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Reductionism in Biology: An Example of Biochemistry

Abstract

In this paper, I argue that the multiple realizability argument against reductionism does not work in biochemistry and that biochemistry as a reductionist project is a progressive research program. Since the anti-reductionist argument that appeals to the multiple realizability thesis doesn't work and since biochemistry that incorporates the principle that biological functions of biomolecules in living cells can be understood in terms of chemical and physical properties of those molecules is a progressive research program, I conclude that plausibility of reductionism is still worthy of further study.

I

Reductionism in biology is concerned with the relation between biological knowledge and chemical or physical knowledge.[1] There is the idea of theory-reduction, which concerns with whether and how a biological theory can be reduced to a chemical or a physical theory. There is the idea of explanatory reduction, which concerns with whether or how biological representations can be explained by chemical or physical representations.[2] In this paper, I will only focus on biochemistry and I will not discuss the nature of reduction relation. Instead, I will argue that the multiple realizability thesis does not show that type-type reduction is not possible at least in biochemistry. Second, I want to address the issue of reductionism in a different way by looking at a science (biochemistry) that forms a reductionist research program. To do so, I would like to answer the question of whether this reductionist research program leads to new empirical knowledge about the biological systems or whether it distorts our understanding of those systems. To answer this question, I would like to use Imre Lakatos' Theory of Scientific Research Programs. The reason I choose Lakatos' Theory is: 1. It specifically addresses the issue of whether research traditions are progressive i.e., whether they lead to new empirical knowledge. 2. Other theories of science such as falsificationism or inductivism (with the exception of Thomas Kuhn – I could as well use Kuhn's Theory and make similar points about this science since Kuhn's notion

1 Alan Love and Ingo Brigandt, "Reductionism in Biology", Entry in *Stanford Encyclopedia of Philosophy.*

2 Ibid.

F. Stadler (ed.), *The Present Situation in the Philosophy of Science*,
The Philosophy of Science in a European Perspective, DOI 10.1007/978-90-481-9115-4_16,

of progress in terms of increase in effectiveness of puzzle solving would do the same job) are not fitted to evaluate research traditions as integrated wholes. I acknowledge that conclusions I reach about Biochemistry Research Program on the basis of Lakatos' Theory will be sensitive to the appropriateness of that theory in understanding science. However, I will not address the broader issues about which theory of science is better.

II

The multiple realizability thesis has been introduced into philosophy by Putnam and Fodor.[3] The idea is this: the *same* kinds of higher level properties can be realized by *diverse* kinds of physical properties. If there is a higher level generalization of the form "If *M* then *B*" where *M* and *B* are higher level kinds, there are multiple physical properties P_1 to P_n that would realize *M* and there are multiple physical properties P'_1 to P'_n that would realize *B*, where *Ps* not only need not but also typically are not equal to *P's*. The relation of this thesis to reductionism is as follows: if a higher level type can be realized by diverse physical types at a lower level, the type-type reduction is not possible since there is no unique lower level type to which a higher level type can be related to. In philosophy of biology and philosophy of mind, the correctness of the thesis has been taken for granted because it has been thought that examples are everywhere (although its implications have been debated, see Sober[4]): just like one can make an automobile from very different physical materials and yet realize the function of being a car, in the same way minds and living organisms can be built up of diverse physical properties and yet do not lack anything in terms of their functions at higher levels.

The claim that multiple realizability is coherent was criticized by Larry Shapiro.[5]

> To say that a kind is multiply realizable is to say that there are *different* ways to bring about the function that defines the kind. But, if two particulars differ only in properties that do not in any way affect the achievement of the defining capacity of a kind then there is no reason to say that they are tokens of different realizations of the kind. Differently colored cork-

3 Hilary Putnam, "Psychological Predicates", in: W. Capitan and D. Merril (Eds.), *Art, Mind and Religion*. Pittsburgh: University of Pittsburgh Press 1967, pp. 37-48. Hilary Putnam, "Philosophy and Our Mental Life," in: *Mind, Language and Reality*. Cambridge: Cambridge University Press 1975, 291-303. Jerry Fodor, *Psychological Explanations*. Cambridge, MA: MIT Press 1968. Jerry Fodor, *The Language of Thought*. New York: Thomas Crowell 1975.

