MNF Education

Molecularization in nutritional science: A view from philosophy of science

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Scope: Over the past decade, a trend toward molecularization, which could be observed in almost all bioscientific disciplines, now appears to have also developed in nutritional science. However, molecular nutrition research gives birth to a series of questions. Therefore, we take a look at the epistemological foundation of (molecular) nutritional science.
Methods and results*:* We (i) analyze the scientific status of (molecular) nutritional science and its position in the canon of other scientific disciplines, (ii) focus on the cognitive aims of nutritional science in general and (iii) on the chances and limits of molecular nutrition research in particular. By taking up the thoughts of an earlier work, we are analyzing (molecular) nutritional science from a strictly realist and emergentist–naturalist perspective.
Conclusion*:* Methodologically, molecular nutrition research is bound to a microreductive research approach. We emphasize, however, that it need not be a radical microreductionism whose scientific reputation is not the best. Instead we favor moderate microreductionism, which combines reduction with integration. As mechanismic explanations are one of the primary aims of factual sciences, we consider it as the task of molecular nutrition research to find profound, *i.e.* molecular-mechanismic, explanations for the conditions, characteristics and changes of organisms related to the organism–nutrition environment interaction.

Keywords:
Emergence / Mechanismic explanation / (Molecular) nutritional science / Reductionism / Systems biology

Things are similar: this makes science possible.
Things are different: this makes science necessary.

Richard Levins und Richard Lewontin [1]

1 Introduction

The "Death of a science", said philosopher of history, *Oswald Spengler* (1880–1936), "occurs when it will stop being an event for anybody". If one follows this apodictic thesis, the diagnosis of nutritional science today should be the most encouraging. The academic seedling of nutritional science has in the past years grown strongly and gained strength and seems never to have radiated so much energy in the scientific community as in these days. Nutritional science is *en vogue*! Parallel to this development, nutritional science has entered a molecular stage. A trend toward molecularization that could be observed in the last decades in almost all bioscientific disciplines, now appears to have also developed in nutritional science [2–9]. Nearly everything – even epidemiology [10–13] – has taken a molecular turn. This development is also to be recognized institutionally, *e.g.* by

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installing professorships for molecular nutrition [14], by establishing of special journals like *Molecular Nutrition & Food Research* [15] and by implementation of a special section called *"Molecular Nutrition" in the British Journal of Nutrition* (for example, see [16].

The ambitious undertaking of *Molecular Nutrition Research* gives birth, however, to a series of philosophical–epistemological questions regarding its own disciplinary legitimation. Because *what* really distinguishes molecular nutrition research in detail, whatever its nature may be? *What* are its objectives? *What* can and should it accomplish, and *where* are its limits? [17, 18]. These special questions reflect those general ones, which are related to the disciplinary self-conception and the aims of nutritional science as a whole; a discussion which in the recent past both nationally [19–29] and globally [30–32] has attracted increasing interest. In this context repeatedly it was pointed out that nutritional science had to clearly define itself as a scientific discipline [25, 29].

We are glad to comply with this demand in that we present with this paper a draft on the epistemological foundation of (molecular) nutritional science. In doing so, our paper will take up the thoughts of an earlier work [17, 18] and reflect on them in a greater depth. To this end, we first present an analysis of the much discussed scientific status of nutritional science and its position in the canon of scientific disciplines. We then will focus on the cognitive aims of nutritional science in general and on the chances and limits of molecular nutrition research in particular (Fig. 1). It is our objective to interpret and help to understand the molecular trend in nutritional science as an epistemologically justifiable development (see the glossary for specific termini from philosophy of science).

2 The crucial question: what is science?

Not only students in nutritional science once in a while ask themselves the question whether their discipline is after all a science *sensu stricto*. To clarify this point, it is first necessary to characterize science in general. So, the crucial question is: *What* is science?

For analytical purposes, it is appropriate to subdivide the question in two subquestions: on the one hand, "what are factual or empirical sciences?", *i.e.* disciplines that deal with the research of concrete or material objects (such as chemistry, biology and psychology), and on the other hand, "what are formal or fictional sciences?", *i.e.* disciplines such as mathematics, semantics and logics which deal with the forms of constructs, such as concepts, statements and arguments [33, 34]. In the framework of this paper, only factual sciences are relevant since nutritional science is one of them [17].

Unfortunately, the philosophy of science cannot offer a uniform answer to the question of "what are factual sciences?" that would correspond to the common philosophical practice [35–37]. Some philosophers of science have even ventured to express the relativistic-anarchistic view that, in principle, there was no difference at all between science and non-science, best expressed by paraphrasing *Paul Feyerabend's* (1924–1994) shattering and well-known credo. According to this philosopher of science, there is no clear definable difference between myths and scientific theories [38]. In fact, Feyerabend [38] told us that

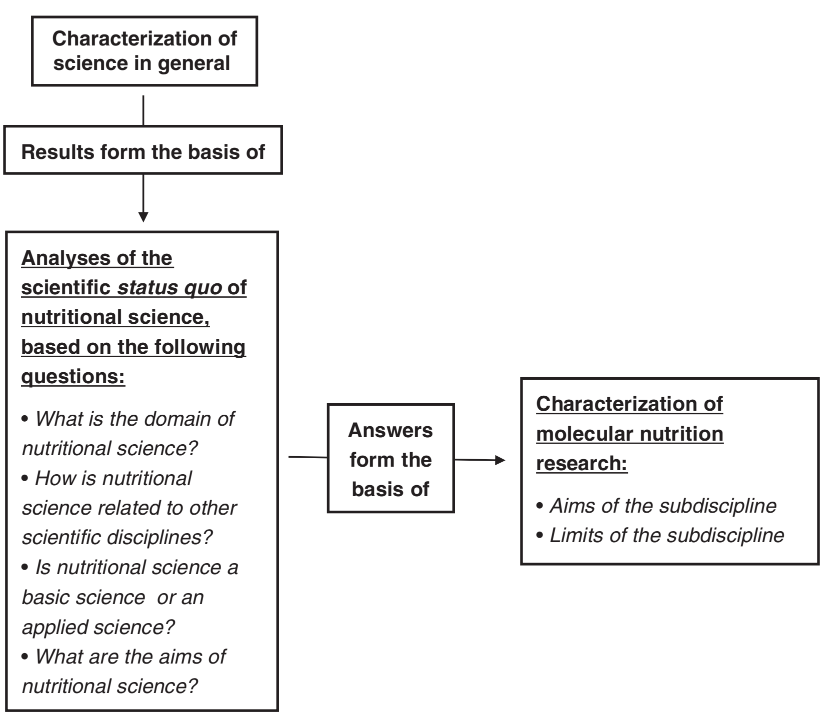

Figure 1. Visualization of the structural organization of this study.

science is one of many forms of life that man has developed, and not necessarily the best – it is noisy, impertinent, expensive and spectacular. Period! Against such an epistemic anarchistic background it comes as no surprise that many contemporary philosopher of science fail to be able to characterize and demarcate science from non-science [39].

However, in contrast to such a relativist position, we [17] agree with other authors [34, 37, 40–43] holding the view that factual sciences, understood as research fields producing genuine knowledge [37], can be clearly distinguished from other non-scientific forms of recognition. However, we grant that factual science cannot be defined on the basis of a single feature or on the basis of a single and universal demarcation criterion like *Karl Raimund Poppers* (1902–1994) widely quoted attribute of falsifiability [44, 45]. For the characterization of science, a whole catalog of criteria is needed instead. According to the position held here [46], any specific discipline of factual science has the following ten features (F) [37, 47, 48]:

(F1) A general philosophical background consisting of the ontological ("How is the world constituted?"), epistemological ("How do we recognize the world?"), semantical ("What is truth?"), axiological ("What are the ethical values that hold true for us"?) and moral ("How shall we behave and act"?) principles held by the scientists and practiced in their research activities. Accordingly, the view of the (neo)positivists like *Moritz Schlick* (1882–1936) and *Rudolf Carnap* (1891–1971) maintaining that factual science operates or should operate in a philosophical and metaphysical vacuum, is misleading [49, 50]. Clearly, if factual science is to be more than an end in itself, limited to the use of certain methods of generating data, and pursues instead a genuine interest of gaining knowledge and finding explanations, then, before any empirical studies, we have to ask how the world and the subject (mind) recognizing it must be constituted for recognition to be possible at all. The corresponding basic metaphysical and epistemological assumptions are the following [37, 48, 51]:

(i) *Ontological realism*. The hypothesis of a mind-independent world. Contrary to that antirealistic positions like radical or social constructivism claim that there is no reality independent of our existence [52]. If that view were correct, nothing without our mental imagination could be empirically studied and explained. In a nutshell, without ontological realism there is no room for factual science in general (for more about realism see [53]).

