

Discussion questions - week 5

- Discuss the advantages and disadvantages of various methods of identifying and analyzing groups of co-regulated genes, including hierarchical clustering, principal cluster analysis, and ChIP-on-chip.
- Discuss the quantitative considerations involved in using mathematical methods of clustering to cluster samples (or experiments) rather than genes, and some of the applications of this approach in developmental biology, cancer biology, and biomedical research.
- Discuss the advantages and disadvantages of oligonucleotide vs. cDNA microarray technologies.
- Discuss the pros and cons of using the “guilt by association” method can be used to make inferences about the functions of genes and gene expression clusters.

Discussion questions - the ENCODE Project

- The authors state that: “Distal DNaseI hypersensitive sites have characteristic histone modification patterns that reliably distinguish them from promoters. Which specific histone modification patterns were found to be characteristic of promoters versus enhancers?”
- The authors state that: “many functional elements are seemingly unconstrained across mammalian evolution. This suggests the possibility of a large pool of neutral elements that are biochemically active but provide no specific benefit to the organism”. Explain the exact biological meaning of this quote. Would a transposable element be an example of such an “active but neutral” DNA element? Why (or why not)?
- The authors state that “DNA replication timing is correlated with chromatin structure”. Explain operationally how they measure “DNA replication timing”. Which specific histone modifications were most closely associated with early replicating sequences? With late replicating sequences?

Discussion questions - alternative splicing

- Discuss the advantages of RNA-Seq versus SAGE for (i) small RNA profiling, and (ii) analysis of alternative splicing. What method would you chose when both levels of analysis are needed?
- Yeo et al. found that exonic splice enhancers were generally well conserved across the vertebrates, but intronic splice enhancers differed considerably between fish vs. mammals. Do these elements interact with different gene families? What are the implications for the evolution of alternative splicing?
- What are the four basic types of alternative splicing patterns? What sequence length constraints apply to an alternatively-spliced, protein-coding exon if it is functional? What is the alternative? (i.e. define at least two, biologically different types of “non-functional” alternatively-spliced protein coding exons).

Discussion questions - RNA structure

- Wan et al. used a technique they called “parallel analysis of RNA structure” (PARS) to determine that the 5’ UTR and 3’ UTR of mRNAs tend to be less structured, while the protein coding sequences tended to be a bit more structured and also contained a 3-base periodicity in their structure. Explain how these experiments were conducted and the biological meaning of the results.
- Wan et al. also found that the start and stop codons tend to be the least structured points along an mRNA. Provide at least two explanations (structure vs. function) for this result.