

5 The Robustness of Gene Networks

5.1 Concepts

Morphogen Soluble molecule influencing the cell fate specification of a target cell. Typically the morphogen is secreted at a distance from its target. A morphogen can specify more than one cell type by forming a *concentration gradient*; in that case, the morphogen is said to convey *positional information*.

Modularity The degree to which a developmental process consists of separate elements^{1,2}. High *pleiotropy* implies low modularity.

5.2 Front and Back

5.2.1 A Simple Question

Every multicellular organism shows a distinct regional organization of cells, tissues and organs, otherwise known as its *body plan*. How exactly are cells organized into the different parts of an organism? This question is at the center of the whole of developmental biology and is, therefore, too broad for this lecture. However, to get a “feeling” for the answer(s) to this question we are going to consider one example of regional specification in some detail: anterior-posterior (AP) patterning in the early embryo of *Drosophila*³. This is one of the “success stories” of molecular developmental biology.

5.2.2 Maternal Influences

Crucial spatial information is conferred on the oocyte before fertilization. In the ovary, *nurse cells* transcribe *maternal* genes, and the resulting mRNAs are transported into the oocyte; the proteins resulting from the translation of these mRNAs regulate the transcription of *zygotic* genes. Four of these maternal genes are critical to the formation of the AP axis:

- *bicoid* (*bcd*) and *hunchback* (*hb*) for the formation of head and thoracic segments
- *nanos* (*nos*) and *caudal* (*cad*) for the formation of abdominal segments

Initially, the *hb* and *cad* mRNAs are distributed evenly throughout the egg, while the other mRNAs show a distinctive spatial organization along the AP axis:

- *bcd*: anterior (A)

- *nos*: posterior (P)

After fertilization, the mRNAs begin to be translated into proteins, and the following genetic interactions occur:

- BCD protein inhibits the translation of *cad*
- BCD binds to the enhancers of the *hunchback (hb)* gene, activating its transcription
- NOS protein binds to *hunchback (hb)* mRNA, preventing its translation in P

As a result, the following expression pattern is established in the early embryo:

- BCD and HB proteins: A→P gradient
- NOS and CAD proteins: P→A gradient

5.2.3 Segmenting the Embryo

The maternal genes regulate the *segmentation* genes that divide the early embryo into 14 *parasegments* along the AP axis. The larval and adult segments are generated based on these parasegments. Three groups of segmentation genes are expressed sequentially:

Gap genes are activated or repressed by the maternal genes, and divide the embryo into broad regions consisting of several parasegment primordia; e.g. *Krüppel (kr)*, *knirps (kni)*, *hunchback (hb)*.

Pair-rule genes are activated or repressed by gap genes, and subdivide the gap gene regions into parasegments; e.g. *hairy (h)*, *even-skipped (eve)*, *fushi tarazu (ftz)*.

Segment polarity genes are activated or repressed by pair-rule genes, and differentiate the parasegments into anterior and posterior compartments; e.g. *engrailed (en)*, *wingless (wg)*, *hedgehog (hh)*.

5.2.4 Robustness or Pleiotropy?

Comparative analyses suggest that insect segments are homologous. In addition, the sequences and expression patterns of segment polarity genes are more highly conserved among insects than those of the other groups of genes mentioned above. In addition, the segment polarity gene network appears to be robust to perturbation, leading to the suggestion that it could explain the genetic and morphological conservation². Alternatively, that might be explained by high interactivity between modules, leading to a high degree of pleiotropy^{1,4}.

5.3 Revision

The lecture notes for the previous lectures have been updated to correct minor mistakes. Three books^{1,5,6} have been added to the reserves section of M. D. Anderson Library.

5.4 Next Lecture

In the next lecture you will be given the first test. In the following lecture we will move to the topic of biases in development.

5.5 Literature Cited

1. Raff, R. A. *The shape of life: genes, development, and the evolution of animal form* (University of Chicago Press, Chicago, 1996).
2. von Dassow, G., Meir, E., Munro, E. M. & Odell, G. M. The segment polarity network is a robust developmental module. *Nature* **406**, 188–192 (2000).
3. Gilbert, S. F. *Developmental biology* 7th edn. (Sinauer Associates, Sunderland, MA, 2003).
4. Galis, F., van Dooren, T. J. & Metz, J. A. Conservation of the segmented germband stage: robustness or pleiotropy? *Trends Genet* **18**, 504–509 (2002).
5. Minelli, A. *The development of animal form: ontogeny, morphology, and evolution* (Cambridge University Press, Cambridge, UK, 2003).
6. West-Eberhard, M. J. *Developmental plasticity and evolution* (Oxford University Press, New York, 2003).