(ii) *Ontological naturalism*. The assumption that there is only one causally self-contained world that exists inherently without being influenced by supranaturalistic entities (spirits, gods, and demons). To put it in simple words: Everything in the world is sound and fair play [54]. Without this metaphysical hypothesis, epistemic operations, such as measuring and experimenting, would lose their status of scientific methods. Because in a world exposed to all kinds of supranaturalistic manipulations everything is possible and therefore nothing can be experimentally verified, nothing can be predicted [50, 55].

(iii) *Ex-nihilo-nihil-fit principle*. The hypothesis that nothing comes out of nothing and nothing disappears into nothingness.

(iv) *Principle of lawfulness*. The assumption that all material objects behave according to a law and not arbitrarily.

(v) *Principle of antecedence*. The thesis that causes precede their effects in time and not *vice versa*. According to this thesis, the past determines the present, which in turn determines the future. The principle of antecedence has to be distinguished from the *principle of causality,* which, in the strict sense, postulates that every event has a cause. However, as we know from the quantum physics, there are also spontaneous events without a cause, so that the principle of causality is false in contrast to the antecedence principle. In short: antecedence $\neq$ causality (for more about causality see [56]).

(vi) *Epistemological realism*. The hypothesis that, in principle, the real world can be known, even if only partly, approximately and imperfectly. Obviously, this kind of epistemological realism is not of the naïve kind which implies that we are able to recognize the world as it exists by itself. And in fact the concepts and models we have created represent the world symbolically and imperfectly, but not as a copy or reflection [48].

(vii) *Principle of parsimony*. This is the methodological maxim going back to William of Occam (1285–1349) according to which explanatory assumptions should not be multiplied beyond necessity, in particular with respect to theoretical entities. In short: *Entia non sunt multiplicanda praeter necessitatem* [57].

(viii) *Fallibilism* and *meliorism*. According to these two methodological principles, all our knowledge is fallible as well as justifiable and should therefore be improved as far as possible [48].

(F2) A specific domain or **universe of discourse,** *i.e.* a collection of actual or putative concrete objects and their characteristics, conditions and changes past, present and future. Thus, anything that is known can be known scientifically. However, this form of scientism should not be mistaken for the thesis that only things are real that have been scientifically explored.

(F3) A collection of aims of the members of a particular research community with regard to the study of their domain. The aims include in particular the description, explanation and prediction of the states, properties and changes of the elements of the specific domain. Whereas basic science is characterized by exclusively concentrating on achieving a gain in knowledge without giving any consideration to its practical applicability, applied science has a practical orientation, *i.e.* it is oriented to solving a concrete real-world problem.

(F4) A specific problem field representing the sum of all actual or potential questions that are (or can be) dealt with by the scientists studying a domain.

(F5) A fund of knowledge, *i.e.* the collection of current and solidly confirmed individual items of knowledge (data, hypotheses, theories) that have previously been obtained by the members of a given discipline.

(F6) A set of methods, *i.e.* the collection of all verifiable and explainable methods the members of a field of science (can) fall back on in exploring their domain. They include specific methods, be they experimental or statistical, and that which is called the general scientific method meaning a systematic sequence of certain epistemic operations consisting roughly of: defining the problem – generating the hypothesis and data – testing – interpreting. Reference has to be made here to the important though often neglected difference between methodics and methodology. Whereas the former is a collection of methods, the latter is normative epistemology and, thus, a meta-discipline constituting a central component of the philosophy of science. Its function is to clarify what is reliable and approved knowledge and how it is to be obtained.

(F7) A specific background knowledge. It includes a collection of current and reasonably confirmed individual items of knowledge (data, hypotheses, theories) obtained in adjacent fields of scientific research and relevant to studying the given discipline.

(F8) A formal background. The collection of all logical and mathematical theories used by the members of a given scientific community in studying the elements of their specific domain.

(F9) A research community is part of the scientific community in general. It consists of persons who have received a scientific education, carry on an intense exchange of information with one another and initiate or continue a tradition of scientific research.

(F10) A society, the whole range of culture, economy and politics that hosts a given research community and encourages or at least tolerates the activities of its members.

In addition to the ten features mentioned above, a factual scientific field also satisfies the following two conditions [37, 47]:

(F11) There are strong connections between a specific field of research and other disciplines (the systemicity condition), and

(F12) components F3 to F7 change, however slowly and gradually, due to the research results obtained in the given discipline or in related fields, which Imre Lakatos (1922–1974), a prominent philosopher of science, has called ''theoretical progressiveness'' [58].

On the one hand, the characterization of science presented above accepts the insight of sociology of science that scientific activity does not take place in a social vacuum [42]. On the other hand, this draft also takes into account aspects from philosophy of science emphasizing the special methodological characteristics of science [59]. In this way, the two extreme positions of ''*every* scientific activity is only a social construct'' (context determines contents) and ''there are no social factors whatsoever influencing scientific activity and findings'' (contents without context) are avoided. Thus, the position presented here is a way in the middle between a radical externalism and an internalism defined too narrowly [40–42].

3 Nutritional science – scientific *status quo*

The general characterization of factual science described above can now be applied to nutritional science. Thus, we have to examine whether and to what extent the distinctive features of science outlined above are inherent in nutritional science [17].

It is obvious to everybody that there is a nutrition research community (F9) organized in national and international groupings specializing in nutrition whose activities are increasingly supported by society (F10) and are based, at least *in praxi,* on the ontological and epistemological basic assumptions outlined above (F1). The formal background (F8) of nutritional science has further widened since the advent of bioinformatics; the development of mathematical models has since become an established practice, which is reflected, *e.g.* by the special section on ''mathematical modeling'' created for this purpose in the *Journal of Nutrition* (for example, see [60]). With our knowledge in the related fields of science, especially biosciences, steadily increasing in the past few years, the specific background knowledge (F7) of nutritional science has also further grown. Nutrition research uses a multitude of methods most of which, however, originate from related fields, such as biostatistics, physiology, or cell biology. A genuine set of methods of nutritional science (F6) is therefore of marginal importance. Finally, the fund of knowledge (F5) of nutritional science has meanwhile grown and includes a flood of data and hypotheses, many of which, however, have not been related to one another in a systematic way. This is the reason for complaints about the resulting knowledge fragmentation [61, 62]. The problem shall be solved with (i) the help of holism [61], (ii) nutritional system biology [63] and (iii) with the aim of evolutionary medicine [62, 64–68].

From the conceptual point of view, the difficulties of nutritional science are inherent in its domain (F2), its aims (F3) and its specific problem field (F4). There is, for instance, no agreement in the research community (F9) on a clear definition of the unsolved fundamental problems of nutritional science. In our opinion, such a collection of problems, in analogy to the Hilbert collection of mathematical problems [69] would be very helpful for the advancement of research and teaching in nutritional science. The study of nutritional science should analogously be accompanied by a specific set of questions and problems, because only one who is capable of *asking* significant and relevant questions will *find* significant and relevant answers [70]. In our opinion, such fundamental questions might be found, if developmental and evolutionary biology would become one of the main subjects of nutritional science. Finally, concerning the domain (F2) and the aims (F3) of nutritional science, opinions have been divided for years. Is nutritional science, for instance, a specialized variant of general physiology and biochemistry [71, 72]? Or is it rather a transdisciplinary specialty [73] of human and social sciences [2]? Is it predominantly an applied science [23, 74] that *should* also see itself as such, *i.e.* a field of applied science? Or should it primarily be basic research committed to modern biosciences [19]? Where does nutritional science stand in the canon of the other sciences? Is it an independent science [24]? If so, what does its independence consist of? And what about the aims of nutritional science, and which of them should be in its scientific focus? Those which are oriented toward socio-political tasks [24] and overlapping ethical objectives [29]? Or is the principal aim of nutritional research to investigate the interaction between the organism and nutrition at the biotic level [19]? To answer these questions the domain of nutritional science has to be further analyzed.

