twenty nanometers, and their RNA to protein content was nearly equivalent, whereas in the original microsome fraction the respective ratio was approximately 1:8. This sounds quite straightforward, yet there were, once again, nontrivial difficulties with the technique of representation: what was recovered from the detergent-insoluble sediment in terms of RNA-rich "ribonucleoprotein," in its RNA/protein composition largely depended upon the concentration of the solubilizer. So the representation, or "definition" of the particle was a matter of the preparative operations performed on it, and because the solubilization procedure brought all subsequent incorporation activity in the test tube to a halt, there was no representational correlate to the preparative, operational definition in terms of biochemical function.

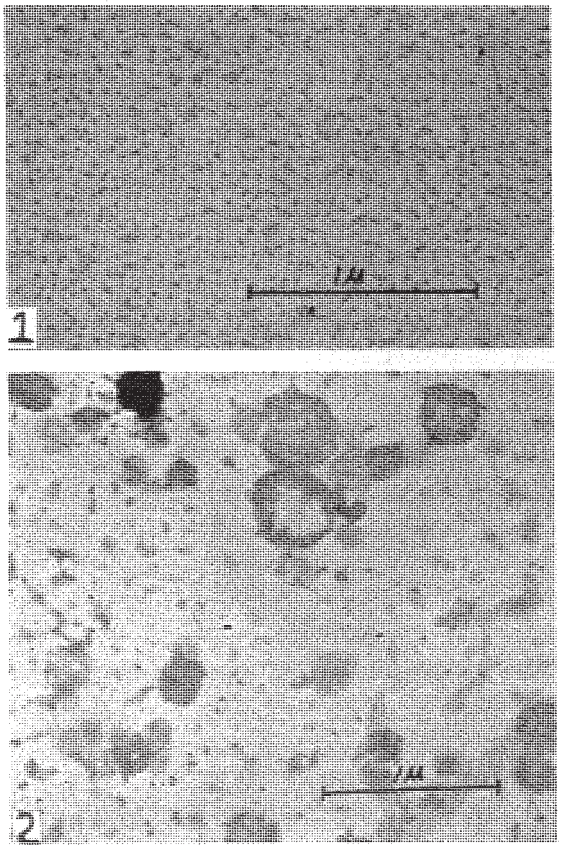


Figure 13.2. Electron micrographs of microsome fractions: (1) micrograph of deoxycholate-insoluble particles from a microsome fraction, magnification 45,900 ×; (2) micrograph of an untreated microsome fraction, magnification 35,200 ×. Reproduced from John W. Littlefield, Elizabeth B. Keller, Jerome Gross, and Paul C. Zamecnik, "Studies on Cytoplasmic Ribonucleoprotein Particles from the Liver of the Rat," *Journal of Biological Chemistry* 217 (1955): 111–23.

In this situation, alternative spaces of representation had to be opened in order to "stabilize" the particle by way of a triangulation or calibration procedure.

One of these representations operated on size and shape. Because the particles had a dimension of only some twenty nanometers, the procedure was bound to the use of electron microscopic visualization. Yet the use of

this technique brought with it serious operational problems of another order: that of specimen preparation for inspection. Because electron microscopy is based on the physical interaction of an electron beam with the object to be visualized, the specimen is prone both to destruction by the beam and/or to deformation by the addition of electron-dense heavy metal solutions used to "stain" and fix the biological material. Because of preparation differences, Zamecnik's particles measured between 19 and 33 nanometers, quite a considerable variation, whereas Palade's osmium-treated particles were only 10 to 15 nanometers in diameter.[51] Were the particles homogenous and small, or were they heterogenous and larger? The problem could not be solved within the representational space of electron microscopy.

A further technique of representation brought into play was the sedimentation pattern and sedimentation coefficient of the particles derived and calculated from analytical ultracentrifugation. Zamecnik's particles appeared as a major "47S peak" in the optical record (see Fig. 13.3). This peak resembled the main macromolecular component already described for rat liver by Mary Petermann and her coworkers.[52] A broader peak running ahead of the 47S particle disappeared upon treatment of the material with 0.5 percent of the detergent. But there was also a smaller peak running behind the 47S particle, which did not disappear upon the

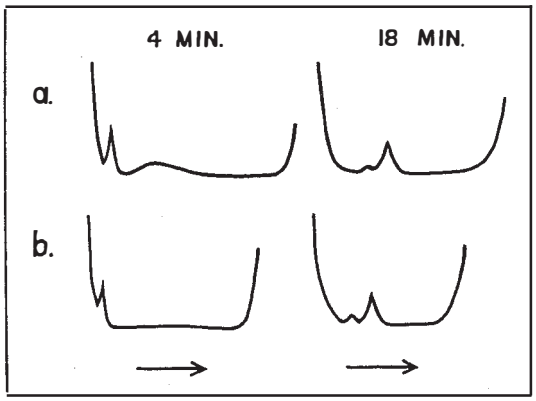


Figure 13.3. Ultracentrifugal analysis of microsomes after four and eighteen minutes at 37,020 rpm in a Spinco model centrifuge. The sedimentation direction is indicated by the arrows. Reproduced from Littlefield, Keller, Gross, and Zamecnik.

