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Short Communication

Side effects of problem-solving strategies in large-scale nutrition science: towards a diversification of health

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Solving complex problems in large-scale research programmes requires cooperation and division of labour. Simultaneously, large-scale problem solving also gives rise to unintended side effects. Based upon 5 years of researching two large-scale nutrigenomic research programmes, we argue that problems are fragmented in order to be solved. These sub-problems are given priority for practical reasons and in the process of solving them, various changes are introduced in each sub-problem. Combined with additional diversity as a result of interdisciplinarity, this makes reassembling the original and overall goal of the research programme less likely. In the case of nutrigenomics and health, this produces a diversification of health. As a result, the public health goal of contemporary nutrition science is not reached in the large-scale research programmes we studied. Large-scale research programmes are very successful in producing scientific publications and new knowledge; however, in reaching their political goals they often are less successful.

Problem solving: Interdisciplinarity: Science policy: Health

Studying complexity

The character of scientific inquiry, inside and outside nutrition science, is rapidly changing. As questions grow more complex[1], scientists often work in large collaborations spanning multiple disciplines[2–5]. Scientific problems are tackled in novel ways, as the following illustrates[6]:

> ‘Scientists need to know what lunch consists of, what *defines* a lunch [...]. Some of us are exploring the intricacies of lunch, reducing it to our intellectually preferred level of understanding. The physical biochemistry of toasting (why does the bread turn brown rather than some other color, say aquamarine?); the physiology of water homeostasis in lettuce, and how to keep it from wilting; the molecular biology of casein digestion by bacteria (and what makes cheese taste so good); and innumerable studies on pastrami and its relatives. This is, in short, why science is so hard. We ask so many h ard questions, at so many different levels. [Now] look how many people have contributed to our study of lunch, and none of them comes up on a PubMed search for “lunch”.’

Additionally, the realisation has emerged that relationships between science, industry and society are changing[7,8] and scientists are increasingly devoting resources to contextual issues, such as communication and ethics, in addition to bench research[9]. ‘Soft’ issues, including communication, and norms and values equally contribute to the complexity of contemporary science.

Collaborations amongst large numbers of different scientists are actively sought by policymakers on the basis that a multidisciplinary approach will solve complex problems and resolve political goals, for example, a cure against a disease, the construction of a tool, health promotion and reduction of public health costs. Nutrition science and especially its newest sibling, nutrigenomics, are equally subject to this trend.

Over the course of the last 5 years, we have studied nutrigenomics with a focus on the complexity of solving problems in multi-site, multi-disciplinary settings. We have chosen two research programmes fitting this multi-sited, multidisciplinary character, to study in more detail, namely the Gut Health research programme, an eight-laboratory collaboration, funded by Senter/IOP (Innovatiegerichte Onderzoeksprogramma) in the Netherlands, and The European

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Nutrigenomics Organisation (NuGO) funded by the European Union FP6 programme. Both are multi-million Euro research programmes, involving hundreds of scientists. In the present article, we will mainly refer to the Gut Health research programme. Over the last few years, we have conducted thirty in-depth, conversation style interviews, performed extensive observations at programme meetings, conferences and symposia in the Netherlands, Poland, Spain, Italy, New Zealand and Australia and spent several months observing in four different laboratories (about 1 month each), sometimes participating in bench work, a method called 'participant observation'[10].

In the present study, we demonstrate that large-scale collaboration is very difficult and that it may not yield the desired outcome: solving or contributing to resolution of a complex problem. We also highlight one of the effects of the large-scale collaborations: the ability to modify or even change the notion of health. The present article presents a short communication of our main findings, written as a historical report. A lengthy empirically supported analysis can be found elsewhere[11]. While not every research initiative is the same, the analysis presented here helps in the understanding of similar dynamics of collaboration and their effects.

