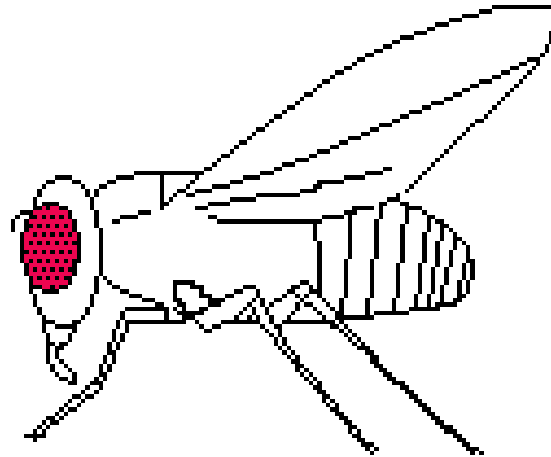


Spatial organization is a key difference between unicellular organisms and metazoans

Unicellular: Cells change function in response to a temporal plan, such as the cell cycle.

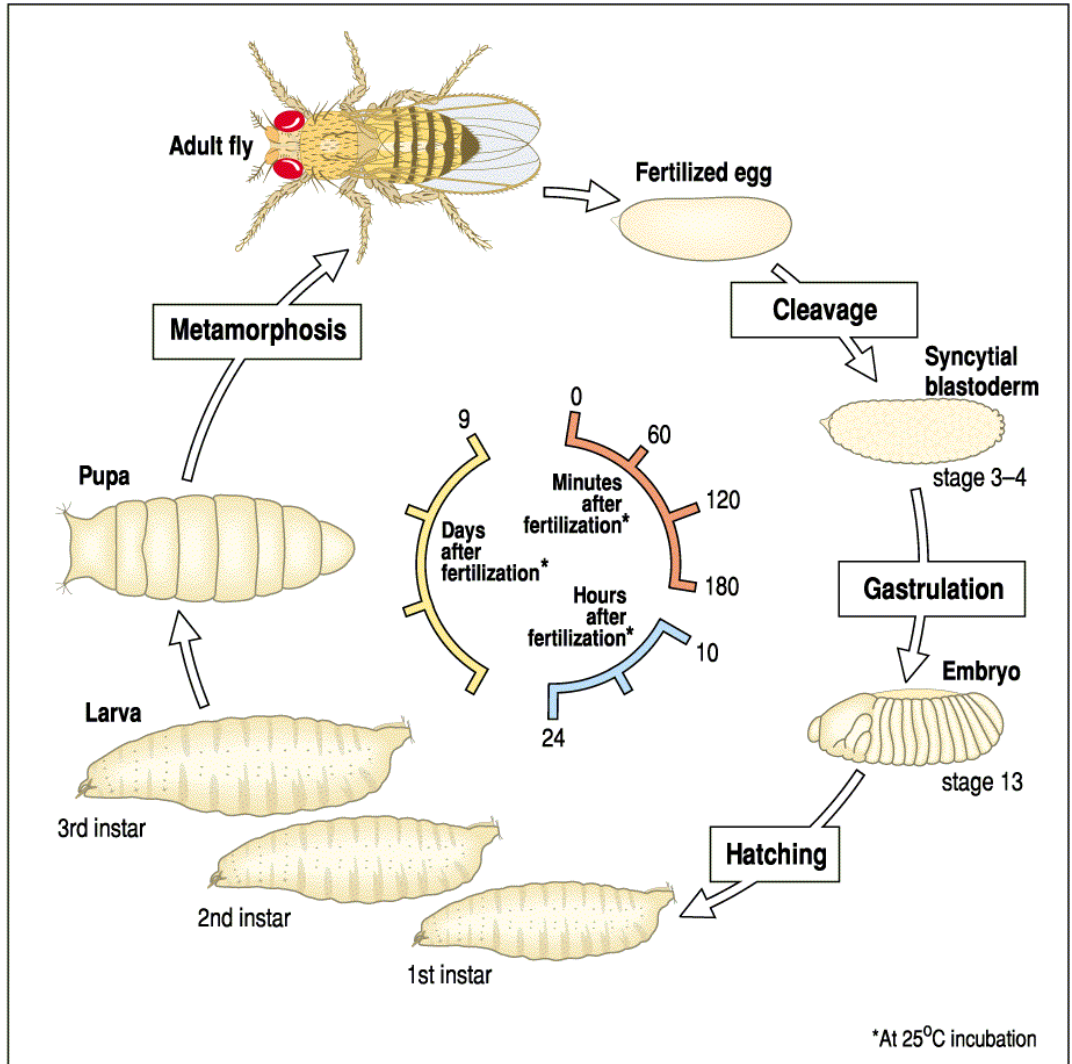
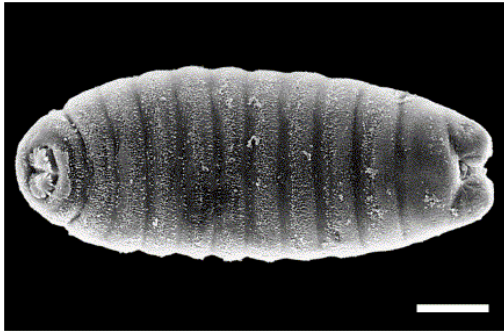
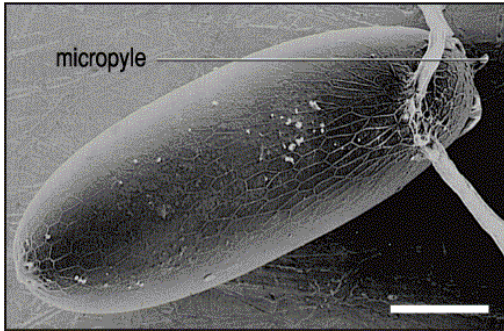
Cells differentiate **as a population** in response to environmental signals, e.g. sporulation, motile behaviour changes. Cells may change behaviour on a temporal plan, including but not limited to the cell cycle.

Metazoan: Specialized cell functions and differentiation occur based on **cell lineage and spatial location** within a body plan. Within this body plan, cells retain their specialized function despite environmental changes.

