

## Nutri-informatics: a new kid on the block?

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**Abstract** From an epistemological point of view, nutritional physiology has been developed, like other factual sciences such as physics, from a purely descriptive to a mechanistic-explanatory scientific discipline. Nowadays, nutritional physiology has entered the molecular stage. Based on this micro-reductionism, molecular targets (e.g., transcription factors) of energy intake, certain nutrients (e.g., zinc) and selected plant bioactives (e.g., flavonoids) have been identified. Although these results are impressive, molecular approaches in nutritional physiology are limited by nature since the molecular targets of nutrients seem to have no ontic priority to understand the nutritional phenotype of an organism. Here we define, to the best of our knowledge, for the first time Nutri-informatics as a new bioinformatics discipline integrating large-scale data sets from nutritional studies into a stringent nutritional systems biology context. We suggest that Nutri-informatics, as an emerging field, may bridge the gap between nutritional biochemistry, nutritional physiology and metabolism to understand the interactions between an organism and its environment.

**Keywords** Micro-reductionism · Nutrigenomics · Nutritional systems biology · Nutri-informatics

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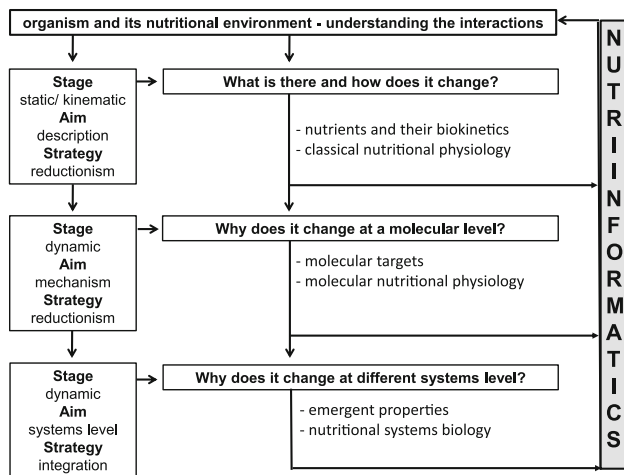
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Based on a view from history of science, it is interesting to note that factual sciences such as physics, biology and psychology have developed through the stages of statics, kinematics and dynamics (Bunge 2004). For nutritional physiology (Fig. 1), a similar trend from a purely descriptive to mechanistic<sup>1</sup>-explanatory scientific discipline can be recognized (Strohle and Doring 2010). For example, in the stages of statics (“What is there?”) and kinematics (“How does it change?”), nutritional physiologists identified the essential components of our diet and answered the question, how the status of nutrients may change as function of intake. On this basis, robust dietary recommendations were made for many nutrients. In the stage of dynamics (“Why does it change?”), the physiological and biochemical functions of the nutrients were unraveled. During the last two decades, nutritional physiology has entered a molecular stage (“What is the molecular mechanism?”). This kind of micro-reductionism has contributed to a deeper understanding of nutritional processes. For example, pioneering work on vitamin A as transcription factor ligands has been published for more than 20 years (Chambon 1996). More recently, by applying gene chip technology, we and others have identified molecular targets differentially regulated by dietary restriction (Giller et al. 2013), vitamins (Fischer et al. 2001), trace elements (Fischer et al. 2001; tom Dieck et al. 2003), and plant bioactives (Boomgaarden et al. 2010). Notably, dietary factors do not only regulate gene expression on the mRNA, but also on the micro-RNA level (Boesch-Saadatmandi et al. 2011; Gaedicke et al. 2008).

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<sup>1</sup> We used explicitly the term “mechanistic” (and not mechanistic) because not all mechanisms are physical—dependent on the systems level cellular and physiological mechanisms are relevant (see also footnote 3).



**Fig. 1** Nutri-informatics as a specialized bioinformatics discipline to integrate the different stages, aims, strategies and questions of basic nutritional science

Moreover, genome-wide association studies have been successfully used to pinpoint allelic variants explaining individual differences in macronutrient intake (Tanaka et al. 2013). More recently, nutritional epigenomics has been established to get insights, for instance, into persistent effects of prenatal exposure to famine (Heijmans et al. 2008). Even more sophisticated, the groups of M. Ristow and S. Schuster have shown that silico analyses of genome-scale human metabolic networks per se may help to discover novel pathways that might explain body weight reduction of low-carb diets (Kaleta et al. 2011). A comprehensive overview regarding the advancement of molecular nutrition research has been given by the groups of H. Daniel and B. van Ommen (Daniel et al. 2008).

No doubt, the success of the molecular approach in nutritional science is impressive. Nevertheless, the initial euphoria about the potential of molecular nutritional physiology has given way to a greater realism (see e.g., van Ommen 2007). In fact, molecular targets (i.e., transcription factors) of nutrients seem to have no ontic<sup>2</sup> priority to understand the nutritional phenotype of an organism: the function of a molecular target depends simply on its epigenomic and cellular environment. For example, the identification of genes differentially expressed under caloric restriction conditions in nearly 600 experiments is not meaningful to predict the resulting phenotype (i.e., longevity) of a restricted organism (Swindell 2008). We have recently shown that dedicated so-called Nutri-informatics tools and algorithms (i.e., Ortho2ExpressMatrix) enable functional classification, pathway analysis and

<sup>2</sup> Philosophical term: the reality, irrespective of how or whether it is known.

phylogenetic allocations are useful to relate molecular data with nutritional phenotypes (Ludewig et al. 2014). In this context, the nutritional phenotype initiative (i.e., dbNP) seems to be a very useful enterprise to understand the emergent<sup>3</sup> properties of an organism in response to nutritional cues (Norheim et al. 2012; van Ommen et al. 2010). To the best of our knowledge, the coinage Nutri-informatics was mentioned for the first time more than 10 years ago ([www.molnut.uni-kiel.de/pdfs/Popl\\_Vortrag/kurzfasung\\_nutriomic.pdf](http://www.molnut.uni-kiel.de/pdfs/Popl_Vortrag/kurzfasung_nutriomic.pdf)). Recently, the group of J. Zemleni has provided a comprehensive guidance regarding bioinformatics resources that are useful in nutrition sciences (Malkaram et al. 2012). Thus, the need of bioinformatics in nutritional research emerged with the “omic” era. Overall, Nutri-informatics can be defined as a specialized bioinformatics discipline to integrate large-scale data sets from nutritional studies into a stringent nutritional systems biology context (Fig. 1). In particular, Nutri-informatics should focus, for instance, on analyses of metabolic networks, mathematical simulation of metabolism [i.e., fluxomics (Winter and Kromer 2013)], genome-based identification of essentials nutrients, food genomics, integration of large-scale data sets derived from transcriptomics, proteomics and metabolomics, and promoter-framework analysis to define nutrient-dependent regulons. Thus, we suggest that Nutri-informatics, as an emerging field, may bridge the gap between nutritional biochemistry, nutritional physiology and metabolism. We emphasize that Nutri-informatics should be developed into a basic scientific discipline to understand the interactions between an organism and its nutritional environment, one of the most noble objectives of nutritional science. In addition, Nutri-informatics has a heuristic potential to foster rather applied disciplines. However, the scientific success of Nutri-informatics depends primarily on the formulation of unsolved fundamental and interesting questions, an inherent problem in nutrition science (Strohle and Doring 2010).

**Conflict of interest** Frank Döring declares that he has no conflict of interest. Gerald Rimbach declares that he has no conflict of interest.

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<sup>3</sup> Philosophical term: emergence, a gain of a property of a system which cannot be derived from the characteristics of the individual elements (i. e. molecular targets such as transcription factors) of the system.

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