Solving problems

The work nutrition scientists do, whether alone or in cooperation, and the knowledge they construct, is loaded with norms and values. It is, for instance, about establishing technical norms, such as determining threshold values in measurements or statistical tests, but also about setting norms on what constitutes 'proper' scientific practice, content or behaviour. Scientists use norms but they also set them through standards, materials and methods in which norms are embedded[12] (for example, consensus over default settings). While, in nutrigenomics multiple norms can be identified, here we will focus on the most prominent one: health. Similar to most of nutrition science it has a normative mission: public health, or 'health for all'. This is, by any standard, an immensely ambitious research goal.

In practice, scientists deal with problems, which they are convinced can be solved. Over 20 years ago, Fujimura coined the notion of 'doability'[13] to describe this particular quality assigned by scientists to research questions and problems. Before a problem can be solved, it must be made doable.

Making something doable takes a lot of work. Experimental strategies have to be designed, partnerships have to be built, materials have to be acquired, experiments have to be fine-tuned and much more. Making a problem doable is about changing elements in the research situation to make everything fit together. The elements that are manipulated and modified differ from problem to problem, and solving a problem is thus a matter of puzzling and continued reassessment. Further, it is not just material elements that are subject to modification: many researchers must also manipulate standards, ideas, hypotheses and norms.

When large numbers of scientists cooperate in projects such as Gut Health or NuGO the major research challenges are divided into tasks, which are in turn divided into manageable parts. In the case of the Gut Health programme, problems were divided on a technological axis (the proteomics and the transcriptomics of gut health) and a nutrient axis (probiotics, fatty acids or amino acids as exemplary nutrients). Supplemented with two bioinformatics initiatives (database building and pathway analysis), this resulted in eight sub-problems, each roughly corresponding to a particular laboratory. Both the problem and the organisation that attempted to solve it were made modular: every member laboratory got its own sub-problem to deal with.

Within this modular topography, experiments are carried out, which address each laboratory's own perspective on their element of the problem. Together the scientists in the Gut Health programme worked on 'gut health and function', but simultaneously, none of them did. Similar to the quote near the top of the present article in the case of the concept of 'lunch', the word 'health' will not (or at best: rarely) pop up in the articles resulting from the Gut Health programme. Tackling the individual research questions, belonging to separate problem modules, is perceived to be difficult enough without dealing with the larger research challenge too, and is therefore given priority:

> 'I think that everybody does his own thing, eventually [...]. I cannot say that people who work in a different group add something to my subject. Everybody does one's own thing. I am together with [Z003 and Z002] and others have teamed up in other groups.' *Interview Scientist W006, 20050919*[11].

However, focusing on smaller problem modules creates complex dynamics within the larger research programme. Modules of the overall research challenge are given priority over the larger research question, and in making these problem modules feasible, they are subtly changed, ultimately moving away from the original research challenge.

Cooperation between these modular structured research groups can be very difficult, especially when they have different disciplinary backgrounds. An example of such interdisciplinarity exists between laboratory practice and bioinformatics: here we can even speak of different styles of science – 'wet' and 'dry' research[14,15]. Differences between 'wet' and 'dry' research result in numerous practical problems in daily cooperation. These different styles have different ideas about notions of 'truth', 'significance' or 'relevance'[16]. Since the ingredients of the 'wet' and 'dry' sub-problems are different, both on a material level (different tools, etc), as well as on a conceptual level (different notions and hypotheses, etc), they display different strategies in making problems doable.

Just as the whole is more than the sum of its parts, solving a complex problem is more difficult than solving its sub-problems. Making a sub-problem doable introduces change and making all the sub-problems doable introduces a lot of change. Not all of these changes can easily be incorporated into the overall problem since they can be mutually exclusive (for a number of examples, see Penders[11]), which makes the ties between certain sub-problems weak.

Changing norms

The notion of health is not immune to such change, and so it was observed in the Gut Health programme. To make sure a sub-problem was made doable, for example, to ensure an experiment provided the desired results, the notion of health is subjected to change. Experiments in nutrigenomics solely

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provide data on a molecular level and the concept of health is matched to the research situation accordingly. Influenced by the genomic technology, the notion of health was made 'molecular'. Healthy, or not so healthy, was and is often expressed in terms of molecules, whether proteins, mRNA or metabolites.