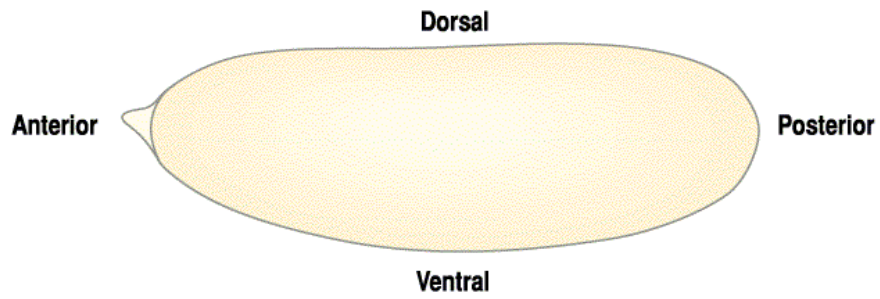


***Drosophila melanogaster* – fruitfly**

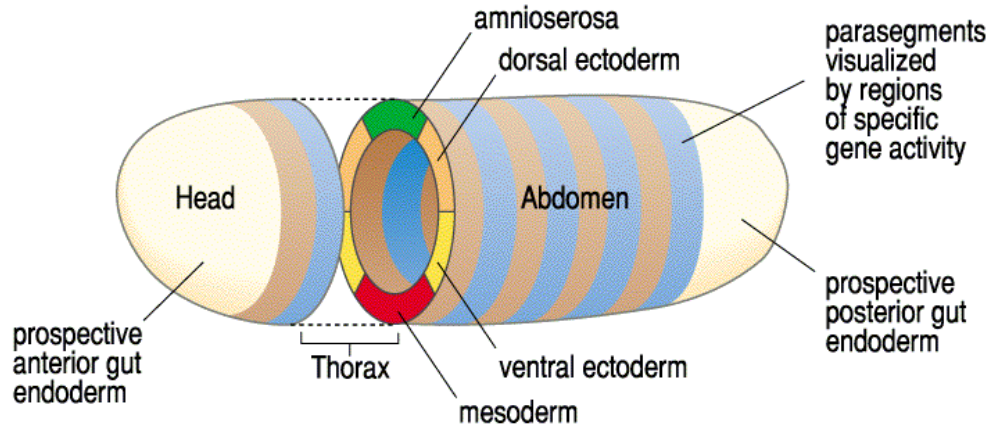
80 years of genetic studies have uncovered many developmental mutations. Molecular techniques have been applied extensively in the past 20 years, culminating in the complete genome sequence (137 Mb) of 13,500 genes in three large and two small chromosomes (www.fruitfly.org).



