The computational foundation of complex biological systems: the role of modelling and analysis

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We argue that future success of systems biology will depend on fundamental research into the computational foundation of biological systems, and not simply on increasing the power or accuracy of existing computational or experimental techniques. This fundamental research must seek to investigate the structure, communication and dynamics within biological systems, and formulate appropriate computational frameworks and paradigms that aid their modelling, analysis and visualisation.

Modelling is the creation of a hypothesis about a biological process or sub-process. The model does not necessarily seek to emulate the process but can be instantiated with real-world data and must produce outputs that can be falsified by experimental evaluation. Analysis techniques such as simulation, animation or verification via model checking enable the building and execution of models *in silico* in order to obtain various dynamic characteristics and the querying of models to establish causal relationships between events. The goal of modelling is to achieve realization, a situation when a variety of simulations or verifications of the model consistently produce outputs that cannot be falsified by biological experimentation. The hypothesis building and experimentation process is iterative and dependent on close interaction between biologists and computer scientists. The critical test for success will be the ability to obtain novel scientific discoveries as a result of such a programme of research, and generate unpredicted insights into biological processes which could not be achieved by classical experimentation.

The challenge of understanding biological systems will require a joint effort towards creating computational models based on large-scale biochemical datasets and confronting these models with experimental reality. This requires fostering of inter-disciplinary collaboration, technological advancement and appropriate training programmes.