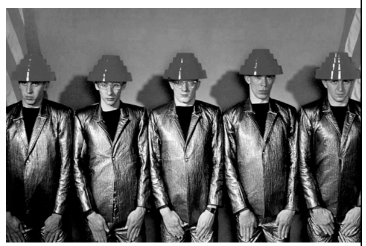
Evolutionary Developmental Biology



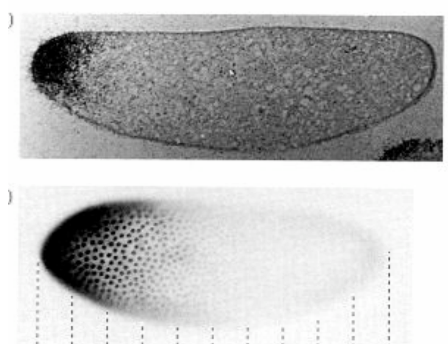
EVO DEVO

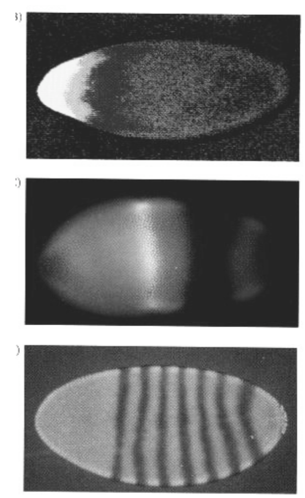
a.k.a. “EVO-DEVO”

Gene regulation in fruit flies

- *Maternal effect genes*, which are genes in the mother’s genome for RNAs that are pumped into each egg cell, regulate. . .
- *gap genes*, which determine large areas of the embryo, and which regulate. . .
- *pair-rule genes*, which are expressed in alternating bands and specify the future segments of the embryo, and which regulate. . .
- *homeotic* genes, which determine segment identity, and which regulate. . .
- *realisator genes*, which cause segment differentiation

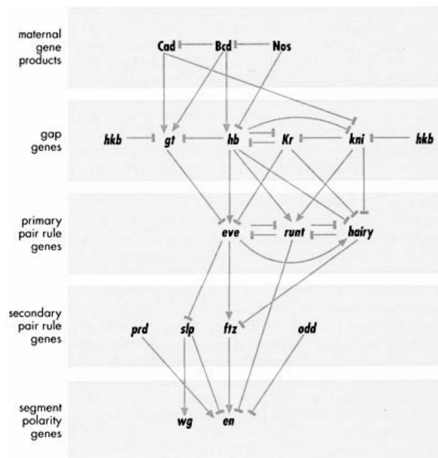
Drosophila egg, showing the location of the maternal mRNA *bicoid* (top) and the localization of the bicoid protein, forming a gradient from the future head end to the tail end



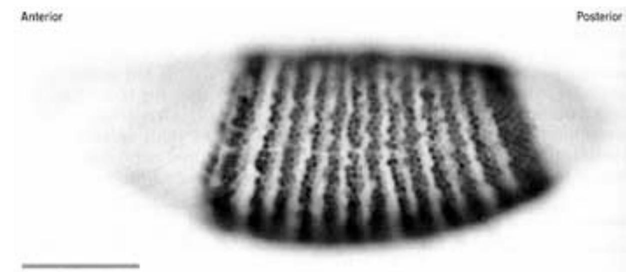


Maternal genes regulate *gap genes*; for example, *bicoid* (top) regulates *hunchback* (middle, shown in orange) and *Krüppel* (middle, shown in green). Gap genes regulate *pair-rule* genes such as *fushi tarazu* (bottom). Both gap and pair-rule genes regulate homeotic genes.

Just a part of the gene regulatory cascade, and we haven't even *got* to the homeotic genes yet. . .



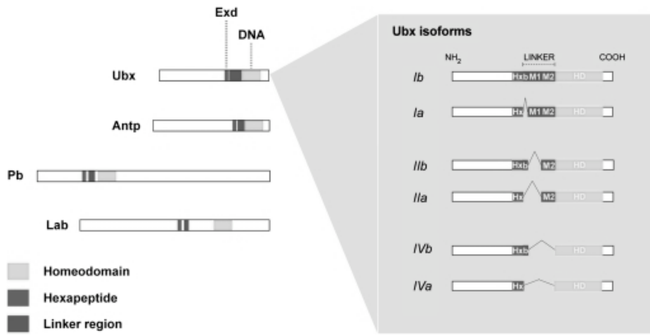
Early-stage *Drosophila* embryo, stained to show the expression patterns of the pair-rule genes *even-skipped* (dark blue) and *fushi tarazu* (brown). Pair-rule genes regulate *segment-polarity genes* (which I ain't getting' into here) and *homeotic genes*.