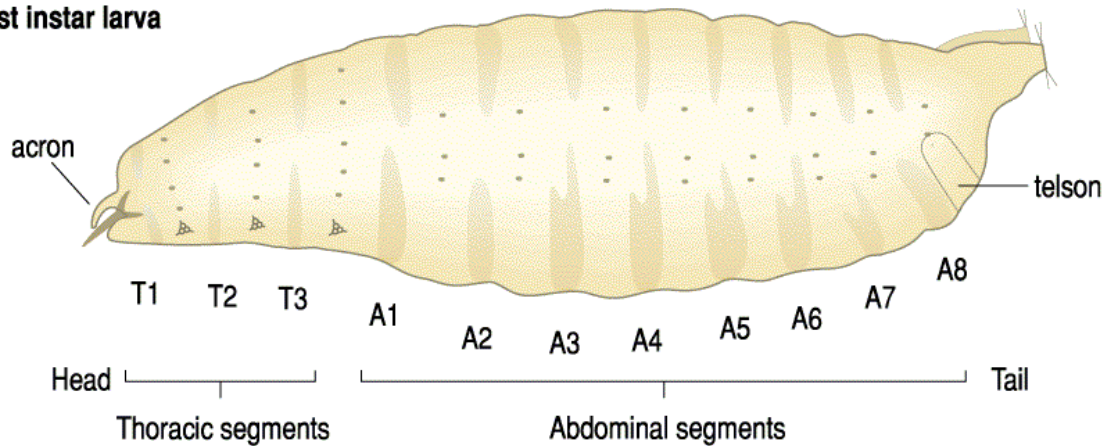
Egg

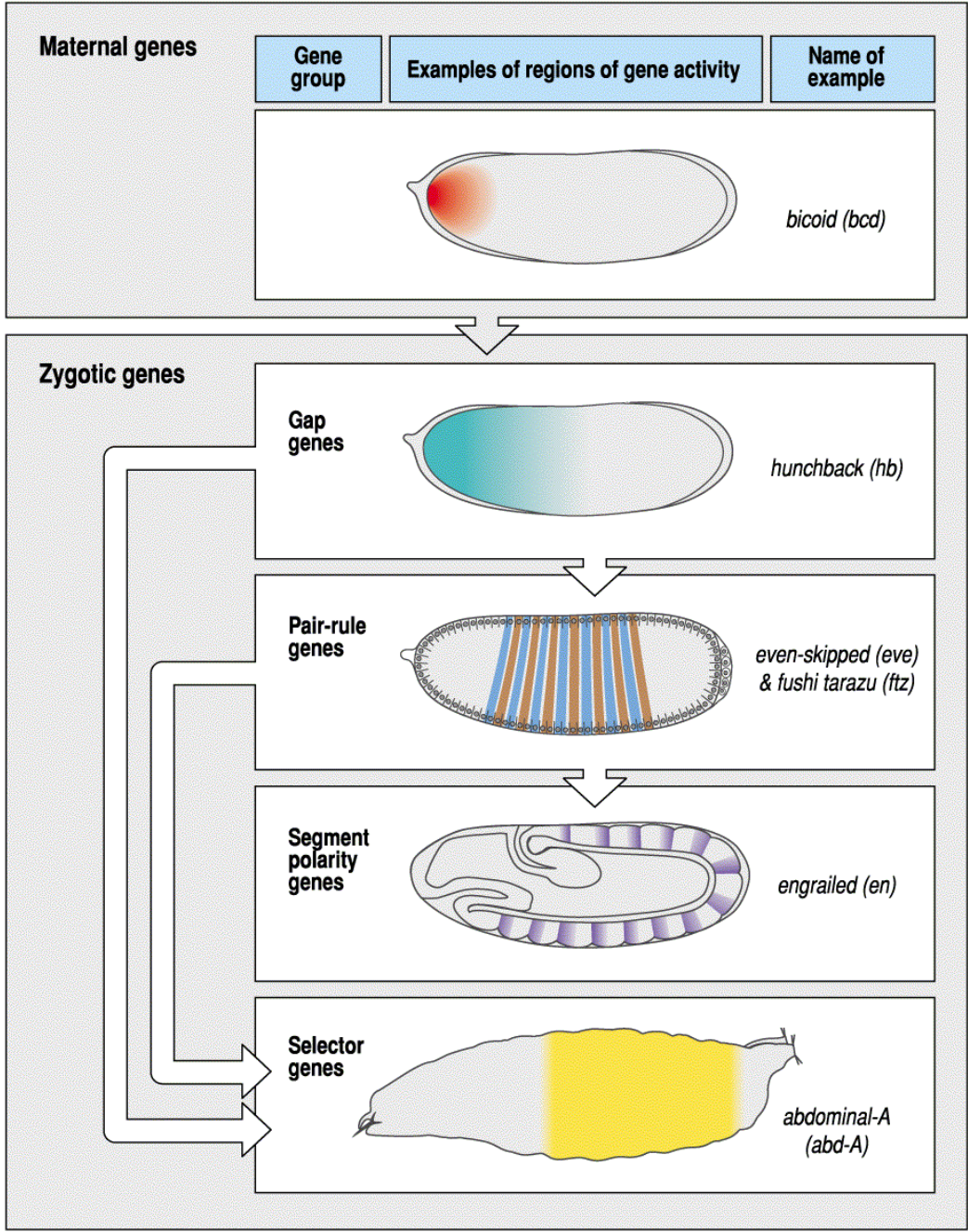


Embryo



First instar larva





Larva

Metamorphosis

Adult fly

salivary glands

Imaginal discs for:

mouth parts

antenna

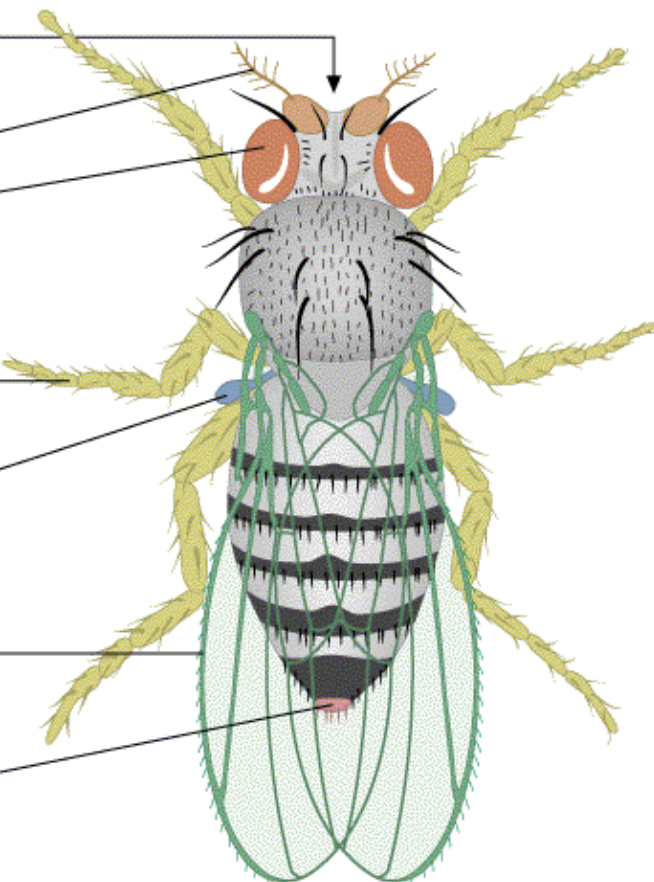
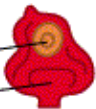
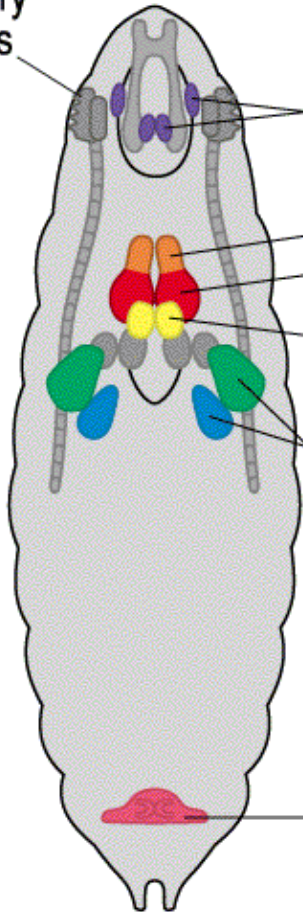
eye