4 What is the domain of nutritional science?

Obviously the question about the essential object and/or basis of reference of nutritional science is easy to answer. Just as the domain of other factual sciences is already expressed in their name – chemistry, for instance, is dealing with chemical, biology with biotical and sociology with social matters – the same seems to be true of nutritional science. According to the above, the basis of reference of nutritional science is nutrition. But *what is* nutrition? In the eyes of many this typical ontological question may appear trivial, at least irrelevant to practical research – because what does the answer means and what depends on it? A lot, we think. In fact, the view on what nutrition is can fundamentally influence the way research is done. If, for instance, nutrition is considered primarily a highly complex physiological and biochemical process [71, 72], nutritional research will logically limit itself to physiological and biochemical studies; psychosocial aspects would be excluded *per definitionem*. Thus, the ontological question of "What is nutrition?" is of methodological significance.

What then is nutrition? Nutrition is an organism–environment interaction, though a specific one. Nutrition denotes all interactions between organisms and their biotic and abiotic dietary factors that have an effect on the activity of the organisms and/or their subsystems. More specifically, nutrition can be analyzed as a *process* including a sequence of events. In the first approximation, this sequence consists of the selection, incorporation and metabolization of the respective dietary factors by the organism. It has to be noted here that for the organism dietary factors can be functional, afunctional or dysfunctional. Functionality means that the nutrition factor is of benefit to the organism's survival or reproduction. In contrast, dysfunctionality means that the dietary factor is harmful to the organism. If the dietary factor has neither a beneficial nor a harmful effect on the organism's continuing existence, it is an afunctional dietary factor [18].

Our analysis of the notion of nutrition leads to two epistemological consequences [18]:

Descriptive: If nutrition is considered an organism–environment interaction, it is an *ecolocical process* to be represented ecologically in an appropriate way. Nutrition as a special form of the organism–environment interaction thus is a domain of specialized ecology. Plant nutrition is therefore an object of *plant ecology* studies, animal nutrition of *zooecology,* and human nutrition of *human ecology, i.e. anthropology,* if we follow this logic. In other words: nutritional science, as a science of human nutrition, is *specialized anthropology* and can thus be neither pure natural nor pure social science. Nutritional science – similar to geography, forestry [75] or agricultural science – is a *multidiscipline*, as it studies the object of "nutrition" with the help of various factual disciplines, *i.e.* human biology, social sciences, and psychology. Therefore, nutritional science can be characterized as a biopsychosocial–anthropological multidiscipline, as Fig. 2 visualizes. It should be noted that human biology comprises many subdisciplines, such as physiology, biochemistry, developmental biology, and evolutionary biology, all of which are relevant to nutritional science. The same is true for social sciences, which includes among others sociology as well as micro- and macroeconomics.

Contrary to the above, there is nothing indicating that nutritional science would be a true *interdiscipline* at the present moment. Unlike a multidiscipline that overlaps with other fields of science in terms of basis of reference and set of methods, an interdiscipline offers additional hypotheses or theories combining various disciplines [47, 76]. An example of an interdiscipline is modern evolutionary biology, which is not only a multidiscipline consisting of genetics, biogeography, and ecology, but also integrates various theories, *e.g.* by developing the synthetic evolutionary theory (the combination of Darwin's natural selection theory with modern genetics) [77]. A similar integration has so far not been accomplished in nutritional science, as far as we can see.

Normative: If the result of the above analysis of nutrition as a form of organism–environment interaction is correct, the following normative postulates can be established:

(i) The complete interaction of man as a biopsychosocial and highly "unnatural" [42, 78] being with his nutritional environment can only be approximately understood when biotic, (mental) psychic and social aspects are taken into account. For analytical purposes it may, of course, be necessary and legitimate to give epistemic

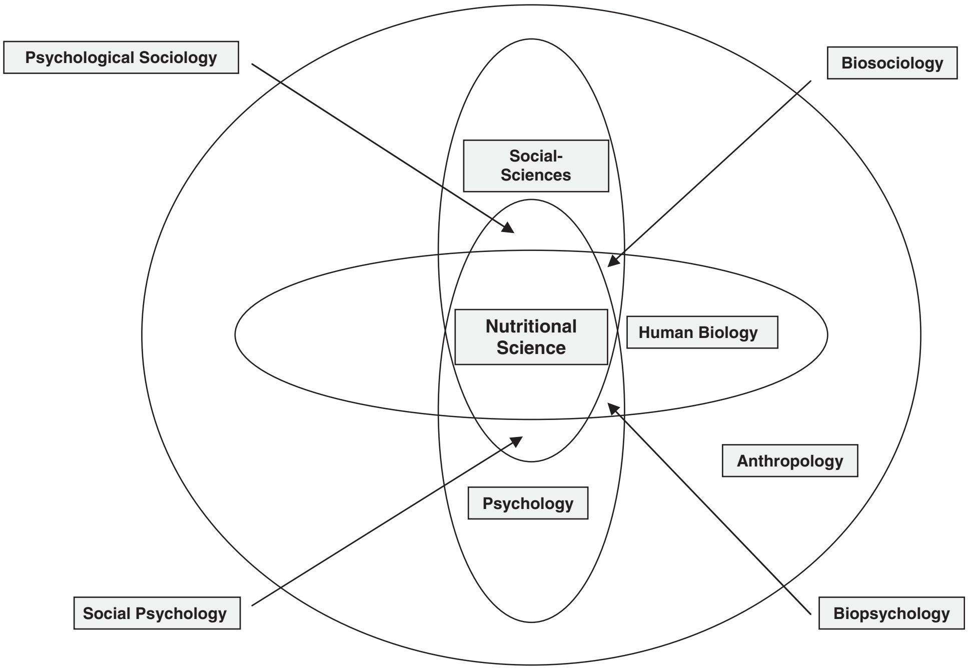

Figure 2. Nutritional science as a biopsychosocial-anthropologic multidiscipline [17].

preference to one particular aspect. Human beings, *e.g.* are organisms capable of learning and perception, which would justify the study of nutrition from the purely psychological point of view. Or: humans are biosystems, their interaction with nutrition factors can therefore be justified from the purely biological angle [14, 79, 80]. This, however, should not lead us to an erroneous ontological thesis that nutrition represented *nothing* but a physiologic-biochemical process.

(ii) As a multidiscipline, nutritional science needs scientists with differing backgrounds in terms of contents and the set of methods they use. Only then will it be possible to counteract the conceptual impoverishment of this field of science.

(iii) A nutritional scientist must master the art of combining width and depth. This is the only way of keeping track of the multifaceted subject of ''nutrition'' on the one hand and going into depth far enough to develop a scientific understanding, on the other hand.

5 Nutritional science – basic science or applied science?

Starting from the above analysis of the domain another aspect comes in sight, which is important to how nutritional science sees itself, *i.e.* the question of the scientific status of nutritional science. Is it a basic or an applied science? Often the view is held that nutritional science is an applied science [23, 24]. And some authors [29] suggest that this view was appropriate and desirable because, after all, society could expect nutritional science to propose specific solutions to urgent societal problems. Nevertheless, there are other courageous authors defending the idea that nutritional science is a basic science [19]. Thus, the situation among the proponents of nutritional science is similar to that which is characteristic of general ecology. There, too, a controversial discussion has been going on for years about the question whether ecology is, or should be considered, a basic or an applied science [48].

Before commenting on the situation of nutritional science, it is appropriate to raise the question about the characteristics and differences between basic and applied science in general [48, 76]. Compared to basic science, applied science deals with a narrower domain, *i.e.* a subunit of the scientific object of its corresponding basic science. The same applies to the fund of knowledge of basic science and its application-related counterpart. Basic science distinguishes itself by serving the one and only purpose of contributing to the progress of knowledge without paying any attention to practical applicability. In contrast, applied science has a practical orientation, *i.e.* its interest in knowledge is focused on solving a concrete problem in the world in which we live.

