DEB and biochemical networks: a top-down view

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The past decades have brought an enormous amount of information on living systems. But although technical advances make data collection ever easier, the scientific community seems to remain unable to gain a bigger picture. One strategy to get a broader perspective is to treat living cells as a network, well-known in disciplines such as engineering and the social sciences. Hence, the past five years have seen a growing interest in the structure of so-called biochemical reaction networks (see e.g. [1, 2, 3]. The most basic feature of a network is its architecture. If you arrange a large collection of nodes (representing molecules in the case of a biochemical network), you can connect them in a number of ways: e.g. by linking nearest neighbours, or by selecting them at random and joining them together. A third strategy is to give a few of the nodes a very large number of connections and to allow the rest to have relatively few. These three kinds of networks exhibit different global features, even if it is assumed that they contain the same number of nodes and the same number of connections [4]. The number of connections per node for both regular and random networks e.g. has a roughly Poissonian distribution with an average value that gives a characteristic scale to the network. In the third kind of network, the number of connections per node falls approximately off as a power law. Because there is no characteristic peak value, this type of network is called 'scale-free'. Based on data from the WIT database [5], the topologic organisation of metabolic networks in 43 different organisms from life's three domains has been investigated [6]. These reaction networks have turned out to be scale-free. Some molecules, like pyruvate and coenzyme A are 'hubs', whereas the average molecule undergoes just one or two reactions. Furthermore, metabolic networks seem to be highly clustered,

and the network diameter, which is defined as the shortest biochemical pathway averaged over all pairs of substrates is surprisingly small (i.e. the 'small-world effect') [7]. Interestingly, it has been found that the metabolic network diameter is approximately the same for all the 43 organisms from the WIT database, irrespective of the number of substrates found in the given species [8]. This means that the connectivity per node must increase as the number of nodes increases. In contrast, all non-biological networks examined to date have a fixed average connectivity per node, which implies that the diameter of the network increases logarithmically with the addition of new nodes [9, 4, 10].

Up to now, quite some features of biochemical reaction networks have been mapped, but there is no theoretical background and therefore no hypotheses can be formulated. As Mr Newman put it in his review article: "We count triangles on networks or measure degree sequences, but we have no idea if these are the only important quantities to measure (almost certainly they are not) or even if they are the most important". Applying DEB to biochemical reaction networks may yield contraints on the architecture and other features of these networks, and hence might give new hypotheses. One way of putting this into practice would be to start with a very simple network and then building it up in a way consistent with DEB. However, it might also be possible to start by imposing constraints on a whole pathway/network at once. As an example could serve a very recent article by Kooijman and Segel [11], in which they applied the DEB-philosophy to a linear metabolic pathway. In this fashion, they were able to derive values for the handshaking parameters and the binding probabilities of the substrates in the pathway, given the reaction rates and the concentrations of the different enzymes involved.

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