Homeotic Genes

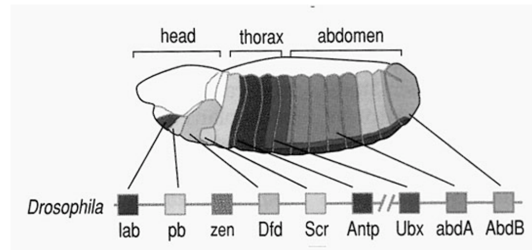
- Homeotic genes contain a 180-bp sequence called a *homeobox* that codes for the DNA-binding part of the protein (the *homeodomain*).
- Homeotic genes lay down segment identity
  - As such, homeotic genes determine the placement of major structures
  - For example: the homeotic gene *Ultrabithorax*, or *Ubx*, regulates a set of a dozen genes that collectively control thorax development.

Computer model of the *Ubx* protein (shown in gray) binding to DNA (shown in orange). This *helix-turn-helix* protein interacts with RNA polymerase II to control the expression of other genes.



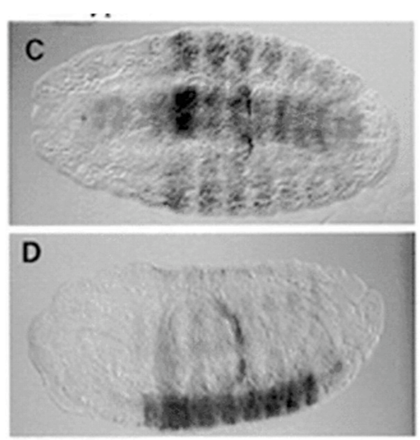
Actually, it's weirder than that: *Ubx* RNA transcripts can be spliced in six different ways to produce six different proteins (isoforms) with slightly different functions in development. I won't go into this further, but it adds some interesting wrinkles to the story. . .

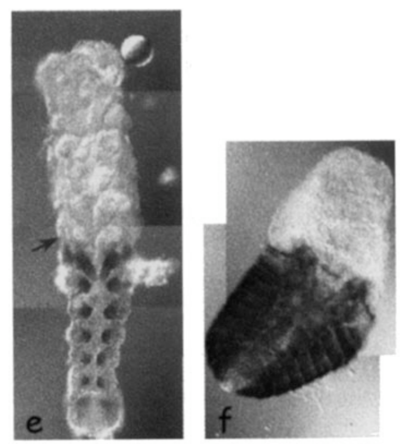
The Hom/HOX cluster of homeotic genes regulates anteroposterior patterning. This map shows a fly embryo. Each HOX gene is color-coded to show where it is active in the embryo.



Note that the order of genes on the chromosome is the same order as their order of expression along the axis.

These *Drosophila* embryos have been stained with antibodies to the *Ubx* protein (brown), showing where the protein is being produced in the embryo.





The same pattern can be seen in other insects—these are cockroach embryos (nine-day on the left, ten-day on the right) that have also been stained with antibodies to the *Ubx* gene product. The dark brown regions show where *Ubx* is actively being transcribed.

Wing development

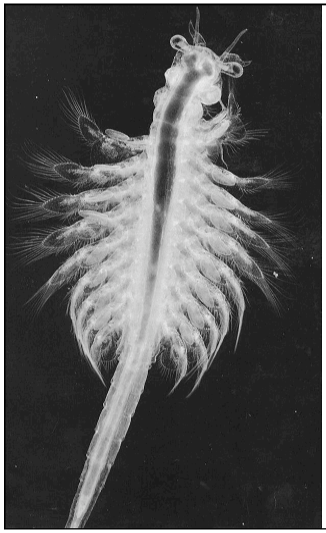
- *Ultrabithorax* (*Ubx*) is activated in the posterior thorax (third segment) and abdomen
- In insects, *Ubx* acts to repress thoracic structures
  - If *Ubx* is knocked out, every abdominal segment becomes a second thoracic segment. (And every abdominal would develop wings and legs, if the embryo could survive.)