leg

haltere

wing

genitalia



Drosophila development: the body plan

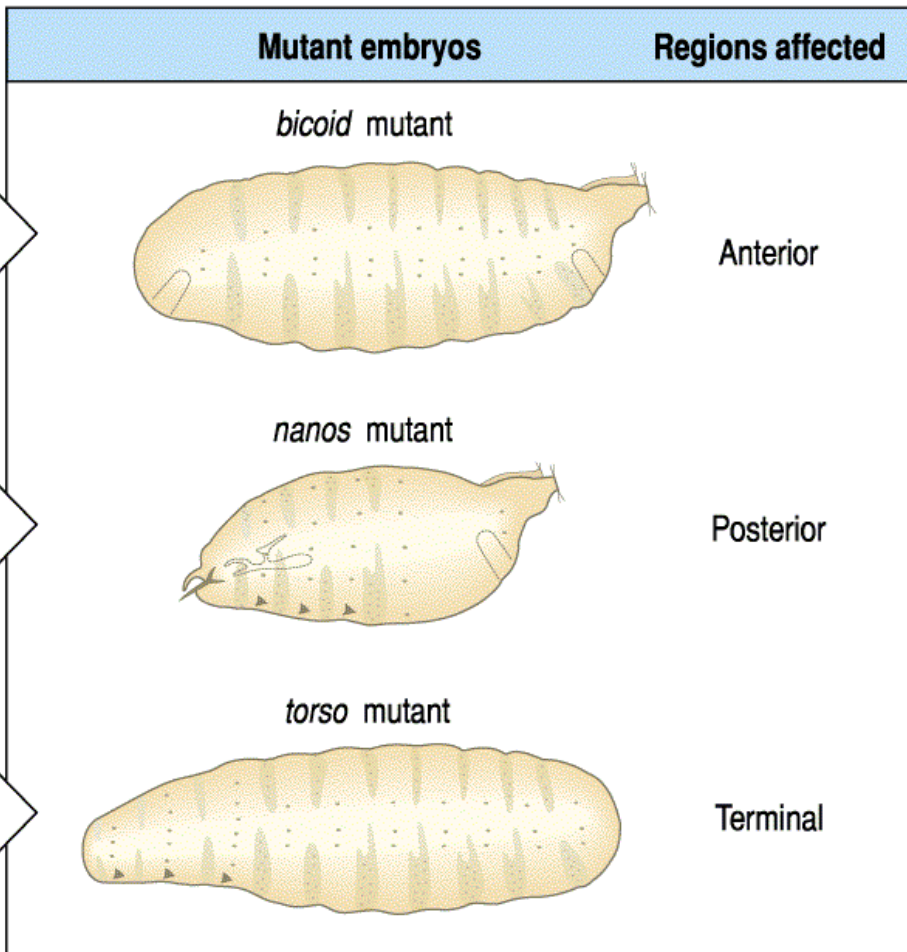
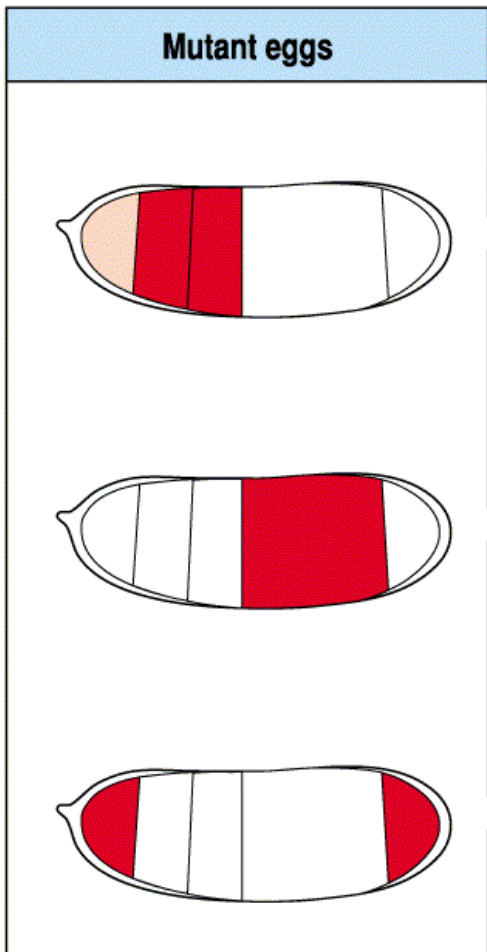
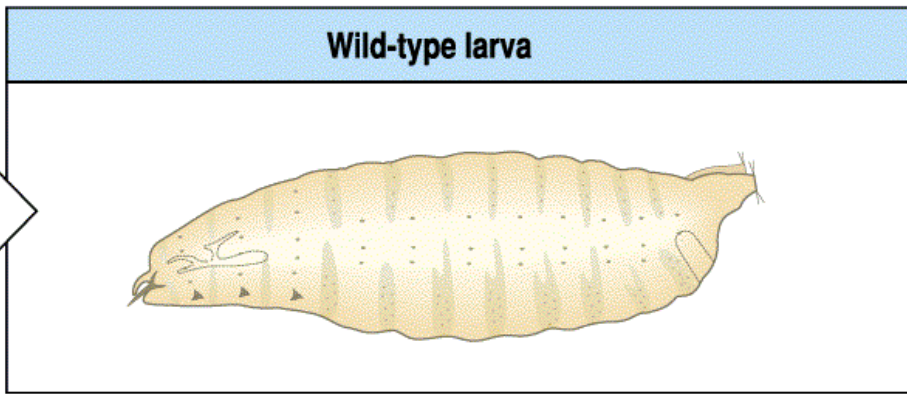
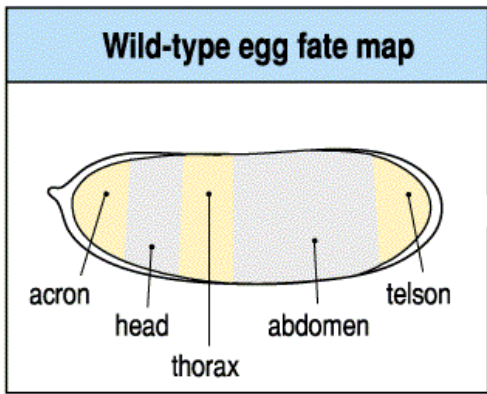
- Genes that control development in *Drosophila* are very similar to those that control development in vertebrates.
- *Drosophila* is the best understood developmental system with great impact upon our knowledge of all development. Bilateral symmetry is established by the A/P and D/V axes.
- The larvae has an anterior acron, three thoracic and eight abdominal segments and a posterior telson.
- Early patterning occurs in the syncytial blastoderm and it becomes multicellular at the beginning of segmentation.
- Concentration gradients of proteins (transcription factors) can diffuse, enter nuclei and provide positional information.

Drosophila development: maternal genes

- Maternal genes establish the body axes.
- Maternal gene products, mRNAs and proteins are expressed in the ovary.
- Zygotic genes are expressed by the embryo.
- About fifty maternal genes set up the A/P and D/V axes: the framework of positional information (spatial distributions of RNA and proteins).
- Zygotic genes respond to maternal gene expression.
- First broad regions are established, then smaller domains (with a unique set of zygotic gene activities) in a hierarchy of gene activity.

Drosophila development: the A/P axis

- Three classes of maternal genes set up the A/P axis
- Maternally expressed genes distinguish the anterior from the posterior.
- Maternal effect mutants result in females that can not produce normal progeny.
- Three mutant classes are 1) anterior, 2) posterior and 3) terminal classes.
- Anterior class: loss of head and thorax (sometimes replaced with posterior).
- Posterior class: loss of abdominal segments.
- Terminal class: missing acron and telson.
- bicoid, hunchback, nanos and caudal are key to A/P axis formation.