From this we finally have to differentiate the field that is called ''technology'' in the philosophy of science [75]. Unlike basic science and applied science, technologies primarily serve the purpose of influencing certain processes. They aim at making the findings obtained by basic sciences and applied sciences useful for the defined approach to a practical problem. Technologies thus include planning and making as well as using and monitoring things or processes with a practical benefit. According to their domain, we differentiate between *physicotechnologies* (engineering science), *biotechnologies* (human and dental medicine, veterinary medicine), *psychotechnologies* (pedagogics, clinical psychology) and *sociotechnologies* (jurisprudence) [76].

Nutritional science as a basic science: If nutritional research is practiced as a basic science, the interaction of man with his nutritional environment will be studied with the exclusive aim of achieving a gain in knowledge. Whether psychic, social or biotic aspects are taken into consideration is irrelevant. In view of the normative postulate outlined above, we would rather maintain that basic research in nutritional science should address all biopsychosocial aspects of nutrition [17]. Examples of basic research oriented questions in nutritional science may be: *Biological:* What is the role of the intestinal fatty acid binding protein in fat assimilation [81] and how its regulation can be characterized [82–85]? *Psychological:* How do cognitive conditions influence the selection of food [86]? *Sociological*: What effect does socialization have on dietary habits [87–90]?

Nutritional science as an applied science: Application-related nutritional research distinguishes itself by studying questions concerning our knowledge about the interaction of man and his nutritional environment in a practical situation. Thus, in this respect studies of nutritional science are conducted with a view to the potential practical relevance of the insights gained. In fact, most nutritional scientists are dealing with application-related issues and/or pretend to do this. It is therefore correct to classify nutritional science as "primarily an applied science" as Müller *et al.* [24] have done it. Examples of application-related questions in nutritional science could be: *Biological:* How does the level of protein intake influence the risk of disease, and what could this insight mean for nutrition technology [91–94]? *Psychological:* Do obese people have specific abnormal dietary habits [95]? *Sociological*: Is there any connection between the socio-economic conditions and the prevalence of nutrition-related diseases [96]? What sociotechnological consequences could result from such findings?

Nutrition technology: When we proceed from nutritional knowledge to practical action, we enter the field of nutrition technology. According to the definition of technology presented above, nutrition technologies include all activities connected with the design, planning and supervision of nutrition-relevant objects or processes. Examples of activities in the field of nutrition technology could be: *Biotechnological:* production of folate-enriched foods to improve folate supply [97]. *Psychotechnological:* development of didactic elements in dietary education (*e.g.* food dietary pyramides [98, 99]. *Sociotechnological*: development of a list of measures for a nutritional socialization oriented toward the aim of prevention.

As the statements above and the popular publications on nutritional science, such as the *American Journal of Clinical Nutrition*, the *Journal of Nutrition or Molecular Nutrition & Food Research,* show very clearly, nutritional science is practiced today as both a basic and an applied science, and as a technology. And all three orientations should be maintained and further developed in future: applied nutritional science in conjunction with nutrition technology for mainly *practical reasons*, because in this field we can expect solutions to specific problems; and basic nutritional science for mainly *cognitive reasons*, as gaining knowledge is the purpose of science. Figure 3 visualized the relationships between basic science, applied science, and technology in the field of nutrition.

6 Description and subsumption as aims of nutritional science

For nutritional science to be recognized as a factual science, it should, as outlined above, pursue the same *cognitive aims* as every other factual science, independently of whether it is studied as a basic or an applied science. This mainly includes the *description*, *subsumption* and *explanation* [43, 47, 100, 101] of the conditions, characteristics and changes related to the organism–nutritional environment interaction with regard to both the organisms and the nutritional environment. (In this context, we do not comment on another important cognitive aim of factual science, *i.e.* the development of predictions. For details, see [102]).

Epistemologically the description of facts is the *first step of recognition*, psychologically it is the *first step of understanding*. As an epistemic operation, a description represents an organized quantity of factual statements [43, 47].

Examples of descriptions as they are used in nutritional science could be:

(i) "Person x has taken up $< y$ mg of vitamin C in the time interval t_0–$t_{>0}$";
(ii) "x suffered internal bleedings at time $t_{>0}$";
(iii) "x died at time $t_{>>0}$"

Such a description of facts helps us to understand the sequence of certain events over time, it answers the question about the *statics* (What is there? How is it?) and *kinematics* (How does it change in the course time?) of facts and conditions [100].

Building on the level of description, in a *second step of recognition* the facts described can then be recognized as a

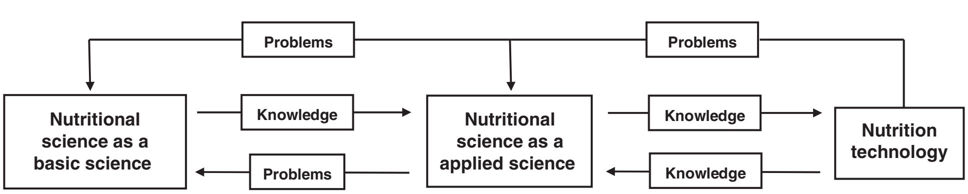

Figure 3. Visualization of the relationships between basic science, applied science, and technology in the field of nutrition.

Excursus 1. Laws and law statements

Although the term of ''natural law'' is a central term in the factual sciences and is also found in relevant textbooks of nutritional science, there is still the question of what it really says. As we have seen in connection with the basic ontological assumptions of factual sciences, this question can only be reasonably answered if we assume that things follow a law in their course. If they do not, any object (*e.g.* minerals) could be developed from any other object (*e.g.* vitamin C), events could go forward or backward and thus nutrient absorption could precede nutrient digestion. In short: in a lawless world things would happen as they do in an animated cartoon or a science fiction film [51]. And as quite obviously this is not the case, we must assume that natural laws exist in actual fact and independently of our knowledge. This, however, raises the question of what these natural laws are in detail. Today, we have a naturalistic answer to this question [51, 103, 104]. It is in short: *Natural laws are unvarying bonds between the characteristics of things, so that we may say: if thing x has the characteristic A, then it also has the characteristic B, and when A changes, B will change along with it.*

This leads to two important conclusions:

(i) As a characteristic, natural laws only exist in conjunction with things (*in rebus*), but not before (*ante res*) or after them (*post res*). Things therefore do not obey certain laws, but, due to their properties, they can in certain circumstances only behave as they do and not in any different way.

(ii) If in the cosmologic evolution qualitatively new things are generated, also new natural laws will be created. Just as biotic natural laws will not form before biosystems have developed, social laws only exist if, and as long as, there are social systems.

(iii) Natural laws as a characteristic of the real world cannot be formulated by scientists, but, if anything at all, statements can be made *about* these laws. Therefore, a strict separation must be made between our statements (hypotheses) about natural laws and those laws themselves. It is the task of factual science to represent natural laws in a cognitive form, *i.e.* as statements about laws. If this difference between the level of existence and the level of cognition is not made, the mystic-magic impression may easily be created that things would obey our statements about laws.

special case of a general pattern or law (Excursus 1 [43, 48]). However, additional data and hypotheses are needed for this purpose. If, in addition to the descriptions (i) and (iii), there is a law saying that ''all people taking up $< y$ mg of vitamin C in the time interval t_0–$t_{>0}$ will die'', the death of x can be identified as a special case of this general law. Thus, we have learned that: ''x died *because* all members of *Homo sapiens* die who take up less than y mg of vitamin C over a certain period of time''. This insight presents a conclusion resulting from the following premises

Premise 1: All persons taking up $< y$ mg of vitamin C in a time interval t_0–$t_{>0}$ will die.

Premise 2: x has taken up $< y$ mg of vitamin C in the time interval t_0–$t_{>0}$.

Conclusion: x has died.

As in a description, this type of *subsumption* is an organized quantity of factual statements with the conclusion, however, being the *logical* consequence of the known facts – an operation usually called the deductive-nomological model of Hempel and Oppenheim [105].

Thus, to learn what facts exist that are relevant to nutrition and of which general law they are a special case, we can be content with descriptions and subsumptions. These two epistemic operations are usually quite sufficient to contribute to solving real-world dietary problems. This has been impressively demonstrated by application-oriented nutritional science in the past. If, however, we are interested in the question why and for what reason the final state described in example (iii) has occurred and how it is related to (i), descriptions and subsumptions are no longer adequate. In that case, we have to take the *third step of recognition*, *i.e.* the step of *mechanismic explanation* [101].