4 Elliott Sober, "The Multiple Realizability Argument against Reductionism", in: *Philosophy of Science* 66, 1999, pp. 542-564.

5 Larry A. Shapiro, "Multiple Realizations", in: *The Journal of Philosophy* 97, 12, 2000, pp. 635-654.

screws, alike in every other aspect, are not tokens of different realizations of a corkscrew because differences in color make no difference to their performance as a corkscrew.[6]

We can extract the following criterion from this passage:

> If there are two *different kinds of realizers* of *the same higher level kind*, then they must differ in their causal powers that are relevant to the function of a multiply realized state.

Contrapositive of this conditional statement runs as follows:

> If *different realizers* of *the same higher level kind* don't differ in their causal powers that are relevant to the function of a multiply realized state, then those realizers *are not different kinds of realizers* of *this higher level kind*.

This criterion implies that no matter how diverse realizers of a given state may seem, as long as they share a common causal power related to the function at a higher level, with respect to that higher level type, realizers don't fall under *distinct kinds* at the lower level. They may differ in other physical or chemical characteristics. It is highly dubious, according to Shapiro, that realizers at a lower level would differ in their relevant causal capacities in bringing about the higher level properties and we would still call them the realizers of *the same higher level type*.

Realizers of a higher level type may fall under distinct kinds with respect to many properties. For example, we can build pendulums from many different kinds of physical material but if all these realizers obey pendulum law, they do not constitute *different kinds* of realizers *with respect to the function of pendulums*.[7] In the same way, physical or chemical properties that realize biological properties of a living cell may or may not fall under distinct kinds depending on which characteristics we are interested in them. If we are interested in their relation to biological property in question (their ability to bring about biological properties), they may not fall under different kinds. If on the other hand, we are interested in classifying their other physical properties that are not relevant to their ability to bring about those biological properties, they may fall under distinct kinds. If this is true, it is then at least possibility that realizers of a given biological function may have at least some chemical or physical characteristics that are relevant to their ability to bring about that function. Then, the type-type reduction is at least a possibility. There is no implication in this thesis that all biological knowledge can be reduced to chemical and physical knowledge. It may be that some parts of biology resist this. However, it entails that the claim that reductionism is in principle not possible due to multiple realizability is false. It follows that the fact that the state is "multiply realized" does not entail that there cannot be kind generalizations about lower level physical or chemical properties relevant to the realization of a higher

6 Ibid., p. 644.

7 Robert Batterman, "Multiple Realizability and Universality", in: *British Journal for the Philosophy of Science* 51, 2000, pp. 115-145.

level type because (again) distinct realizers of a system may exhibit some features that are universal with respect to the behavior under consideration.

Consider the relation between protein function and its structure and sequence. To make sense of this relation, we should specify exactly what we call a higher level type (in this case about the specific function of a protein). Then, we must be clear about the relevant lower level property that we may say responsible for that specific function. For example, the same protein may be responsible for several functions or a protein having different sequences may realize the same function. Does it follow from this that multiple realizability thesis is right and consequently reductionism is false? No. If the two sequences are different and yet still realize the same function, then the relevant question is what part of the sequence is responsible for the function. What is a kind? Should we take two sequences as different lower level kinds because they differ only in one place or many? Sometimes only one change in the sequence may be enough to call them different kinds but sometimes even if they differ in many places it may not be. This depends on what function we are investigating. So whether something counts as a relevant kind at the lower level depends on the function we are interested in. If there is a part in the sequence that makes a difference in the realization of the function that is the relevant property we should be focusing on as a lower level kind. If we can identify such a part and if that part is common in all of the realizers of the function (in all the different sequences that realize the function) then we have identified a kind at the lower level with respect to the function in question. If a higher level generalization is "all proteins have some biological functions" and we want to reduce this to a lower level kind, then we should direct our attention to their chemical or physical attributes that enable all of them to do some biological functions. If a higher level generalization is "Protein X has a biological function Y" and we want to reduce this to a lower level kind, then we should look at the chemical or physical features of this protein that we can assign responsibility for that specific function. So a higher level type can be generalizations about a single protein or all proteins; but depending on a specific kind of higher level generalization, the lower level physical or chemical generalization may be different.