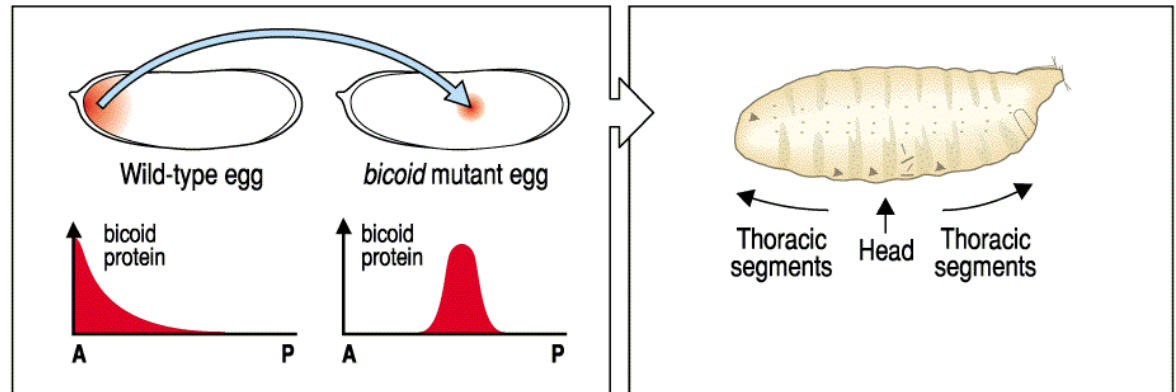
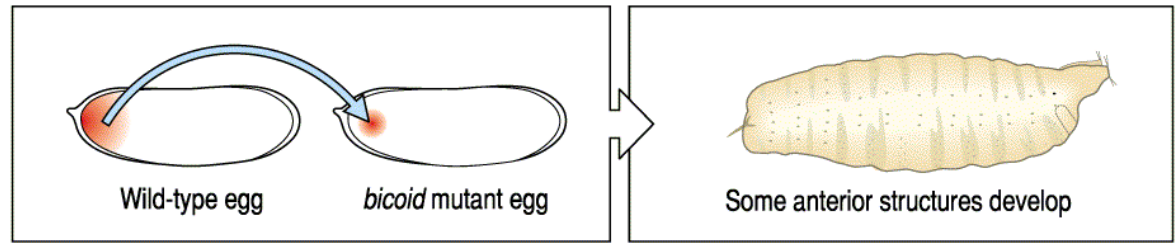
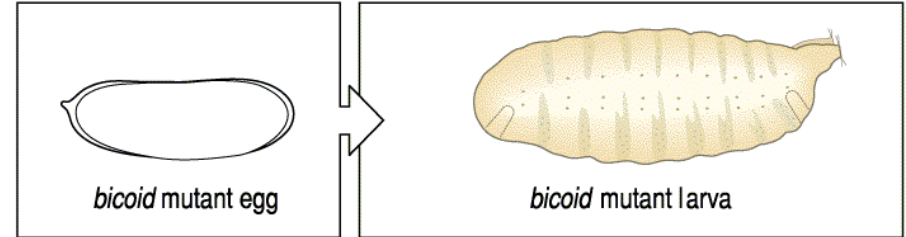
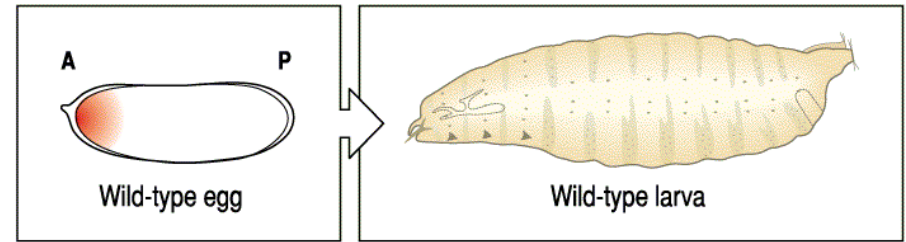
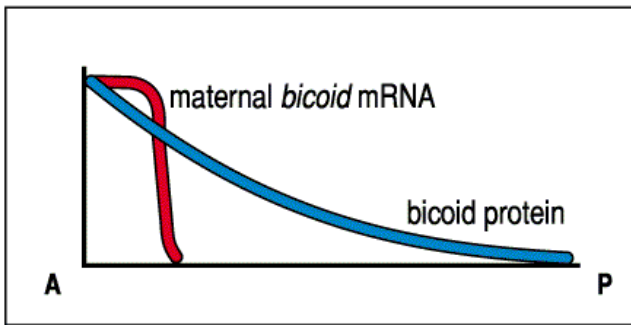
Drosophila development: maternal genes

- bicoid is sequestered in the oocyte during oogenesis.
- bicoid sets up a A/P morphogenic gradient and controls the first steps in embryo development and, thus, is essential to the developing organism.
- *bicoid* mRNA is localized to the anterior end of the unfertilized egg.
- After fertilization, the mRNA is translated and a concentration gradient is formed along the A/P axis. (bicoid was the first evidence of a morphogen gradient.)

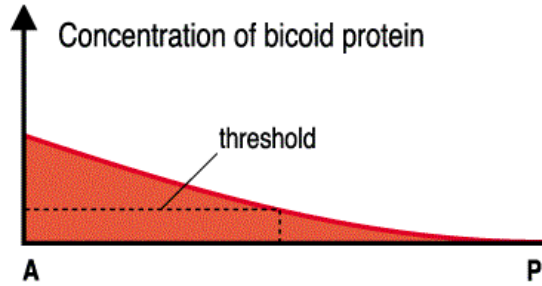
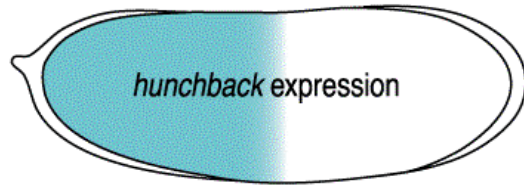
Maternal *bicoid* mRNA



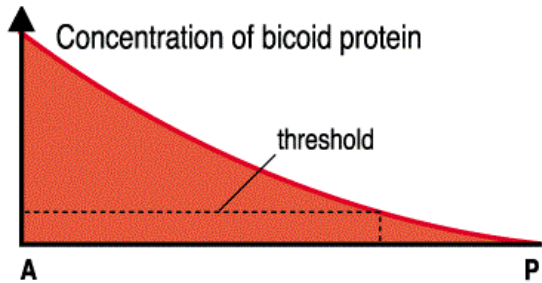
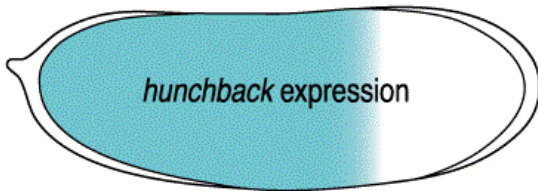
***bicoid* protein**