Since there were multiple sub-problems, which were addressed in several laboratories, many modifications to the concept of health took place. Different laboratories used different micro-array platforms, which require different sample preparation protocols and procedures. Influenced by the modularity of the research situation, health was made situated. This implied that the norms for the boundary between health and disease (whether fully articulated or more implicit), which concentrations of which molecules are considered normal or abnormal, differed between them. For an individual to be healthy according to the (implicit) norms for health in laboratory A did not mean the same individual was healthy according to laboratory B.

The presence of different styles of science within nutritional genomics introduced further diversity. Whether working in a laboratory or behind a desktop computer, the quest for doable research problems was equally prominent. However, the research situation was different. Laboratories deal with molecules and bioinformatics departments deal with datasets. Different styles of science speak in different (technical) languages, but they also conceptualise elements in the research situation differently. Whereas health in a laboratory was understood in terms of molecules, to bioinformaticians health was thought of in terms of data distribution and its subsequent analysis. Thus, the notion of health was not stable across styles and 'wet' (molecularised) and 'dry' (computation-based) concepts of health could be identified. Thus, location and specialisation are important in the understanding of health and approach to research challenges.

Scientists were and are really good at making the problems they deal with doable. They mobilise everything around them to make their experiments work and get their papers published, and they did so on a daily basis. This is the normal and accepted state-of-affairs of scientific inquiry. However, whilst scientists deal with sub-problems, the larger research challenges are described in research proposals and programmes, policy documents and funding reports. Societal relevance is drawn from that overall problem and its do-ability results from the integration of the local, situated doabilities of the sub-problems.

In the process of constructing these doabilities, multiple healths have come into being, some of them molecularised, some of them computation-based and all of them situated. The process of solving the sub-problems resulted in them diverging in the pursuit of research that can be done successfully and re-integrating can grow increasingly difficult.

Diversifying health

The larger a scientific collaboration, the greater number of sub-problems, the more difficult integration becomes. In the case of Gut Health, an eight-laboratory project, this integration appeared unsuccessful, notwithstanding the success of the isolated modules. The programme modules were very successful, publishing many articles, producing successful PhD theses and acting as the basis for raising further funding. With respect to its public health goal, success is still far away, while simultaneously many scientific accomplishments are celebrated. One can thus conclude that this big science programme failed and succeeded at the same time. Similar dynamics can be observed in other large-scale scientific endeavours. Take for instance, the 'war on cancer'. As a scientific project, many triumphant solutions to sub-problems can be claimed, but as a public health project, its overall goal of eliminating cancer still remains very much unattainable[17].

What can be considered 'health' or 'healthy' is not, and has never been, static. Changes occur in the ways in which health is understood or materialised in biomedical technology and technical norms or protocols. In social theory the molecularisation of health is suggested as a prominent trend[18]. In the present study of large-scale nutritional genomics practice, we observed that many versions of health exist in parallel and some can be thought of as molecularised, but not all of them. The uniform goal of a 'health for all' has not been brought any closer, while various different concepts of health proliferate. This diversification of health has made contributing to public health more difficult than ever. Furthermore, as knowledge on the molecular basis of nutrition increases and research questions grow even more complex, even more conceptualisations of health may arise.

Large-scale nutrigenomics was meant to contribute to public health and, while scientifically sound and increasingly successful, nutrigenomics has yet to address this overall goal. Our research has shown that this was not related to good or bad intentions or overpromising. If anything, the existing promises have acted to bring scientists together and keep them together[11]. However, the problem-solving strategy employed in contemporary large-scale research has unintended side effects: fragmentation and the subsequent prioritisation of fragments over whole. These side effects should provide us with food for thought with respect to the organisational, economical and scientific merits of large-scale research.

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