7 Mechanismic explanation as an aim of nutritional science

As the above example shows, a subsumption only represents an input–output relation: an inadequate intake of vitamin C will lead to the person's death. Such a *black box statement* is rather superficial and not really satisfactory from the scientific point of view. In fact a deep scientific explanation must present a mechanism acting as a mediator between input and output. Such a *translucent box statement* explains the pattern created by the subsumption on the basis of a mechanismic hypothesis or theory. The result of such an epistemic operation is called a ''mechanismic'' [43, 101, 106, 107] or an ''ontic conception'' [108] of explanation. In philosophical jargon we may also say: a mechanismic explanation subsumes the subsumption and therefore is at a higher cognitive level than the latter. Because epistemologically a mechanismic explanation presupposes more data and hypotheses than a subsumption, and ontologically it penetrates the domain more profoundly by referring to mechanisms – be they visible (phenomenal) or invisible (transphenomenal) [48].

For an illustration of what has just been said, let us come back to the above vitamin C example. With the help of an additional mechanismic statement, the death of x can be explained in the following way:

Premise 1: All people taking up $< y$ mg of vitamin C in the time interval t_0–$t_{>0}$ will suffer inner bleedings at time $t_{>0}$.

Premise 2: Such bleedings are fatal in humans.

Premise 3: x has taken up $< y$ mg of vitamin C in the time interval t_0–$t_{>0}$.

Conclusion: x has died.

By a mechanism we understand a process that follows a law within a system (Excursus 2) and under given circum-

Excursus 2. System and emergence

The system concept is essential to all modern factual sciences, although it is mostly used in a nonanalyzed way. It is simply taken for granted that it is known what a system is. But what exactly *is* a system? In a modern, science-oriented and materialistic ontology the answer is given as follows [48, 102]: Material objects (things) may be *elementary, i.e.* uncompounded, or consist of several components and form a *compounded thing.* Such objects, called *complex things,* are generated in two different ways: either by *aggregation* or by *combination*. Aggregates are characterized by the absence of a major connection between the components, so that this whole is noncohesive and can easily disintegrate into its individual components again. Clouds or sand piles would be an example of such *noncohesive wholes.* In contrast, wholes created by combination distinguish themselves by a stronger interaction of the components. Such *cohesive complex things* are called s*ystems*. Thus, a cell is a system of cell organelles, cells form an organ system, and organs form multicellular systems of organisms, such as the human being.

The cohesiveness of systems is to be attributed to the *binding relationships* or simply links between the components. Such a binding relationship between two system components *x* and *y* exists when the condition of *y* changes if there is a relationship with *x.* Otherwise, the relation is a *nonbinding* one, as in aggregates.

Strictly speaking, all material systems, such as human beings, have the following characteristics [102]:

(i) a **composition *C***, *i.e.* the total of all components of a system, such as the human organ systems,
(ii) an **environment *E***, *i.e.* all things outside the system which are influenced by it or its components or can take an influence on the system, such as the chemical, biotic and social environment of humans,
(iii) an internal structure (**endostructure S_i**), *i.e.* all relationships between the components of a system, such as the relationship between the subcellular components of a cell,
(iv) an external structure (**exostructure S_e**), *i.e.* all relationships between a system or its components and the material objects in its environment, such as the relationship between the cell and the extracellular environment. The total of exo- and endostructure forms the **overall structure *S*** of the system.

Corresponding to the three system characteristics *C, E,* and *S,* any material system *s* can be represented as a simple qualitative model *m* – a so-called *CES model* - to be expressed as:

$m(s) = (C(s), E(s), S(s))$.

The methodological relevance of this insight to practical research will be made clear in the present contribution. May it suffice here to have a look at a term closely associated with the system concept, *i.e.* system characteristics. Such system characteristics, often also called *emergent properties,* can be understood in two different ways:

(i) Qualitative characteristics of a whole which none of its components have individually *(''The whole is more than the sum of its parts'')*. Example: ''life'' as an emergent characteristic of cells, since the individual molecular cell components themselves do not have this characteristic.
(ii) Qualitative characteristics which a material object acquires when it becomes a component of a system. Example: the DNA incorporated in the extragenomic and cellular supersystem, has other properties than an isolated DNA thread. Finally, the process generating such emergent characteristics is called *emergence,* whereas the loss of such system characteristics may be called *submergence.*

stances will lead from an initial to a final state – the *modus operandi* of a system, and therefore a mechanismic explanation will answer the question about the *dynamics* (Why does it change?) of facts and conditions [100] and/or the underlying factors [43, 102, 109] (more about mechanisms [106, 109]). Only when such an explanation has been given, has a domain been known satisfactorily from the scientific point of view [110]. Similarly, the process of knowledge in the factual sciences as a rule develops from description to subsumption and finally to mechanismic explanation.

From the history of science angle, it is interesting to observe that apparently all factual sciences go chronologically through the stages of statics, kinematics and dynamics: physics as well as biology and psychology have developed from purely descriptive to mechanismic-explanatory sciences [100, 106]. For nutritional science, a similar trend can be recognized in the field of nutrition physiology [111–114]. Thus, in vitamin C research, for instance, the three stages mentioned can be easily identified: in the static stage (''What is there?'') it was said that a vitamin C deficiency will lead to scurvy. The question ''How does the vitamin supply status change as a function of uptake?'' (kinematics) was answered by means of vitamin C kinetics, and on this basis reliable recommendations were made for vitamin C uptake. In the stage of dynamics (''Why does it change?'') the physiological function of vitamin C and its role in connective tissue integrity was shown.

As a matter of fact, the statistical correlations uncovered by descriptive and experimental nutrition epidemiology (such as association of vitamin C deficiency and scurvy symptoms), require an explanation, *i.e.* identification of a mechanism. Thus, the (negative) methodological rule says: without knowing the mechanisms there is no mechanismic explanation and therefore no true understanding of the object studied. This means that mechanisms precede explanation *ontologically* and explanation precedes understanding *epistemologically* [106, 109]:

Mechanism (ontological level)
↓
Explanation (epistemological level)
↓
Understanding (psychological level).

8 Microreductive explanation and microreductionism

Mechanismic explanations, according to the thesis developed so far, are the aim of factual sciences and thus of nutritional science. Consequently, the explanation provided in connection with the vitamin C example above should be satisfactory as far as cognition goes. But is it really? In fact, many nutrition scientists may consider this type of explanation superficial, as it says nothing about how and why a vitamin C deficiency leads to inner bleedings and finally to death. This means that a more profound type of explanation would aim at explaining the physiological condition of "internal bleedings caused by vitamin C deficiency" at the cellular and biochemical level by referring to the role of ascorbic acid in collagen synthesis (Excursus 3). The death of x would then be explained as follows:

Premise 1: All people taking up $<y$ mg of vitamin C in the time interval t_0–$t_{>0}$ will show a reduced cotranslational prolyl/lysyl hydroxylation of procollagen at time $t_{>0}$.

Premise 2: This molecular defect leads to an impairment of the structural integrity of the connective tissue collagen in humans.

Premise 3: This leads to brittle blood vessels and inner bleedings and death after a prolonged period.

Premise 4: x has taken up $<y$ mg of vitamin C in the time interval t_0–$t_{>0}$.

Conclusion: x has died.

This type of mechanismic explanation is also known as *microreductive explanation* or *top-down explanation* which means that a fact concerning the organism as a whole (the *macrofact* "death of *x*") is explained by deduction of the statements that relates to a fact concerning one of its subsystems (the *microfact* of "reduced cotranslational prolyl/lysyl hydroxylation of procollagen"). Or to put it in simple terms: a microreductive explanation explains the behavior of a complete system by deducing it from that of its subsystems [48]. Correspondingly, atomic processes are explained on the basis of the insights into the behavior of subatomic particles (electrons, protons, neutrons); we try to understand cellular processes on the basis of insights into their subcellular components, and the behavior of multicellular organisms is finally explained at the cell biology level. This type of explanation then is the same that we can consider characteristic of modern natural sciences including biosciences. The underlying epistemological position is called *microreductionism* or simply *reductionism*. It says that a system is considered sufficiently recognized and explained if we know what components it is made of [43, 102, 109].