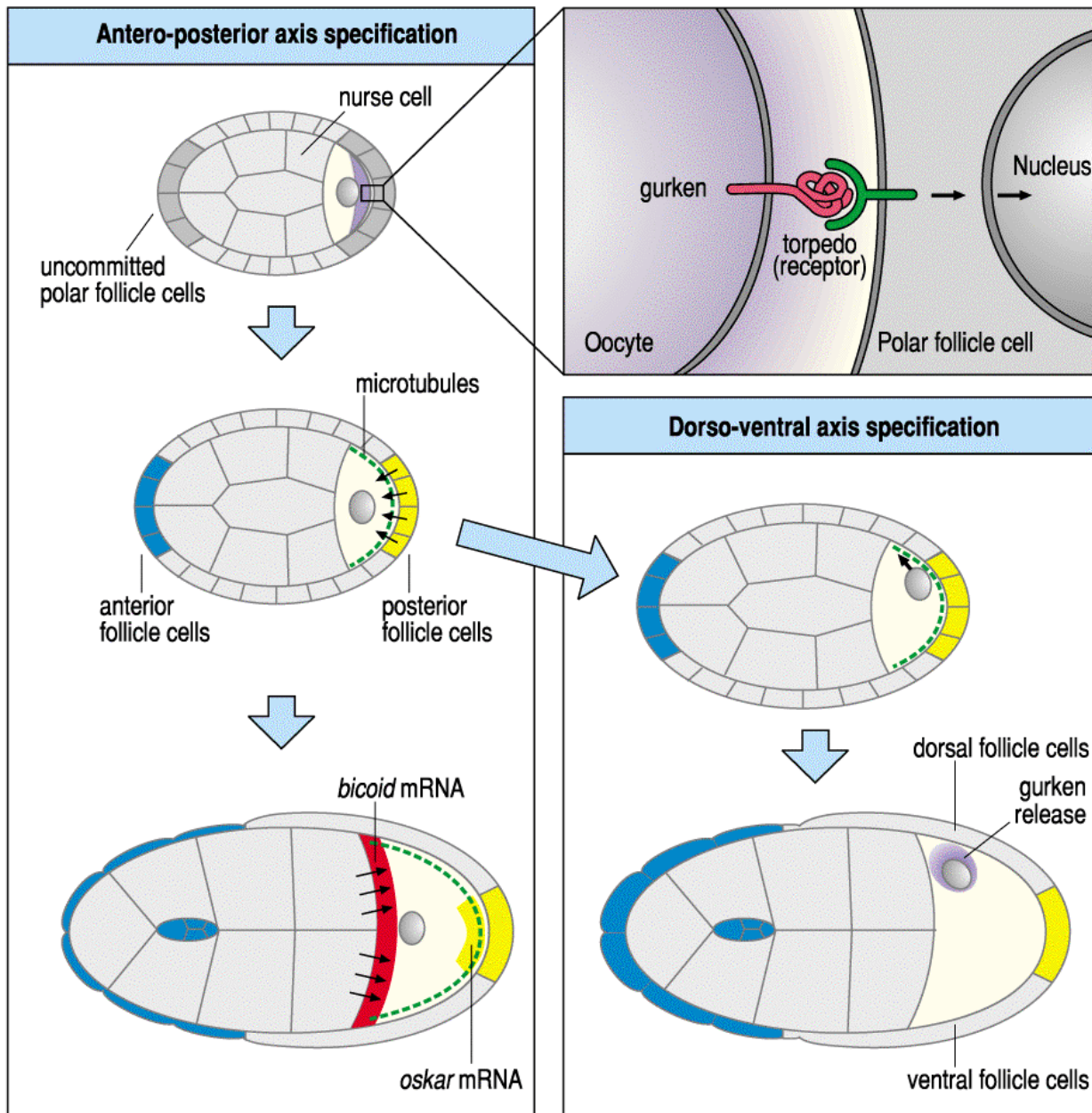


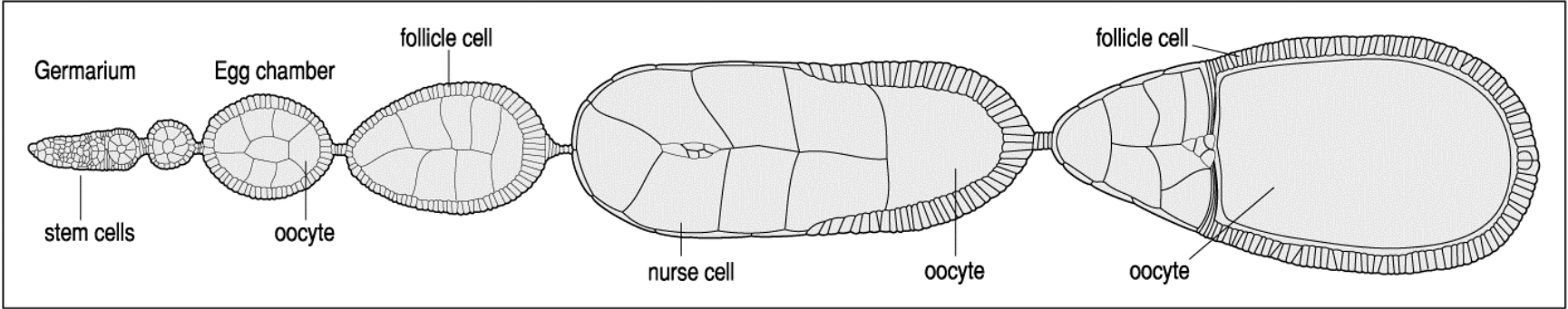
