**Sample Questions** (That we might consider studying this semester)

**I) Macrophages** crawl preferentially onto hydrophobic surfaces (plastics, metals) in preference to hydrophilic surfaces, and macrophages crawl toward positive electrodes and away from negative electrodes.  Macrophages also accumulate on roughened surface in preference to smooth, and they don't detach in response to proteolytic enzymes, which again is the opposite of all other differentiated cell types.

***1)***  Do these opposite behaviors of macrophages (***hydrophobic, roughness, positive electrodes, enzyme responses***) have the same causes as each other?   How could we prove that?  Or disprove it?

***2)***  Are some normal functions of macrophages served by these opposite behaviors?  Perhaps invasion of inflamed tissues?  Going where other cell types avoid.

***3)*** Osteoclasts develop from macrophages & behaviors opposite to osteocytes.  (Could this help explain or prevent osteoporosis?)

***4)*** Macrophages invade ***atherosclerotic plaques*** and convert into "**foam cells**".

**II)  Guidance of crawling nerve growth cones** to locations of innervation.

Often patterns of innervation are map-like "**neural projections.**" The best-studied example is innervation of the roof of the midbrain by ganglion cell axons from the neural retina.

Are nerve connections guided by gradients of adhesion?  Or by gradients of proteins that stimulate cell detachment where these proteins contact each other.  (hint: Neural projections tend to be upside down and backwards.)

**III)  Are memory and learnin**g created by guidance and/or connection (or maybe by selective detachment) of nerve synapses in the brain?

Is modern science ready to solve Mind-Brain questions?

…because such questions are too complicated?  Or because computers are not good analogies to brain function?  (**Parallel processing** versus **Central Processing Units**.)  What about **Connectionism** and **Artificial Intelligence**?

The concept of **Neural Darwinism** could also be worth discussing.

**IV)  Colinearity of Hox genes**: For some unknown reason, the relative locations in embryos where Hox genes are transcribed have the same spatial order (with few exceptions) as the (genetic map) locations of Hox genes on the chromosomes. This can't be coincidental; but is it a (causal) means for activating the right genes in the correct parts of the body? Or is it more of a side effect?  What are the possibilities?  And what testable predictions are made by alternative hypotheses on this subject?

**V)  Is the "clock and wavefront" theor**y the true mechanism that causes spatial segmentation of somites in embryos?  Many researchers have become convinced this theory must be true.  Time oscillation of concentrations of signaling molecules really does occur; So what else could explain these oscillations? Supporters of clock & wavefront seem never to have considered any other possibilities.  One possibility is operation of a reaction-diffusion system, which could produce time oscillations of its molecules..

**VI)** Has any specific biological pattern ever been conclusively proven to be caused by any version of **Reaction-Diffusion system?**

**VII)** What mechanism "weeds out" lymphocytes whose antibodies or binding sites fit some normal molecule of the body?  Does this weeding-out process occur only during early development, or can it continue through life?  Can it be reactivated?  Are **MS, Lupus, RA** and other **autoimmune diseases** caused by failure of such weeding-out?

**VIII)** How can **bone formation** be stimulated? How can **osteoporosi**s be prevented? (perhaps by preventing macrophages from becoming osteoclasts?

**IX)**  Is the rounding-up of cell aggregates caused by maximization of cell adhesion?

Or is rounding-up caused by strengthening of acto-myosin contraction of those parts of cell surfaces that are not touching other cells of the same differentiated cell types?

Why would cells have such properties?  Are gastrulation and neurulation caused by the same forces as cause reaggregated cells to sort out from cells of different differentiated cell types?  What sorts of evidence could prove or disprove such ideas?

**X)** How does cancer chemotherapy really work?  Why should faster-growing cells be killed more by slowing them down?  Or do cell cycle check points fail to halt cancer cells until damage can be repaired?

**XI)** Does cartilage grow by increased secretion of matrix, by increasing concentrations of covalently-bound sulfates, or by weakening of constriction of collagen fibers? (Or by a mixture of these, or other forces?)

**XII)** Is the Stopak-Harris theory of muscle and tendon formation correct?

(That cell traction lines up collagen and myoblasts.)  What evidence is needed?

**XIII)**  How and why do differences in flexibility of substrata control which cell type stem cells will differentiate into?

**XIV)**  Why can salamanders regenerate legs?  Why can't mammals (and frogs) regenerate legs?  If we knew these reasons, would that information help us invent methods to heal human amputations?