Since its establishment by the French philosopher *René Descartes* (1596–1650), microreductionism has actually proved to be a very successful research strategy. So much so that it could simply be considered identical with scientific methodology. Thus, in the final analysis, the advancement of the natural sciences in the course of the past 400 years seems to have been brought about by the success of microreductionism [43, 102, 109]. It is not surprising therefore that microreductive explanations are also very popular in the disciplines of bioscience. Genetic reductionism such as it has spread in

Excursus 3. The function of L-ascorbic acid (Asc) in the human organism [115–118]

BLAST-based sequence comparisons suggest that the human genome does not contain any L-gulonolactone oxidase (GLO) "coding" gene. This means that in human tissues GLO activity cannot be detected. However, as GLO is required for the synthesis of Asc (2,3-didehydro-L-threo-hexano-1,4-lactone), this finding already leads to the hypothesis that the human organism does not synthesize Asc. If, moreover, Asc is assumed to have a specific biotic function, another hypothesis can be formulate, *i.e.* the hypothesis of the vitamin function of Asc in humans. And it is indeed necessary to supply Asc from outside to maintain the integrity of the human organism. Consequently, if Asc supply is stopped, typical vitamin C deficiency symptoms, called scurvy, will develop after some time. The four major signs of scurvy include *ecchymosis* (subcutaneous bleeding), *fatigue* (exhaution), *gum bleeding* (gingival bleeding) and *hyperkeratosis* (keratinization of the skin). The first-mentioned finding leads to the assumption that Asc has a function in the connective tissue. More detailed studies have shown that in fibroblasts Asc has an effect on collagen synthesis, in myocytes on fatty acid oxidation, and in adrenal medulla on catecholamine synthesis. At the tissue level, a vitamin C deficiency means reduced collagen formation in the connective tissue, reduced fatty acid oxidation in the muscles, and disturbed catecholamine synthesis in the nerve tissue.

In subsequent studies, Asc was identified as an essential cofactor for the dioxygenases (DO) prolyl 4-, prolyl 3- and lysyl hydroxylase. These DO are relevant to the structure and function of collagen, as they cause the cotranslational hydroxylation of proline and lysine residues in the procollagen. Six other Asc-dependent human DO and/or monoxygenases (MO) are currently known: trimethyllysine and γ-butyrobetaine hydroxylase (carnitine synthesis), dopamine β-hydroxylase (norepinephrine synthesis), 4-hydroxyphenylpyruvate dioxygenase (HPPD; tyrosine degradation), peptidylglycine-amidating MO (pituitary peptide hormone synthesis) and HIF prolyl 4-hydroxlase (HIF-1a-dependent gene expression; HIF, hypoxia inducible factor). Finally, it has been possible to clarify the molecular function of Asc as a DO-cofactor: Asc reduces enzyme-bound Fe^{3+} to Fe^{2+} and thus prevents the inactivation of the DO that requires bivalent iron, α-ketoglutarate and oxygen to be active. Asc, as a reducing agent, therefore has an enzyme-protecting function. Thus, the enzymatic functions of Asc in connection with collagen biosynthesis are due to its properties as an electron donator. Other effects of vitamin C, such as the promotion of intestinal iron absorption, the protection against LDL oxidation, or the reduction of monocyte aggregation, are also connected with the electron donator function of Asc. In addition, a recent publication [119] shows that the Asc-dependent type I collagen prolyl 4-hydroxylase hydroxylates, and thus stabilizes, the argonaute 2 protein. As argonaute 2 is an essential component of the RISC complex (RNA-induced silencing complex), Asc also seems to play a role in the posttranscriptional regulation of gene expression.

the biosciences since the detection of the DNA structure by Watson and Crick [120, 121] may be the most striking indicator that most biodisciplines feel committed to the microreductionist research program [122, 123]. Thus, today almost every approach to research and attempt at explanation in the biosciences has a primarily genetic orientation [124, 125], so that some authors have spoken about "the doctrine of DNA" [126] and called our current scientific era "the century of the gene" [127]. Correspondingly, in developmental biology there is a trend to reduce ontogenesis to differential gene expression and to explain morphology and physiology in terms of molecular genetics [128–130] and/or chemistry and physics. Thus, the microreductionist statement of *Francis Crick* (1916–2000): "*The ultimate aim of the modern movement in biology is to explain all biology in terms of physics and chemistry*" [131] has obviously been confirmed. The exponentially growing flood of data in the field of genomics is perhaps the most evident sign of the molecular–microreductionist revolution in the modern life sciences [132].

9 Molecular nutrition research as a mechanismic-explanatory discipline

The time of a pure phenomenalistic type of descriptivism (motto: "Describe the phenomena, but do not explain them!") is definitely over in the factual sciences where mere description and subsumption is no longer adequate [43, 106], nor is it in nutritional science. If it is correct to say that mechanismic explanation is one of the primary aims of factual sciences [48], we can understand why nutritional science has entered a molecular stage, as molecular nutrition research is the attempt to find profound mechanismic explanations for the organisms' conditions, properties and changes that are related to the organism–nutritional environment interaction. Molecular nutrition research is rightly expected to make "essential contributions to our understanding of the nutritive effects on complex biological processes" [19]. And obviously, the commitment to the microreductionist research program mentioned above is a guarantee that the molecular approach will be crowned with success also in nutrition research.

Molecular nutrition research has in fact contributed already to a deeper understanding of the phenomena of nutrition physiology. The mechanismic-biochemical substantiation of the lipostatic theory, for instance, is one example. It says that the level of fat storage controls energy supply. For decades, the connection between the depot fat and the control of energy supply could only be expressed at the level of description and subsumption. Only by means of positional cloning of the leptin gene was it possible to identify leptin, the fatty tissue hormone responsible for energy supply [133]. Then the leptin-mediated physiological responses to weight loss and weight gain were decoded at the molecular level, *i.e.* the relevant central and peripheral leptin receptor-mediated signal paths could be detected mechanismically [134]. Seeing the lipostatic theory from the molecular perspective also led to the recognition that the fat tissue was an endocrine organ. The detection of the respective adipokines and their receptors also made it possible to identify nutrition-depending organ interactions including the effect of fatty acids on adipokine release and inflammatory processes. Thus, the example of leptin shows that molecular nutrition research contributes to a deeper understanding of facts and conditions related to nutrition physiology and can guide research in an innovative direction. Does the microreductionist approach then represent the ultimate way toward gaining new knowledge in nutrition research as well?

10 Molecular nutrition research and the specter of physicalism

At this point at the latest we should stop our self-criticism for a while. If the research program of microreductionism were really taken seriously, there is no reason why the epistemological reduction should end at the molecular level. The biochemical explanation for the death of x in our above vitamin C example – reduced cotranslational procollagen prolyl/lysyl hydroxylation – could be further reduced to the atomic or even subatomic level of explanation: if, in the final analysis, chemical processes are nothing but physical processes, it should in principle be possible to explain the electron donator function of vitamin C in the procollagen hydroxylation in terms of biophysics or even quantum physics. Thus, molecular nutrition research would finally be reduced to *subatomic nutrition research*. Will the molecular revolution be followed by the subatomic one? Will we create professorships of subatomic nutrition research in future replacing molecular nutrition research? Will molecular nutrition research and/or the microreductionist approach on which it is based lead to physical aporia as its final consequence? Will the nutrition scientists with a molecular orientation in the end, like Goethe's sorcerer's apprentice, be unable to get rid of the microreductionist ghosts they conjured up?

Our answer to the questions raised above is a clear *No*, as we together with other authors [43, 48, 51, 102, 135–137] consider physicalism an illusionary project that has ultimately failed. According to that project, the world should be explained solely from the angle of physics (*radical epistemological microreductionism*), as ultimately all real objects are *nothing* but physical objects (*ontological or eliminative reductionism*) [138–141]; (on the history of physicalism see [142]). From an epistemological perspective, it may suffice to say in this context that chemistry or biology cannot *completely*, at best *partially*, be reduced to physics, neither conceptually nor theoretically or explanatively [143, 144]. Whereas in complete or far-reaching theory reduction the theory to be reduced will follow logically from the basic theory, a partial or moderate theory reduction will lead to additional assumptions that are not part of the basic theory [43]. Most examples hailed as successful microreductionism actually are examples of partial reductionism [145].

