Scale Relativity in Systems Biology of Muscular and Pulmonary Diseases

Charles Auffray[1], Laurent Nottale[2] and the SYSTEMOSCOPE Consortium[3]

1- Genexpress, Functional Genomics and Systems Biology for Health, LGN - UMR 7091 - CNRS and Pierre and Marie Curie University - Paris VI, 7, rue Guy Môquet - 94801 Villejuif, France, Phone: +33-1-49-58-34-97/98. E-mail: charles.auffray@vjf.cnrs.fr; URL : http://fre2571.vjf.cnrs.fr

2- Universe and Theories, LUTH - UMR 8102 - Paris-Meudon Observatory, Denis Diderot University - Paris VII and CNRS - 92195 Meudon Cedex . Tel: +33-1-45-07-74-03. E-mail: laurent.nottale@obspm.fr; URL : http://luth2.obspm.fr/~luthier/nottale

3- Dominique Charron, INSERM U 662 and IUH, Denis Diderot University - Paris VII; Jean-Pierre Françoise, UMR 7598 - CNRS and Pierre and Marie Curie University - Paris VI ; Bertrand Laforge, LPNHE - UMR 7585 - Pierre et Marie Curie University - Paris VI and CNRS; Jean-Jacques Kupiec, Centre Cavaillès, Ecole Normale Supérieure ; Giuseppe Longo, LIENS - UMR 8548, Ecole Normale Supérieure and CNRS ; Jacques Mallet, LGN - UMR 7091 - CNRS and Pierre and Marie Curie University - Paris VI; Christophe Pison, Valdur Saks, CHU Albert Michallon Hospital, Joseph Fourier University of Grenoble and INSERM EMI 221.

TRANSCRIPTOME 2005 will highlight the transition from Functional Genomics to Integrative Systems Biology for Health, after the successful meetings held in Paris (2000), Seattle, (2002) and Tokyo (2003) which led to a shared vision of Systems Biology as an integrative and iterative process based on interdisciplinarity and networking, and the formation of the SYSTEMOSCOPE International Consortium with Pr. Leroy Hood and Zhu Chen (Auffray et al., 2003a, b). We proposed as a working hypothesis that self-organization of living systems results from a conjunction of a stable organization with chaotic fluctuations (Auffray et al, 2003b), and recognized the need to measure small variations of a large number of weak signals with high throughput technologies developed under quality assurance.

To tackle the complexity of biological systems, and stimulate applications in preventive and predictive medicine, it appears necessary to integrate analytical approaches of discovery with systems theories and non-linear dynamics. The members of the French SYSTEMOSCOPE Consortium have endeavoured to develop a trans-disciplinary research and training program in systems biology, based on their extensive experience in mathematics, informatics, physics, biology and medicine.

We are designing and implementing a systems biology demonstration pilot project to measure dysfunctions of energy metabolism and modulations of gene expression profiles in skeletal muscles of patients with pulmonary diseases or cardiac failure, before and during rehabilitation of systemic myopathy. To ensure reliable experiment description and data integrity, and obtain the accurate and consistent data required to capture the multiple moderate but biologically important fluctuations which escape meta-analyses, we will use standardized measurement, annotation and biovalidation technologies. We intend to identify underlying functional and regulatory networks, to measure influence of the immune and nervous systems through genetic polymorphism studies, to formulate working hypothesis and test them, to iterate the process and assess improvement of models and methods.

We are using mathematical and computational tools to infer, model and simulate functional networks from large-scale expression datasets combined with genetic and phenotypic data, and to develop robust measures for biological functions and complexity. We are also simulating cellular differentiation with a selective model of stochastic gene expression regulated by dynamic constraints and epigenetic modifications, and constructing a theoretical framework to model attractors with variable numbers of dimensions in biological systems. Finally, we are combining the elements of modeling of scale relativity (Nottale, 1993) to describe the effects induced by non-linear scale laws, in order to relate properties of complex biological systems to underlying physical first principles.

The principle underlying scale relativity is to introduce at the most fundamental level the observation scales in the description of natural laws, and to found this description on the

principle of relativity extended to these new variables. It allows to construct scale laws which satisfy this principle, and to articulate them with the laws of motion, leading to a generalized quantum mechanics. This conceptual framework transcends classical and quantum physics to provide models for self-organized structures and behaviours which have already proved extremely valuable to describe evolving living systems (Nottale, 2004).

Auffray, C., Chen, Z., Hood, L., Soares, B., and Sugano, S. (2003a) Foreword: from the TRANSCRIPTOME conferences to the SYSTEMOSCOPE International Consortium. C. R. Biologies 326, 867-875.

Auffray, C., Imbeaud, S., Roux-Rouquié, M. and Hood, L. (2003b) From functional genomics to systems biology: concepts and practices. C. R. Biologies 326, 879-882.

Auffray, C., Imbeaud, S., Roux-Rouquié, M. and Hood, L. (2003b) Self-organized living systems: conjunction of a stable organization with chaotic fluctuations in biological space time. Phil. Trans. R. Soc. Lond. 361, 1125-1139.

Nottale, L. (1993) Fractal space-time and microphysics: towards a theory of scale relativity, World Scientific.

Nottale L. (2004) The theory of scale relativity: Non-differentiable geometry and fractal space-time. In Computing Anticipatory Systems, CASYS'03 - Sixth International Conference, Daniel M. Dubois, ed., American Institute of Physics Conference Proceedings 718, 68-95.
http://luth2.obspm.fr/~luthier/nottale/arcasys03.pdf