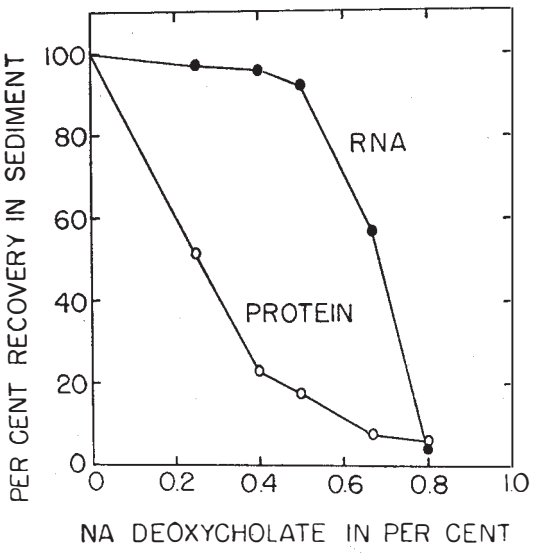


Figure 13.4. Effect of sodium deoxycholate concentration on the recovery of RNA and protein from a 105,000 × g microsomal sediment. Reproduced from Littlefield, Keller, Gross, and Zamecnik.

same treatment. Was the ribonucleoprotein portion of the microsomal fraction itself heterogenous after all? Again, the question could not be answered within the framework of this representational technique alone.

Still another representation of "ribonucleoprotein particles" was the characteristic change of their biochemical composition as a function of the increasing solubilizer concentration. This was a typical biochemical representation. Raising the level of detergent caused the nonsolubilized protein remaining on the particles to decrease more or less monotonically, whereas for RNA, a clearly definable boundary showed up (see Fig. 13.4). Below 0.5 percent deoxycholate, virtually all RNA of the fraction remained in the unsoluble material. Beyond this value, however, the RNA was gradually lost to completion. This biphasic behavior of the RNA with respect to the solubilizer could be taken to point to an edge at which the biochemical representation indicated a qualitative change in the cohesion behavior of the particle.

For all representational techniques, there was no conceivable external reference concerning the shape and composition of the scientific object under preparation. Its shape could not simply be derived by comparison of a "model" particle with a "real" particle; it gradually took some shape

from a correlation of representations constructed from different biophysical and biochemical techniques.[53] And because the material was no longer active in the test tube with respect to amino acid incorporation after the different isolation procedures, there was no functional reference for comparison. The experimental representations partially matched each other and partially interfered. The "deoxycholate particle" entered the field of in vitro protein synthesis around 1953, and around 1956 it disappeared again from the scene because no ways were found to render it functionally active. Nevertheless, it had a transitory function quite generally characteristic for the production of epistemic things. It was a tentative invention. It was a step on the laborious path of trying to bring the fractional representation of the cell sap into resonance with some functional sutures of protein synthesis—in the present case, amino acid incorporation into proteins. Ribonucleoprotein particles that were active in vitro became only available some years later in the course of a process that involved the recomposition of the ionic composition of the buffer system, the exchange of the solubilizing material, and the switch to another cellular source for the particles.

Xenotext

In the construction of scientific objects, I see a process in which different representations are made to bear upon each other. Insofar as this process, as a research process, has no predictable outcome, I am inclined to put my constructivist vocabulary in brackets and declare: If there is anything specific for scientific representation, it is to *deconstruct* itself. Within the continuum between epistemic things and technical things, what we usually call a "model" occupies a kind of middle position. As a rule, *qua* epistemic things, models are already sufficiently established to be regarded as promising areas of research and therefore to function as research attractors. On the other hand, they are not yet sufficiently standardized in order to serve as unproblematic subroutines in the differential reproduction of other experimental systems. Thus, an experimental model system has always something of the character of a supplement in the sense Derrida confers on the notion.[54] It stands for something *only the absence of which* allows it to become effective. If the supplement presents itself as a simple addition, it has nevertheless the potential to direct the differential movement of the whole system. The subversion of an experimental system by a supplement shows both aspects characteristic for that movement: it tends

to change the identity of its components, and it fails to do so by its very presence as a supplement. This is because a supplement, by definition, tends to be supplemented by "another" one. A model is a model in the perspective of something at which it fails to arrive. It functions precisely in the sense of a Rotmanian "xenotext." I quote from *Signifying Nothing*: "What it [the xenotext] signifies is its capacity to further signify. Its value is determined by its ability to bring readings of itself into being. A xenotext thus has no ultimate 'meaning,' no single, canonical, definitive, or final 'interpretation': it has a signified only to the extent that it can be made to engage in the process of creating an interpretive future for itself. It 'means' what its interpreters cannot prevent it from meaning."[55]