The formation of segments in *Drosophila melanogaster*: a logical analysis.

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We present here a qualitative analysis of the genetic regulatory network made up by the segmentation genes, which determine the number of segments formed along the anterior-posterior axis of the *Drosophila melanogaster* embryo. Segmentation genes belong to two main classes: the maternal and the zygotic genes. The maternal genes are transcribed during oogenesis and their products (maternal organisers) deposited in the oocytes. The zygotic segmentation genes further split into three categories depending on the number of segments affected by their mutations: the gap genes affect several contiguous segments; the pair-rule genes affect complete alternate segments; finally, the segment polarity genes affect each segment. The segmentation genes constitute a hierarchical system, in which the interactions take place in a temporal order: the maternal organisers determine the activation of the gap genes; these together with the maternal organisers determine the activation of the pair-rule genes, which, in turn, determine the activity of the segment polarity genes. The cross-regulatory interactions between these genes help to the refinement of their final expression patterns.

On the basis of published data, we have derived a logical model for the key segmentation genes. As the segments in both the head and the tail are not very well defined yet, our analysis focuses on the formation of the trunk segments. In brief, we associate a multilevel logical variable and a logical function to each element of the network, taking into consideration whether this element interacts with more than one element in the network, and whether these interactions require distinct functional levels (e.g. concentrations of regulatory factors). In addition, the weights of the different interactions are quantified by logical parameters.

Our model allows the simulation of the kinetics of gene expression observed in the wild type fly, as well as the prediction of the phenotype of various mutants. Furthermore, our analysis emphasises the roles of the various feedback circuits present in the regulatory matrix, while specifying the range of parameter values associated with a proper functioning of these feedback circuits. For example, we show how positive circuits made of the cross-inhibition between segmentation genes allow the refinement of segmental boundaries. Finally, the disentangling of the segmentation gene network into well-defined sets of feedback circuits sharing one or several elements leads to the reconstitution of the different classes of segmentation genes defined by the molecular geneticists on the basis of mutant phenotypes.

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