The most important counter-argument against the physicalistic and/or radical microreductionist program, however, is not an epistemological but an ontological one [146, 147]. If the emergentistic view outlined in Excursus 3 is correct, new systems are forming in the course of cosmologic evolution with emergent characteristics – characteristics that its isolated components are lacking. Ontologically, it is therefore impossible to reduce these novel types of system characteristics completely to those of their components. Organisms, for instance, are *also, but not only,* physical and chemical objects, of course. In short: all truly biotic characteristics and facts/conditions are, and continue to be, of the same supraphysical nature as all really social facts are, and continue to be, of a suprabiotic nature – or else they would stop being biotic or social. Not even the fact that in the individual case it may be possible to *partially explain* the mentioned system characteristics by an analysis of their components, will alter this situation. Because a fact/condition will not be eliminated ontically by an epistemic operation, such as an explanation [102]. Therefore, a phenomenon of life, such as nutrition, will remain a phenomenon of animated systems even if it can be explained in chemical—physical terms – there is no nutrition of molecules, only of organisms. Figure 4 visualized the differences between physicalism (ontological microreductionism) and emergentism.

11 About the failure of radical microreductionism – the example of the human genome project

The microreductionist research program has no doubt been impressively successful – also in nutritional science. Nevertheless, the thoughts outlined in the last paragraph above have clearly shown that even this approach has its limits. In sober fact and looked at more closely, we must in fact admit that radical reductionism has failed in all disciplines of factual science [145]. This is shown very clearly by the example of the human genome project with its genetic-reductionist background [148, 149] which starts from the assumption that the DNA itself or a ''genetic program'' based on it has all ''genetic information'' needed to determine the development of the organism and its functions [124, 126]. In that case, the organism seems to be nothing else but an epiphenomenon of its genes [125, 128–129]. Thus, the expectations of sequencing the human genome were high. In 1991, Walter Gilbert, one of the most renowned molecular biologists, still upheld the thesis that, once the complete DNA sequence of the human genome was known, we would finally know what makes the human being so special [150].

Today, after we know the sequence of the human genome, the initial euphoria has given way to disillusionment and a greater realism [151]. Although the human genome project represents a masterpiece of great research teams in molecular biology and bioinformatics [152, 153], even stubborn gene freaks must admit that the data it offers are in themselves not able to answer any of the really interesting biological questions. Thus, for instance, it does not answer the question of how a complex multicellular organism will develop from a single zygote.

Today genetic reductionism must in fact be considered disproved [154]: genes simply do not have any ontic, let alone causal, priority in ontogenesis. Genes certainly are necessary factors in the regulation of physiological processes, but they alone are not sufficient because their function is context dependent, *i.e.* the biotic function of a gene critically depends on the extragenomic and cellular environment. One reason being that co- and posttranscriptional processes, such as the alternative use of promotors, alternative splicing, trans-splicing, *antisense* transcription and RNA editing, may lead to the creation of a multitude of proteins with different functions from a protein-coded gene (more precisely: a transcriptionally active region) depending on cell type, developmental timepoint and environmental factors [155, 156]. No wonder then that there is no correlation between the number of genes of an organism and its morphological complexity – a finding known as the *g-value paradox* [157, 158]. However, present findings on how to explain the function of non-protein coding genes, such as

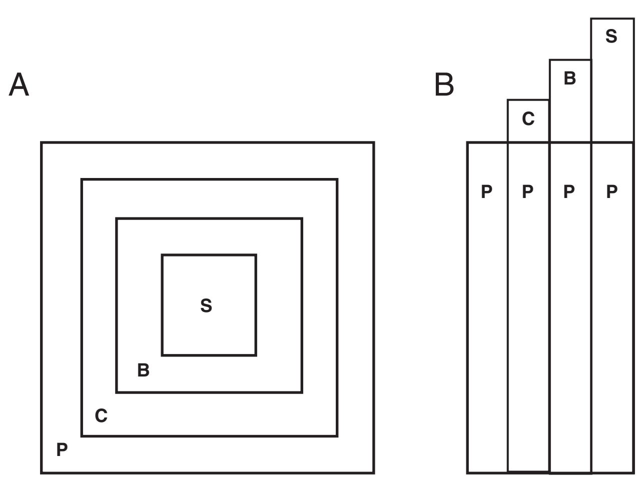

Figure 4. Visualization of the differences between physicalism (ontological microreductionism) and emergentism (referring to [47]). A visualizes the concept of physicalism. According to it, the real world is a system of Chinese boxes. Things at a higher level are just special cases of lower levels. B visualizes the concept of emergentism. According to it, the real world is a telescopic system. Higher levels are composed of things that possess emergent properties in addition to properties of things at lower levels. P: Physical things; C: Chemosystems; B: Biosystems; S: Sociosystems.

the regulatory function of certain pseudogenes [159, 160], suggest that the paradox will at least partially be solved in the next few decades. And yet, the fact that protein coding and non-protein coding genes are incorporated in a network of epigenetic factors we are just now beginning to understand, defeats every idea of genetically determined developmental processes. Another reason being that stochastic processes, such as "developmental noise", are a constituent element of the phenomena of life [161] – a fact that can already be demonstrated today at the gene expression level by modern methods of molecular biology [162–167].

In summary, against the background of the above, we have no choice but call the project of genetic reductionism an illusionary and failed endeavor [154, 168].

12 Microreductionism is dead – long live microreductionism in molecular nutrition research!

How inappropriate all research activities are that exclusively focus on radical microreductionism will be understood in the light of Excursus 3 which presents the characteristics of a material system consisting of the triad "composition – environment – structure". Accordingly, a system is considered fully characterized if all three aspects are taken into account. An epistemological insight resulting from this systemistic thesis will be that a system and/or its characteristics, conditions and changes can only be considered fully known, if both its composition and its environment and structure are included in its examination. We already mentioned above that the biotic function of a gene depends on the interaction with the extragenomic and cellular environment and therefore is context-dependent. Correspondingly, most of what is really of biological interest is *above* the level of the genes and therefore of an *epi*genetic nature. Insights of this kind have finally been the reason for a rising number of biologists to refer to the limits of the microreductionist approach [169–172] or to even speak of the end of "naïve reductionism" [173, 174].

In this situation, we now find ourselves confronted with a (false) paradox in nutritional science. We refer to the impressive success of microreductionist research programs, especially in the neighboring biosciences, and we announce its failure at the same time. Therefore the question is: is molecular, and thus microreductionist oriented, nutrition research a promising project *or* a paper tiger, overrun by time conceptually and methodologically dead even before it was born?

If we pass in review the aspects mentioned above, we recognize that microreductive explanations in the strict, but not in the moderate, variant must be considered a failure. Whereas the success of *complete microreduction* is the exception in all factual sciences, the success of partial or *approximate microreduction* is the rule [100, 106].

Whereas strictly microreductionist explanations are by no means adequate operations for a successful gain in knowledge [102], a moderate microreductionism still has its justification – also in nutritional science. One reason being that the microreductionist program has great heuristic value [175]. Also in nutritional science, the alternative of radical reductionism is not antireductionism, but *moderate microreductionism*. This is the research maxim saying that all system characteristics, conditions and changes in condition should be reduced as far as possible to those of their components without ignoring the relationship of the system in question with its superior system. The condition of an object cannot be fully explained if the object is analyzed separately from the condition of the system in which that object is integrated [145].

This is illustrated clearly when we go back to the vitamin C example described above. With the insight that a vitamin C deficit is associated with a disturbances of the catecholamine synthesis, a microreductive explanation seems to have been found for the macrofact of "tiredness"; a psychic condition was reduced to a biochemical one. In actual fact, however, we are faced here with a *partial* microreductive explanation at best, because a *full* explanation of tiredness as a mental (psychic), *i.e.* emergent, condition of neuronal systems would require, among other things, that findings of neurobiology and neuroanatomy be considered additionally, *i.e.* to integrate the biochemical detail of "reduced catecholamine synthesis" in a wider context.