Wing development

- In flies, *Ubx* represses at least five genes needed for wing development
  - This is what causes the second wing to develop as a haltere—which doesn't happen in other insect groups
  - Mutations in the genes that *Ubx* controls (including the *bithorax* you saw earlier) produce less shocking modifications.

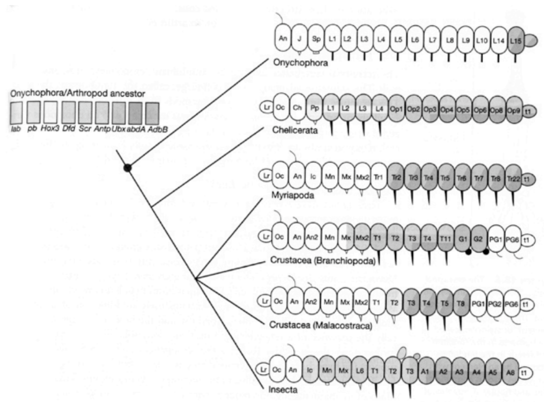
Crustacean *Ubx*

- *Ubx* is present in other arthropods as well, including crustaceans (currently thought to be the closest relatives of the insects)
- But. . . in crustaceans, *Ubx* does *not* repress limb development
  - Ronshaugen and others (2002) were able to insert a crustacean *Ubx* in a fly embryo. . . and found that crustacean *Ubx* doesn't repress limb development
- Implication: The shift from a crustacean-like ancestor to an insect involved changes in the action of *Ubx*



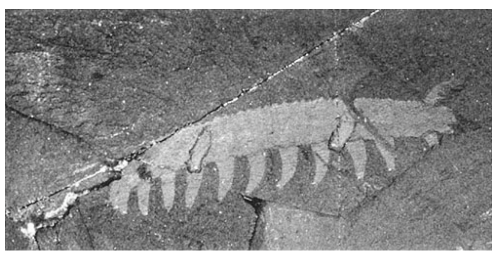
This crustacean (*Artemia*, the "brine shrimp") shows that abdominal segments still carry legs, even though *Artemia* has a *Ubx* gene that plays a real role in normal development.

Changes in *where* Hox genes are expressed seems to be correlated with major shifts in body plans!

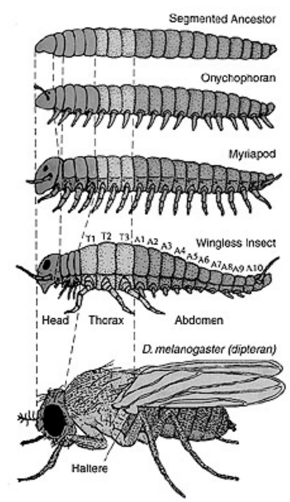


Hang on here. . .

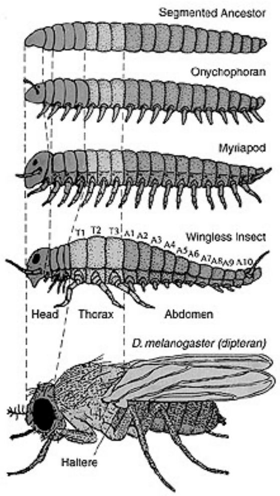
- *Hold it, Dr. Waggoner! I assume* Ubx *had to evolve from something! Doesn't this mean that before* Ubx *gained its present function, insects must have had wings and legs all over their bodies?*
- Why yes, inquisitive young people! In fact, I'm glad you asked that. . . .



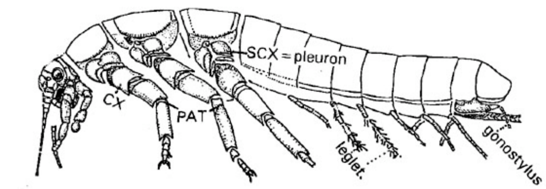
All arthropods are thought to have evolved from an ancestor that looked something like this 510 million-year-old fossil, *Aysheaia*. Notice that all of its appendages are basically of the same type.



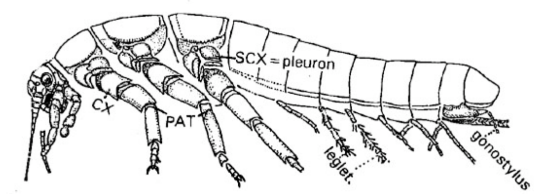
From something like that relatively simple fossil, various arthropod body plans evolved by specializing, enlarging and reducing segments and parts. Specifically, insects are derived from a centipede-like ancestor with numerous legs.