One dose of *bicoid*

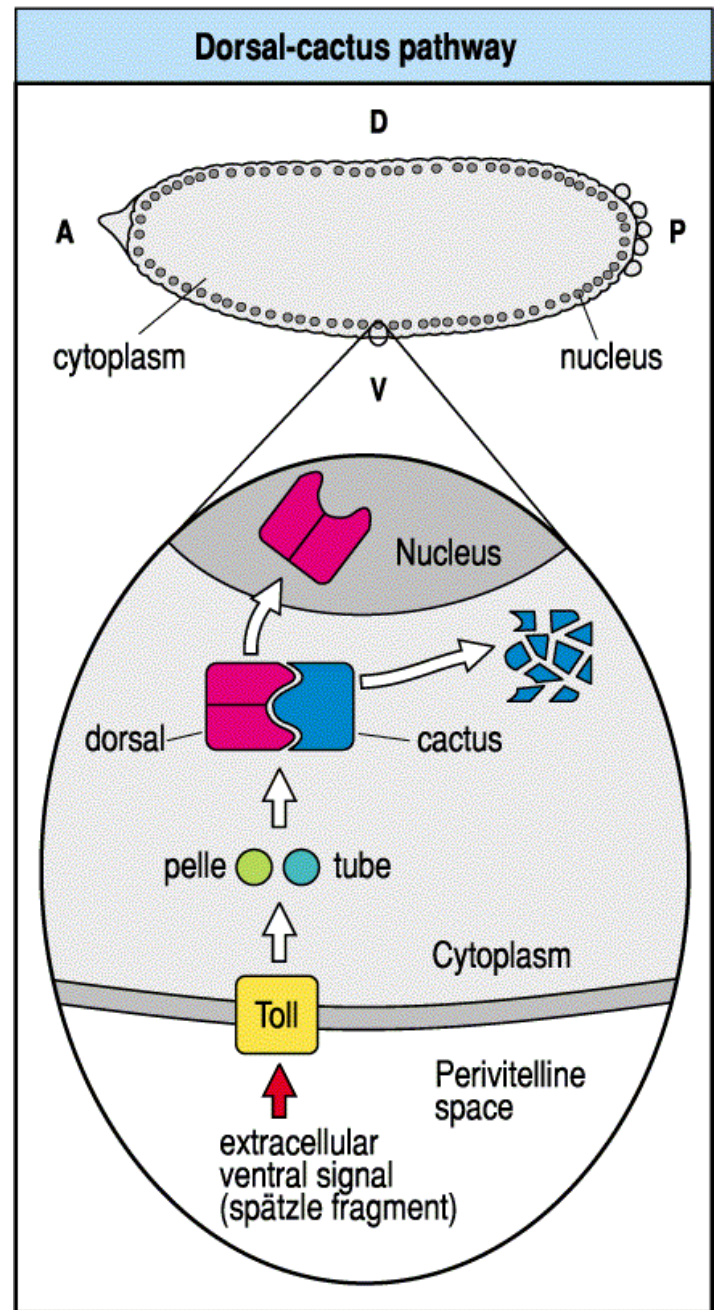
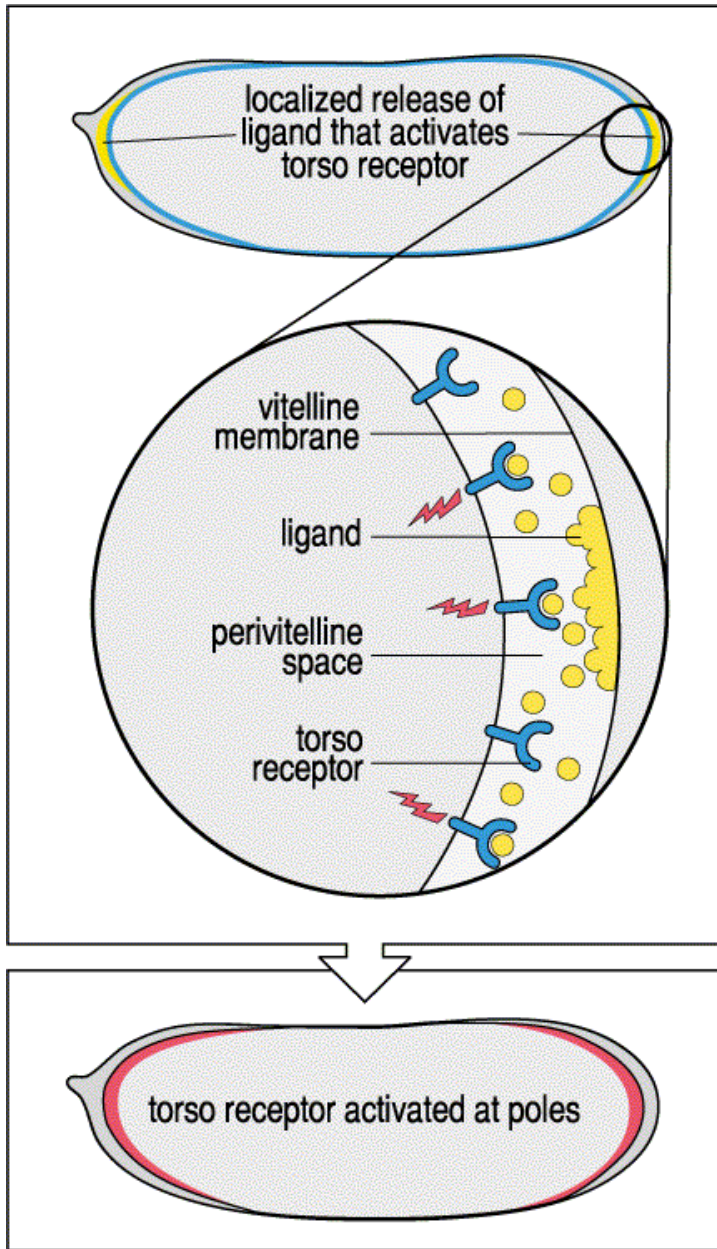