The fact that the context, especially the environment, is important to understanding a system can be illustrated by further examples, *e.g.* by the example of the glucokinase gene (position 7p15 in the human genome) [176]. Thus, the cellular and organismic function of the gene's product, the glycolytic enzyme glucokinase, cannot be understood by focusing only on its biochemical function. As we know, glucokinase phosphorylates glucose to produce glucose-6-phosphate, whereby the K_m value for glucose lies in the range of physiological glucose concentrations. The human genome, however, has several genes "coding" for enzymes with identical activities. But these enzymes have different K_m values and can be detected in different cell types where they have different functions. Thus, glucokinase in the β-cells acts as a primary regulator of the glucose-controlled insulin release [177], whereas in the hepatocytes glucokinase facilitates glucose uptake and is therefore essential for the appropriate regulation of a network of glucose-responsive genes [178]. As this example shows, the cellular function of a gene product depends on the interaction with other cell components. But then the cellular function of glucokinase does not say anything about its biochemical function. Therefore we need a *systemic approach*, such as it results from the CES model presented in Excursus 3. It says that, according to the methodological approach, every system should be analyzed in respect of both its composition and structure and in respect of its environment. Such a systemic approach would combine reduction ("disintegration") and integration [48, 102, 137]. The significance of the last-mentioned operation for our understanding of biotic systems is recognized by an increasing number of biologists who favor an integrating approach. The key word in this connection is "systems biology" which is celebrated as the innovative research program [170, 174, 179, 180], leaving it unclear, however, whether or not it is in the end nothing but the reanimation and costly 'Omic' variant of time-honored physiology [174].

Whatever the decision may be, we cannot go into any further detail here about this development, which is relevant to nutritional science. May it suffice to mention that with the help of the systems biology approach it has been possible, at least in the field of microbiology, to develop a model of the interaction of nutrition factors with the genome by using the respective algorithms [181].

13 Molecular nutrition research – conclusions

Starting from an analysis of the scientific status of nutritional science, the intention of this contribution has been to show where molecular nutrition research stands. The basic questions in this context that are relevant to the way the discipline sees itself will be raised here again. These are the questions of the (i) **research strategy**, the (ii) **cognitive aims** and the (iii) **scientific status** of molecular nutrition research.

(i) **Research strategy.** Methodologically, a mechanismic-explanatory discipline such as molecular nutrition research is bound to a microreductive research approach. We emphasize, however, that it need not be a radical microreductionism whose scientific reputation, as we know, is not the best. We and others favor instead a moderate microreductionism, which combines reduction with integration. Even though we think that the microreductionist program is not adequate in bioscientifically oriented nutritional science, we value the heuristic potential of the microreductionist approach sufficiently to recommend that it be practiced for this reason alone. As Vollmer says [175]: *"[..] if systems can be explained in terms of their components, we will only find out when we try. But if they cannot be reduced, this too can only be found out by trying it persistently."*

(ii) **Cognitive aims.** As mechanismic explanations are one of the primary aims of factual sciences, we consider it the task of molecular nutrition research to find profound, *i.e.* molecular-mechanismic, explanations for the conditions, characteristics and changes of organisms related to the organism–nutrition environment interaction. This also includes the attempt to contribute to a deeper understanding of nutrition physiology phenomena, but without the wish not the ability to reduce nutrition physiology completely to biochemistry and molecular biology. Apart from this explanatory function, molecular nutrition research has

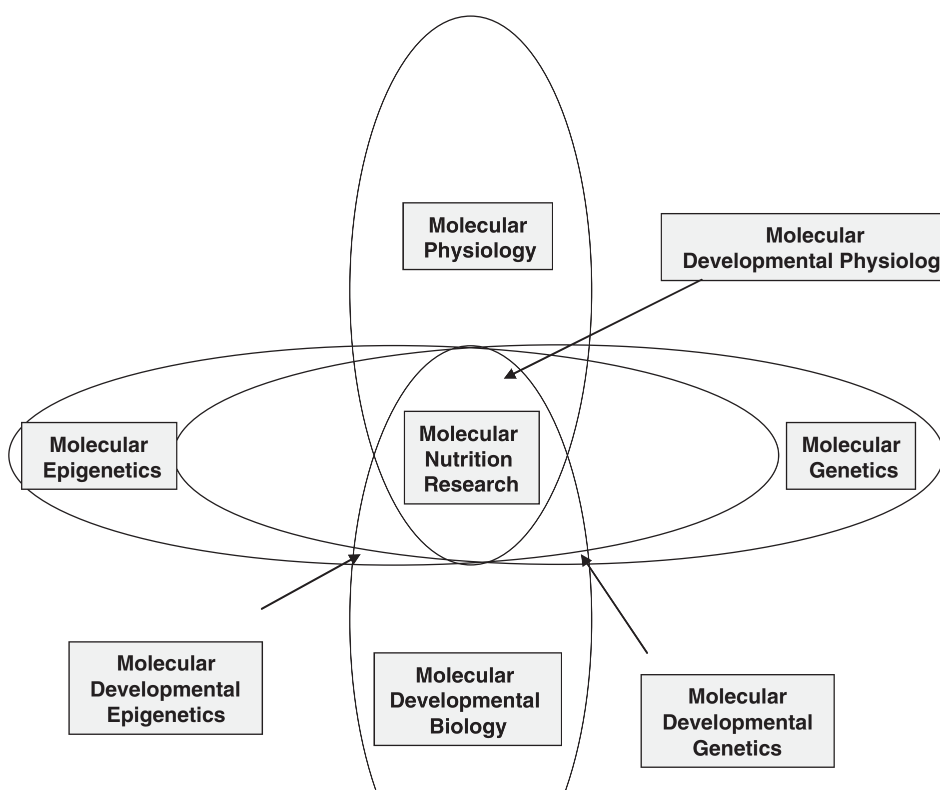

Figure 5. Molecular nutrition research at the interface of various bioscientific disciplines [18].

a heuristic potential for nutrition physiology. Thus, on the basis of molecular findings new working hypotheses for nutrition physiology can be developed. In this sense molecular nutrition research has a guiding function for nutrition physiology. This applies to both the basic and the application-related orientation of nutrition physiology.

(iii) **Scientific status.** As the focus is on the biological aspects of "nutrition", molecular nutrition research can be seen as a special form of bioscience. As a multidiscipline, it is to be located at the interface of other biodisciplines (Fig. 5). From this angle, it is obvious that the most noble objective of molecular nutrition research is the pure gain in knowledge, and this is why we consider it as a basic science. For its legitimation, let me make a psychological remark at the end: molecular nutrition research is simply interesting!

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14 Glossary

Axiology
The theory of values

BLAST
Basic Local Alignment Search Tool, heuristic algorithm to compare nucleotide or protein sequences

Biotic
The characteristics, processes or facts/conditions connected with living systems (biosystems)

Biological
Concerning biosystems and/or representing the →biotic

Emergence
A gain of a property of a →system which cannot be derived from the characteristics of the individual elements

Epistemic
The characteristics, processes or operations connected with gaining knowledge

Epistemological
Philosophical term, concerning knowledge and/or representing the → epistemic

Epistemology
The study of cognition and knowledge; philosophical discipline which deals with knowledge in general and is partly descriptive, partly normative. Normative epistemology is also called → methodology.

Hypothesis, scientific
A well thought-out, explicitly stated/formulated and testable assumption

Method
An explicitly direction for a course of action. More precisely: a rule and/or a number of rules for a structured and systematic procedure.

Methodic
A number of → methods that are used in a particular field

Methodology
Normative → epistemology, a philosophical discipline dealing with the methods of gaining knowledge.

Ontic
Philosophical term: the real, irrespective of how or whether it is known

Ontologic(al)
Philosophical terms: concerning the →ontic and/or representing the ontic

Ontology
A branch of philosophy that deals with the most pervasive features of reality, i.e. the most general characteristics of being and becoming

Semantics
The field that studies the contents of concepts, statements, statement systems (→ theory) and arguments

System
→Ontological term referring to the cohesive whole of parts that have binding relations

Theory
A system of hypotheses related to one another by the logical relation of deduction (hypothetico-deductive system)

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