> In both closely and distantly related proteins the general response to mutation is conformational change. Variations in conformation in families of homologous proteins that retain a common function reveal how the structures accommodate changes in amino acid sequence. *Residues active in function, such as the proximal histidine of the globins or the catalytic serine, histidine and aspartate of the serine proteinases, are resistant to mutation because changing them would interfere, explicitly and directly, with function*[8] (Italics are mine).

Whether this situation is widespread or rear is irrelevant. However, this example illustrates how despite many differences in the sequence we can still call all of

8 Arthur M. Lesk, *Introduction to Protein Architecture*. Oxford: Oxford University Press 2001, p. 172.

them the same kind of sequence with respect to a common property that is relevant to the specific function. The above claim by Lesk says that there is a part in the sequence that is preserved despite the fact that other parts show variations. The explanation is that, the part that is preserved plays a vital role in the realization of the function. So with respect to this specific function, there is a common lower level kind to which that function can be reduced. This is what Shapiro's criterion of multiple realizations predicts.

III

The failure of a priori arguments against reductionism paves the way for a defense of methodological reductionism. The basic idea here is that if a research program with reductionist tenets such as biochemistry leads to new empirical knowledge about biological phenomena, the issue of whether reductionism is justified can be addressed on these methodological grounds. Here the issue does not concern with the truth of reductionist thesis; it mainly concerns with the heuristic value of it – i.e., whether sciences such as biochemistry, biophysics etc. are justified in following reductionist tenets. It is important, however, to note that if a reductionist research program constantly succeeds in the discovery of new empirical knowledge, this will provide plausibility for the reductionist thesis even if it does not justify its truth.

According to Imre Lakatos,[9] the basic unit of science is a research program. Scientific Research Programs (SRP) consist of negative and positive heuristics: negative heuristics determine what is not allowed in SRP and positive heuristics determine what is permitted. SRP also consists of two sets of assumptions: hard core and protective belt. Hard core assumptions are the fundamental principles of SRP (for example, in Newtonian physics they would be three laws of motion plus gravitational law or in evolutionary biology they would be formulations of principles that define how evolutionary forces affect genetic structure of a population) and protective belt assumptions are anything that may be needed to relate these hard core assumptions to the world. When there is a mismatch between theoretical results and the actual observations, negative heuristics say that no change in hard core assumptions is allowed. Positive heuristics say that only non-ad hoc changes are allowed. In the case of a gap between theoretical results and actual measurements, there is no recipe about what kind of changes can close the gap. However, sometimes methodological principles may lead us to make changes in certain directions. For example, in Newtonian physics, commitment to the idea

9 Imre Lakatos, "Falsification and the Methodology of Scientific Research Programmes", in: Imre Lakatos and Alan Musgrave (Eds.), *Criticism and the Growth of Knowledge*. New York: Cambridge University Press 1965. Imre Lakatos, *The Methodology of Scientific Research Programmes*. Philosophical Papers Volume 1. New York: Cambridge University Press 1978.

that nature should be explained in mechanical terms will lead scientists to look for new models that will not violate this maxim (so when one mechanical model fails they will look for another mechanical model that will do the job). In this sense, when we assess an SRP, we are also assessing these methodological maxims as well because such principles may sometimes be responsible for the failure of an SRP. According to Lakatos, failure or success of SRP cannot be put in absolute terms. For him, successful SRP makes both empirical and theoretical progress. Failed SRP is degenerative in the sense that it fails to make empirical progress. Since there is no recipe how to make appropriate changes in SRP when there is a gap between theoretical results and actual measurements, in most part creative and imaginative scientists determine the faith of SRP. In this sense, sometimes even the degenerative SRP may make a comeback.

In order to define theoretical and empirical progress, following Malcolm Forster,[10] let me introduce the term 'model'. A model is basically the combination of hard core assumptions and protective belt assumptions from which we obtain theoretical results that can be related to the world. When a theoretical result we obtain from a model does not match to the actual observations, then another model is called for. According to Lakatos, when we make changes in the old model, these changes should not be ad hoc; i.e., such changes should lead to new predictions and they should be independently testable. If these new predictions are empirically confirmed, then SRP is making empirical progress. If we construct more and more models and they make empirical progress, then SRP that these models belong to is progressive. However, if more and more models belonging to SRP start failing, then it is degenerative.