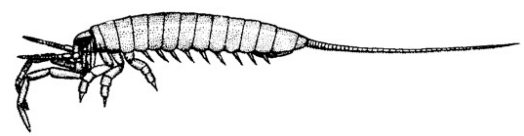
To make an insect out of a "centipede", *Ubx* evolved to suppress the genes that would act in the thorax—one of which is a *HOX* gene that promotes limb development called *Dll* or *distal-less*. *Ubx* essentially says, "Whatever you're doing ahead of the second thoracic segment, don't do it here!")



This early fossil insect, *Ramsdelepidion* (about 300 million years old) had legs on its abdomen! Apparently the *Ubx* gene complex had not completely evolved its suppressive function in this group of insects at this time.

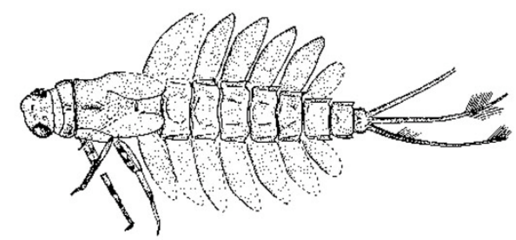


Meanwhile, a small plate that had formed part of the leg was exapted—and grew larger, eventually becoming a functional wing. It's labeled SCX in this diagram of *Ramsdelepidion*.

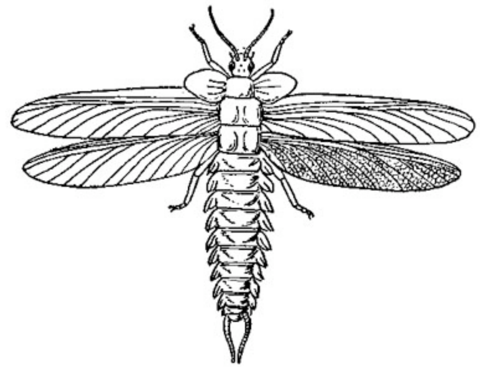


Dasyleptus

Epeoromimus



Other early insects also show morphologies that you would expect if the *Ubx* cluster was not fully functional.



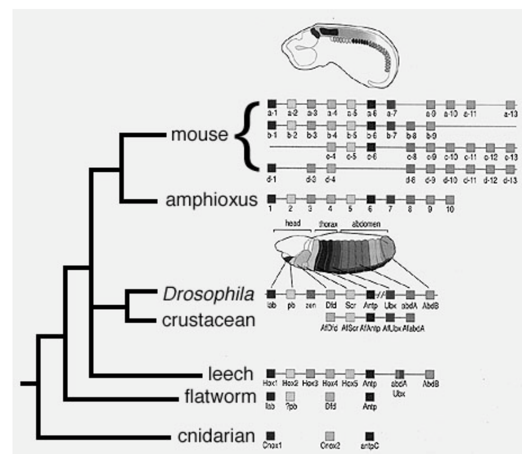
Stenophlebeia is one of the earliest known winged insects in the fossil record. Notice that it has *three* pairs of wings, plus some odd flaps along the sides. . . .

Evolution of the HOX complex

- HOX genes are found in all animals
- Number of HOX genes is correlated, very roughly, with "complexity" (jellyfish have three, fruit flies have nine, humans have thirty-eight)
- *Ubx* homologues are found in mammals. . .
  - In mice, they seem to be concerned with early nervous system development—later in development they are expressed in kidneys, gonads, bone marrow
  - *Ubx* mammalian homologue *HOX-B7* is expressed at an abnormally *high* rate in certain cancers. . .

Evolution of the HOX complex

- Gene duplication is responsible for increases in the number of HOX genes.
  - Vertebrates have four HOX *clusters*— apparently, HOX cluster duplications were important in the earliest evolution of vertebrates.
  - Yet another duplication of the HOX cluster, which happened before vertebrates had evolved, produced the ParaHOX cluster, which is also important in development



Evolution of the *Hox* complex of homeotic genes

The "Universal Evolutionary Toolkit"

- HOX and other homeotic genes have strongly conserved functions
  - Even in very different animals, the same genes control the development of the same structures (such as the head)
- Evolution of homeotic genes, and new interactions among homeotic genes, is a key part of the evolution of new phyla on Earth.