

20.106J – Systems Microbiology
Lecture 8
Prof. DeLong

- Chapter 8 – Brock: Regulation of Cell Activity
- Note from a problem on the test: when O₂ is not the terminal electron acceptor, alternative electron acceptors are used: NO₃, SO₄, Fe³⁺.
- When you split C₆H₁₂O₆ in this manner, you get CO₂ and ethanol, H₂.
Fermentation – no electron transport chain. ATP made by substrate level phosphorylation.
- Next week: we'll start going into genetics, and a history of genetics.

- Turning genes on and off: transcriptional control
- Regulation of prokaryotic transcription.
 - Single-celled organisms have pretty short doubling times – this helps them respond quickly
 - The half-life of most mRNAs is short (on the order of a few minutes).
 - Transcription and translation are coupled in a single cellular compartment
 - Genes are regulated in units called operons. All of the genes necessary for a particular function are generally located on the same operon with the same promoter.
 - This allows uniform control of biosynthetic pathways.
 - Alternate Sigma factors. There are different ones to use depending on where the cell is in its growth cycle.
 - The use of different sigma factors also varies by organism.
 - Transcription factors: DNA binding proteins work in dimers.
 - In the presence of arginine, arginine biosynthesis is turned off very quickly – within around ten minutes.
 - Conversely, in the presence of lactose, lactose-metabolizing genes are induced.
 - The metabolism of lactose in *E. coli* and the lactose operon
 - Diauxic growth – means that cells preferentially use one carbon source over another, in sequential fashion.
 - Graph: they use the glucose, then there is a lag after the glucose is exhausted, and then they start using the lactose.
 - With lactose, the repressor will bind to the promoter unless lactose is around, in which case the lactose binds to the repressor instead.
 - However, just having lactose around isn't enough, because there's also an element of positive control, which has to do with glucose – regulation by cyclic AMP (cAMP) levels, and its interaction with the Catabolite Activator Protein, CAP.
 - Slide: Cooperative binding of cAMP-CAP and RNAP on the *lac* promoter
 - X-ray structure of CAP-cAMP bound to DNA
 - Catabolite control of the *lac* operon.

- Think big picture: with the *lac* operon, there are elements of both negative and positive control
 - The tryptophan *trp* operon: two kinds of negative regulation
 - There's a repressor protein.
 - Also, the mRNA binds with itself where there is complementarity downstream. There's a Trp Leader that controls via attenuation. If there's a lot of tryptophan, then the ribosomes work pretty close to the RNA polymerase, which causes the mRNA to bind to itself right next to the ribosome, causing it to fall off of the mRNA. This is a very fine-tuned, complicated process.
 - The arabinose (*ara*) operon
 - P_{BAD} promoter: very tight, precise control. Used a lot in biotechnology for that reason.
 - Key features of Arabinose regulation
 - The point is that there are a lot of complex levels of control that have to do with feedback regulation.
 - Differences between arabinose and lactose operons
 - AraC can act as both a repressor and an activator of *AraBAD* expression. This is an example of positive control.
 - AraC can regulate its own synthesis too.
 - *Ara* operon provide an example of regulation at a distance by DNA looping.
 - Common mechanisms of regulation of transcription, with variations on a theme.
 - “Flipping promoters” Flagellar phase variation.
 - The bacteria regularly switch back and forth between different types as a method of avoiding host immune response. You can't plate just one type or the other – you'll always get both
 - This is due to another type of transcriptional control: flagellar phase variation.
 - The promoter gets flipped, so that the first gene doesn't get transcribed – instead another one does.
 - How this happens is randomized to provide diversity.
 - More complicated control mechanisms.
 - These cells respond to the environment and communicate with each other with incredible efficiency.
 - For example, take cells that make their own light: They won't do it unless there are other cells of the same type around. It only works if there's a certain density.
 - They send out signals that act sort of like casting votes.
 - This kind of quorum sensing is very important with respect to pathogens.
- Translational control:
 - The “stringent response”: a type of translational control

- When bacteria are starved of nutrients, they immediately shut down gene expression and other metabolic activities.
 - Binding of an uncharged tRNA to the A-site in the absence of amino acids.
 - The Ribosome stalls, and RNAase shuts down
 - This is a global control mechanism that's sensed by the ribosome
-
- Review of gene regulation in bacteria