Does biochemistry contain reductionist tenets? Is it a progressive research program in Lakatos' sense? Biochemistry studies chemical processes and reactions that take place in living cells. There are varieties of different molecules in living cells. Molecules that Biochemistry studies are carbohydrates, proteins, enzymes, lipids and nucleic acids. The guiding idea of biochemistry is that processes of living cells can be understood in terms of the chemical properties of these molecules that form a living cell. One textbook defines the goal of biochemistry as follows:

> The overall goal of biochemistry is to describe life's processes using the language of molecules, that is, applying the principles and methods of chemistry to determine molecular structure from which it is often possible to explain biological function.[11]

10 Malcolm R. Forster, „The Hard Problems in the Philosophy of Science", in: R. Nola and H. Sankey (Eds.), *After Popper, Kuhn & Feyerabend: Recent Issues in Theories of Scientific Method*, Australasian Studies in History and Philosophy of Science, Kluwer Academic Publishers 2000, pp. 231-251.

11 Rodney F. Boyer, *Concepts in Biochemistry*. Hoboken, NJ: Wiley & Sons Inc. 2006, p. 2.

It is important to distinguish between two sets of theories that we may call hard core assumptions of biochemistry research program: 1. There are background theories, such as chemical, physical and biological theories. 2. There are set of principles about the nature, function and interactions of biomolecules that are building blocks of life. It is the second one that is distinctive about biochemistry and the reductionist nature of this research program lies in these second kinds of principles. Since the second claim is distinctive of biochemistry research program, it plays a vital role whether this science succeeds in realizing its goals. Lehninger, Nelson and Cox[12] write:

> The molecules of which living organisms are composed conform to all the familiar laws of chemistry, but they also interact with each other in accordance with another set of principles, which we shall refer to collectively as *the molecular logic of life*. These principles do not involve new or yet undiscovered physical laws or forces. Instead, they are set of relationships characterizing the nature, function, and the interactions of biomolecules.

The list of the principles concerning the molecular logic of life are:[13]

> A living cell is a self-contained, self-assembling, self-adjusting, self-perpetuating isothermal system of molecules that extracts free energy and raw materials from its environment. The cell carries out many consecutive reactions promoted by specific catalysts, called enzymes, which it produces itself.
> The cell maintains itself in a dynamic stady state, far from equilibrium with its surroundings. There is great economy of parts and processes, achieved by regulation of the catalytic activity of key enzymes.
> Self-replication through many generations is ensured by the self-repairing, linear information-coding system. Genetic information encoded as sequences of nucleotide subunits in DNA and RNA specifies the sequence of amino acids in each distinct protein which ultimaltely determines the three-dimensional structure and function of each protein.
> Many weak (noncovalent) interactions, acting cooperatively, stabilize the three-dimensional structures of biomolecules and supramolecular complexes.

The common theme in all these principles is the idea that life can be understood in terms of chemical or physical properties of biomolecules and their interactions. It is because of this common theme that I claim biochemistry is a reductionist research program. Biochemistry research program also includes methods and techniques about how to identify structure and how to relate this structure to a specific function. This involves the use of instruments, for example, NMR spectroscopy, X-ray crystallography, Cryoelectron microscopy and electron cystallography. It also involves certain heuristics about relating structure to function and interpretation of data provided by these instruments. Thus, biochemistry has features of a research program in Lakatos' sense.

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12 Albert L. Lehninger, David L. Nelson and Michael M. Cox, *Principles of Biochemistry*. New York: Worth Publisher 1993, p. 4.

