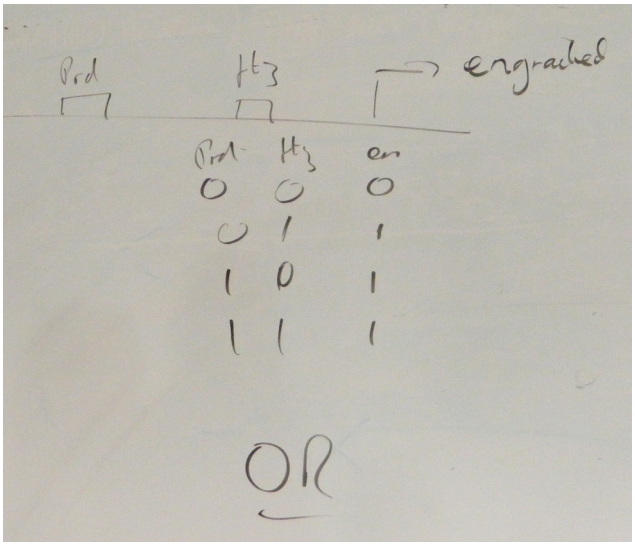
Class notes from DB4 Cellular Mechanisms

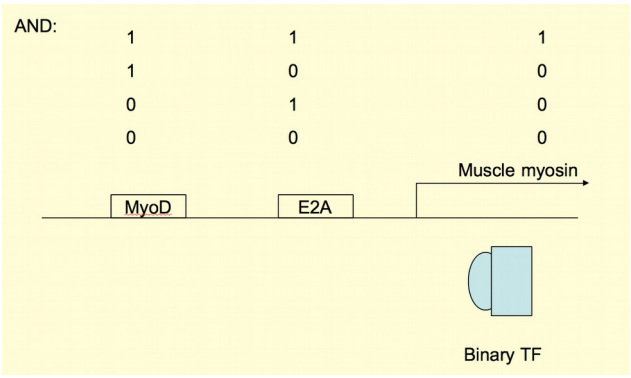
Session 2 2nd October 2014.

We began with you reporting back on your tasks: bringing examples of how genes control other genes. Links to the presentiations you made will be added to the home page of the course, when you have sent them to me. I may also add some whiteboard photos to this document, depending on what is covered by what you send.

I added an extra example; regulation of engrailed by paired and ftz (which is like an OR) – see overleaf, left panel.

We then went on to consider coordinated regulation of linked genes. The first example (2nd table overleaf) was drawn from the prokaryotic world (E. coli) – the galactose operon.

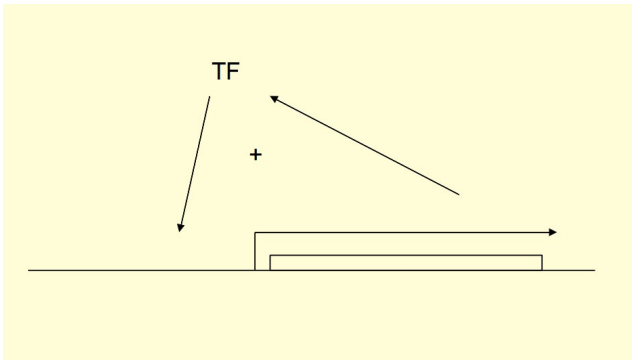


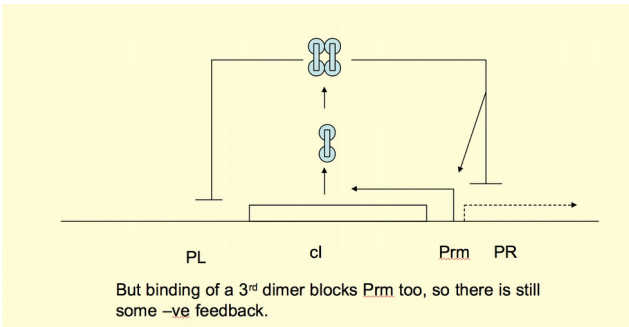


(This is another example)

After the coffee break, we considered very small networks of genes. First, there was The lac z system. I introduced the idea of this being a system for maintaining free galactose (an odd way of looking at things, but it led us on to feedback).

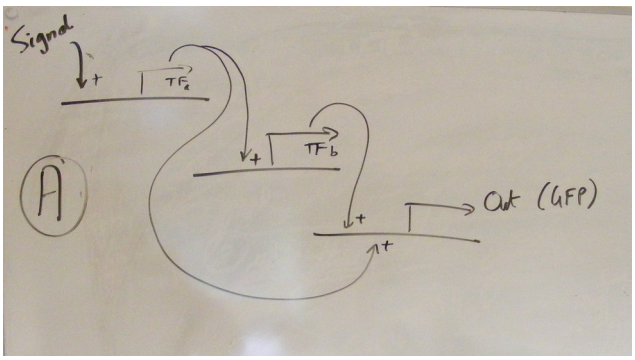
We then went on to consider positive feedback, such as the latch in the left part of the table below, and the positive feedback loop (tempered with some negative to keep cI within reasonable limits) of bacteriophage lambda:

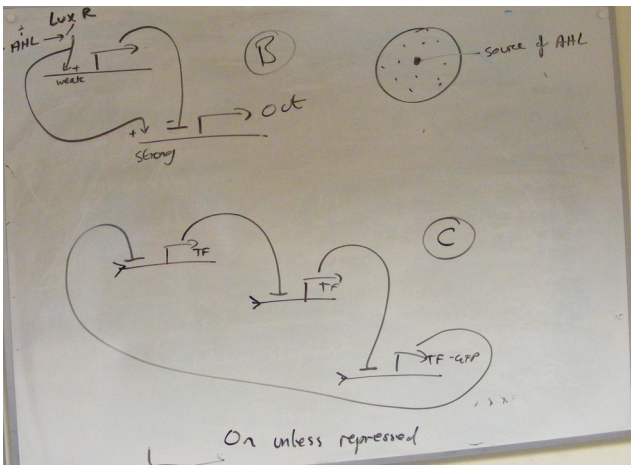




I then told you about an experiment on differentiation of muscle cells (mesenchyme → myoblasts → myotubes), in which researchers sought 'master regulators' of muscle differentiation by conducting a subtractive hybridization experiment between mesenchymal cells and myotubes. The identified MyoD, and demonstrated that expression of that in a variety of mesenchymal cells (adipocytes even) causes them to become muscle. They celebrated having their master regulator. They then did another subtractive hybridization to see what MyoD switched on, and identified myf5 (and other things). They expressed myf5 in cells to see what it swtiched on: Myo D. This, as you pointed out, tells us two things:
1) MyoD and myf5 form a positive feedback loop (latch)
2) Ideas of 'master regulator' may not really apply to mammalian systems (the genes cannot both be the other's boss).

HOMEWORK
I drew three more complex genetic networks on the board, and asked you to work out what they do. For the one that involves an external signal (A), consider this signal coming up from zero, then going back down to zero again. For B, consider the cells to be in a dish with a central source of AHL (which will diffuse to give a gradient). I'll give you the references next week, for now I want you to think.





ALSO, bring some exam questions (e-mailing them to me would be sensible).