Feedback

Q1: During the lambda virus merging with the bacteria, there are two paths. There is an induction event that causes the switch from lysogeny to lysis. What is the cause for the induction?

A1: That might be exposure to UV light (at least in experiments). But basically it is any damage of bacterial DNA that will initiate switching.

Q2: If there are multiple stable states, which one is chosen?

A2: There are several mechanisms that can lead to switching between multiple stable states. But we probably don't know all the ways by which switching is performed in biology – even for bistable switching. However, the threshold mechanisms is certainly one of those: the system will switch once a concentration of certain key species is larger than a specific threshold. It was recently suggested by Kobiler et al. (PNAS, 2005) that the lysis-lysogeny decision in lambda phage infected E. coli makes use of such a mechanism. Also, it is assumed that stochastic effects (perturbations) lead to switching between different stable states. (Cf. SB3 lecture).

Feedback

Q3: How is reverse engineering related to complex systems?

A3: Reverse engineering is the traditional/customary approach to analyse and understand complex systems. It “is the process of discovering technological principles of a system through analysis of its structure, function and operation. It often involves taking something apart and analysing its working in detail, usually with the intention to [re-]construct” (Wikipedia) the system.

Q4: What is the “upper” level of abstraction?

A4: On the highest abstraction level (when using undirected graphs) we abstract from all other details except the relation between the components, for instance proteins (species). We still get insights/gain knowledge from this abstraction level by analysing the structure of the network (connectivity, degree distribution, robustness, community structure, …). The lower the abstraction level, the more details of the real system are taken into account – down to the level where every single component (e.g. molecule) is considered, including its temporal and spatial evolution.

Feedback

Q5: What examples are there of this sort of modelling leading to practical discoveries in biology that could possibly lead to medical applications?

A5: There are dozens of pathways that researchers model to gain insights into the dynamics and functioning such as the NFkB pathway, which is known to control diverse mammalian signalling responses that mediate cell survival, inflammation and immune response. It seems that aberrant regulation of NFkB underlies chronic and acute inflammatory diseases, autoimmune diseases and different types of cancer. NFkB and the signalling pathway that regulates its activity has become a focal point for intense drug discovery and development efforts (cf. Karin *et al.*, *Nat Rev* ***3***, 2004). Nevertheless, it is difficult to estimate how much computer models contribute to practical discoveries. Modelling certainly helps to gain biological knowledge, but usually in an indirect way (by guiding experimentation).