13 Ibid., p. 19.

The question now is whether biochemistry as a research program is empirically progressive. To answer this question, we have to look at the historical record of biochemistry whether its models constructed from hard core assumptions together with protective belt assumptions have led to new empirical knowledge about living cells and whether there are cues that point to expectations about further new empirical knowledge. To show that biochemistry research program has realized its goals to some extent, it suffices to list just some major discoveries about the structure of DNA, the structure and function of proteins, discoveries about the causes of many diseases, developments of new techniques and instruments in solving problems in biochemistry research program. There are more discoveries in the field than the number of Nobel prizes awarded but the selected list of noble prize awards will give some idea about its progress toward providing new empirical knowledge about biological functions: Fisher for enzyme action, Buchner for description of fermentation, Summer for crystallization of urease, Krebs for description of citric acid cycle, Watson and Crick for DNA double helix, Perutz for X-ray of protein crystals, Smith for restriction enzymes, Cech and Altman for catalytic RNA, Mullis for polymerase chain reaction, Horvitz for biochemistry of programmed cell death, Wüthrich, Fenn and Tanaka for NMR, MS structure of proteins, Mackinnon and Agre for Aquaporins and membrane channels and Hershko, Rose and Ciechanover for ubiquitin-mediated protein breakdown.[14]

Furthermore, just looking through paper publications related to biochemistry will show that more knowledge is being produced and on the way. 2005 JCR Science Edition reports that there are 261 journals listed under the category of "biochemistry and molecular biology" between 2003 and 2005. In these journals 236,517 papers published between 2000 and 2005 and the total number of citations these papers produced was 511,212.[15] Between 1971 and 1990, the percentage of biochemistry articles in chemistry papers published in the journal *Nature* is found to be 83 but the percentage drops to 73 in 1990s.[16] Around the same years the percentage of chemistry articles are 13 and the percentage of biology and medicine articles are 49.[17] More information about the performance of scientific fields is available in journals related to scientometric and bibliometric studies of performance evaluation of these fields. The figures I cited above point to some rough and ready ideas about the progress of biochemistry. These figures may include repetitive publications and not significant discoveries. However, even small percentage of these figures will show that this research program is empirically progressive in Lakatos' sense since it is not too harmful to assume that top journals in the field do not publish papers that are not original contribution to the field. There is also inter-

14 Boyer, *Concepts in Biochemistry*, p. 6.

15 Nan Ma, Jiancheng Guan, and Yi Zhao, "Bringing PageRank to the Citation Analysis", in: *Information Processing and Management* 44, 2007, p. 802.

16 D.B. Arkhipov, "Scientometric Analysis of Nature, The Journal", in: *Scientometrics* 46, 1, 1999, p. 62.

17 Ibid., p. 59.

esting statistics about the number of publications related to the subfields of biology. Between 1991 and 1998, in terms of average annual number of papers among the subfields of biology, with 320 papers molecular biology ranks first, with 155 papers medicine comes next, with 109 papers brain ranks third, with 21 papers natural history ranks fourth, and with 20 papers agriculture ranks fifth.[18] Even these figures give some approximate idea about the direction biological sciences heading. These figures should, of course, be detailed and should be subjected to serious analysis to provide more detailed answer to the question of whether sciences are heading in the direction of reductionism; but, as a starting hypothesis from these figures, we can say that biochemistry is progressive research program.

It must be noted, however, that Lakatos' SRP does not allow us to make judgments about the final faith of a research program. For, SRP can be progressive at one time and then may become degenerative later; it may be degenerative at one time but then with the imaginative and creative abilities of researchers working in the field it may become progressive again. So our evaluations of the overall success of a research program will always be relative to the information available to us at a given time period. Accordingly, my claim here is that the best evidence available to us now leads to the conclusion that biochemistry research program is empirically progressive.

IV

The fundamental question of biochemistry is defined as follows in one of the most influential textbook in the field: "Biochemistry asks how the thousands of different biomolecules formed from these elements interact with each other to confer the remarkable properties of living organisms."[19] Through the applications of techniques and concepts from chemistry, biochemists hope to understand this fundamental question. Given their track record in a short time, we should be optimistic about their possible success in answering this question. So we should be optimistic about this reductionist project. I believe we will make more progress in our philosophical projects about reductionism by studying in detail a science whose project is to understand biological phenomena in terms of chemical and physical concepts.

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18 Ibid., p. 67.
19 Lehninger, Nelson and Cox, *Principles of Biochemistry*, p. 1.