Last Time – 10-01-14

- Definition of adaptation
  - Based upon principles established by Darwin; very restrictive, requires evidence of 'selection' = evolutionary approach
  - Need to know original function; how selected?
  - As physiologists, generally look at current benefits
- Overcome some issues by using the ideas of the 'Central Dogma' – challenged and significantly modified, but proteins are considered the phenotype!
- Concepts raised in Ch. 1 (text): challenges confronting all organisms; factors responsible for diversity vs unity

Last Time -17/01/14

Enzymes – general principles (catalysis, regulation, structure)

- Reduce free-energy – 'induced-fit', importance of conformation
- Conformation (structure) – determined by a.a. sequence and microenvironment of protein
  - Types of a.a. and importance to folding (II^o structure)
  - Spontaneous vs assisted folding
  - General model of protein formation
- Regulation – quantitative, qualitative and modulation
  - Quantitative or [enzyme] = rate of synthesis – rate of degradation
    - Change one or both to change [enz] – numerous processes involved in both which may be affected by environmental change
  - Qualitative or type – protein variants/polymorphisms
    - Whole genome duplications – 3 during animal evolution
    - Differential or segmental duplications
      1. isozymes or protein families (ARs) – partial or complete divergence of loci (breed true, fixed in genome)
      2. allozymes – heterozygous loci, SNPs (don't breed true)
    - Detecting variations – methods; limited abilities and $\overline{\text{HET}}$
      1. no correlation at protein levels found between $\overline{\text{HET}}$ and environmental complexity – may be at nucleotide level
      2. significant variation exist, but is there a functional role for it?

Last Time – 21/01/2014

- Type/Qualitative strategy (cont'd) – duplication events
  - Mb/Hb story – major difference in O_2 binding linked to subunit structure (development) and effectors (H^+, DPG, T°)
  - LDH – continue glycolysis (NADH re-oxidation)
    - Composition – tetramer, 2 SU; tissue distribution
    - Isozymes – gene duplication event; M/A and H/B; LDH M_4 or -5, LDH H_4 or -1
    - Kinetics (pyr reductase, lac oxidase; abortive ternary complex), O_2-stability model, evidence
- Modulation strategy – existing enzyme activities; 4 potential categories
  - Modulation by S or small molecules
    - 2 kinetic patterns – hyperbolic vs sigmoidal; defined by V_{max} and K_m ($S_{0.5}$); calculated parameters (different plots)
    - V_{max} related to [E]; K_m α 1/ES affinity; K_m generally above $[S]_{in}$; enzymes generally operate at low [S] not at V_{max}
    - K_m complex term; can be used as a relative term assuming that the enzyme mechanism is the same between conditions

Last Time – 24/01/2014

- Modulation strategy – existing enzyme activities
  - Modulation by S or small molecules
    - 2 kinetic patterns – hyperbolic vs sigmoidal
    - Characteristics of both kinetics – SU numbers, interaction between SUs
    - ex. LDH (hyperbolic, 4 SUs, no interactions)
    - ex. Hb and PyK (sigmoidal; homotropic, heterotropic interactions)
    - Importance in changing K_m or $K_{0.5}$ values, not V_{max} (i.e. changing ES-affinities)
  - Post-translation modifications (PTM) – irreversible vs reversible
    - Phosphorylation/dephosphorylation (P/deP) – critical for signal transduction
    - History via GPase cascade (specificity, amplification)
- Signal transduction – importance with respect to metabolism and changes in enzyme regulation via PTM (reversible)
    - receptor systems – GPCR and RTK; general system
    - GPCR – classes (Family A); ARs as an example
    - intermediate coupling system = g-protein