Six doses of *bicoid*







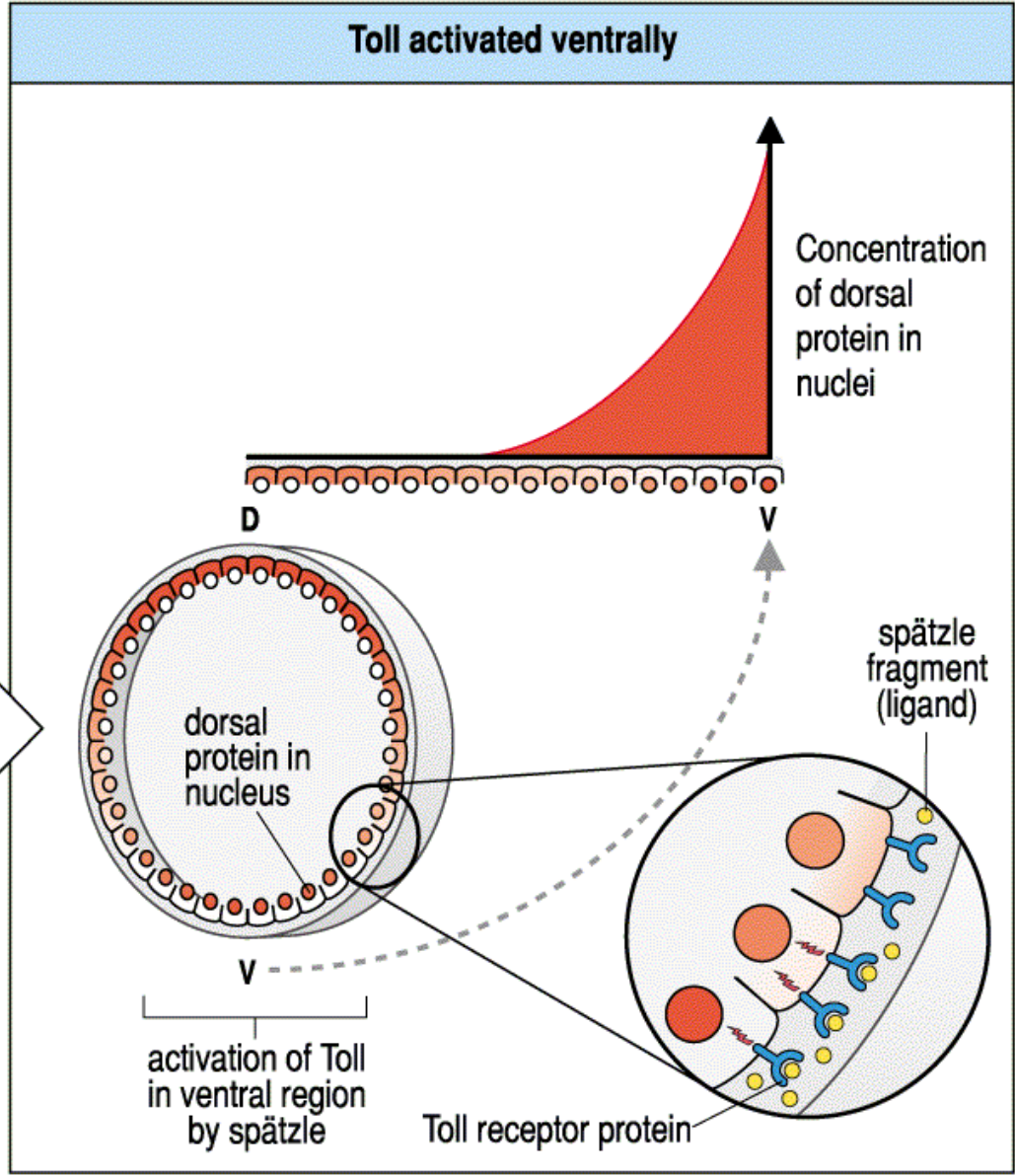
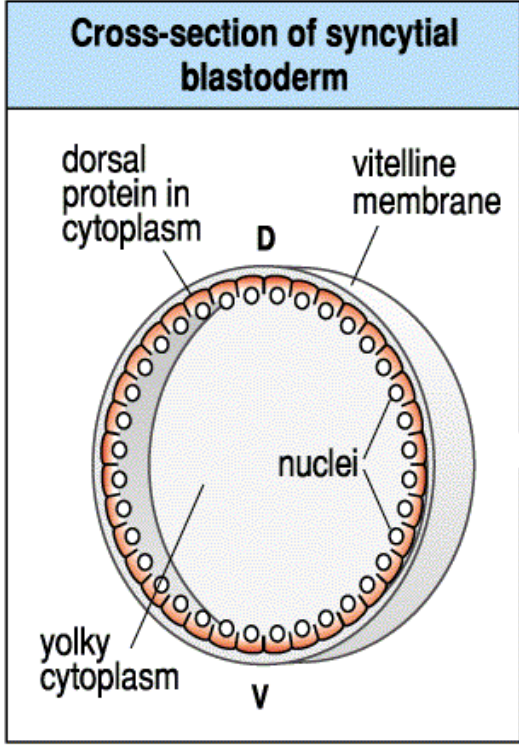


Zygotic gene expression along D/V axis is controlled by dorsal protein

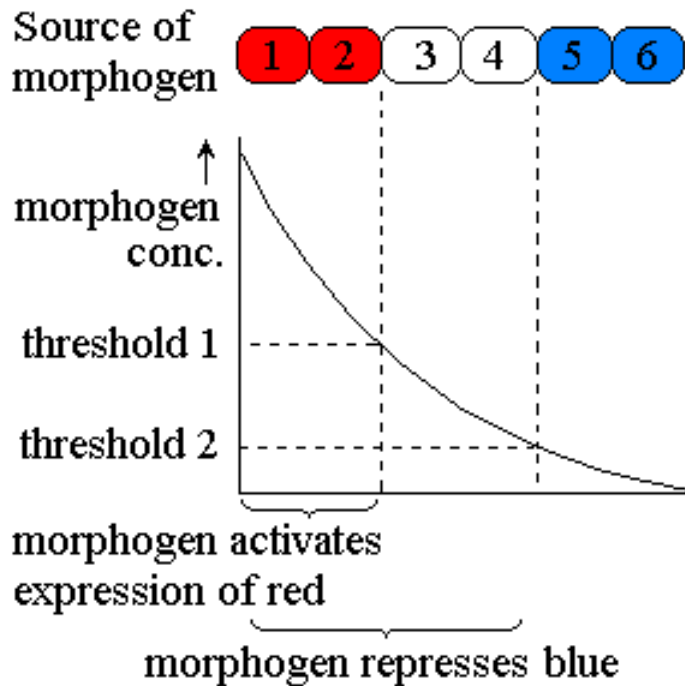
- dorsal drives gene expression to activate and inactivate a number of genes by binding to the regulatory regions of many genes it controls.
- dorsal specifies the most ventral cells as prospective mesoderm.
- High levels of dorsal activates *twist* and *snail* (required for mesoderm induction and gastrulation).
- Low levels of dorsal activate *rhomboid* (which is suppressed by snail) to give rise to the neuroectoderm.
- *decapentaplegic* (*dpp*), *tolloid* and *zerknult* are suppressed by dorsal and are restricted to the most dorsal regions.
- *zerknult* specifies the amnioserosa.

Zygotic genes pattern the early embryo

- The most ventral region become mesoderm (muscle and connective tissue).
- Ventral ectoderm becomes neurectoderm (some epidermis and all nervous tissue).
- Dorsal ectoderm becomes dorsal epidermis and the amnioserosa (an extra-embryonic membrane).
- The endoderm from the terminal regions, give rise to the midgut.



Positional information and the French flag model



Drawing from classical embryology studies, a model explaining the relationship between position and pattern development proposes the existence of hypothetical substances called **morphogens** ([Wolpert, 1996](#)). Diffusion of morphogen from a source creates a **gradient**, and different **threshold levels** set off different responses, e.g. the induction or repression of protein expression.

As development proceeds, different patterns of gene expression within the red domain and the blue domain specialize the cells for particular roles. At a later point, gradients of other morphogens may become established, and now the red domain can respond to the new morphogen in one way, while the blue domain responds in another.