Question 1: Inducing large scale alignment in microphase separated block copolymers:

Block copolymers are macromolecules composed of blocks of chemically distinct repeat units. The different blocks are thermodynamically incompatible but the chemical link between the blocks prevents phase separation on a macroscopic length scale. The blocks do phase separate on a nanometer scale (termed microphase separation).

There exists both a wide variety of experimental results and a wide range of theoretical models to attempt to explain the morphology and microstructure alignment of thin film block copolymers. The matter is of both basic scientific importance and of technological relevance in view of the important role played by polymer films in industry and technology.

Discuss the **thermodynamics** and **kinetics** of microphase separation in block copolymers focusing on the differences between thin film and bulk morphologies. Propose experiments that could be performed to induce large-scale alignment of this nanoscale morphology in thin films

Your proposed experimental plan should include a detailed protocol, including what materials and equipment you would use, and a full experimental procedure. You should also address the following issues:

1) Why did you choose the specific experiment?
2) What information will it provide which is different/superior than other experiments in literature?
3) What kind of results do you expect from this experiment?
4) How would you use the experimental results to evaluate the type of morphology of the thin-film block copolymer?
5) How would you use the experimental results to quantitatively evaluate the degree of orientation of microphase-separated domains?
6) Are additional characterization tools/methods needed?

Your report should be written in the format of a research proposal, and should include the following: justification of proposed research, relevant background, problem identification, project goals, method of approach, expected results, and significance and impact of the proposed research.

Question 2: Development of a bench scale process for production of functionalized nanoparticles

There has been much recent interest in using magnetic nanoparticles in biomedical applications such as drug delivery and enhanced magnetic resonance imaging. For many of these applications, it is desired to covalently bond a protein to the nanoparticles. The proteins can be selected so that a particular type of cell is targeted. One common route is to use amine propyltriethoxysilane (APTES) or amine propyltrimethoxy silane (APTMS); the silane groups react with the surface of the nanoparticles leaving the amine group free to bond to another molecule. Through various types of cross-linking reactions, biomolecules such as proteins can be attached. For example, a glutaraldehyde molecule can then be used to link the amine group to an amine group on a protein. The glutaraldehyde step is challenging since glutaraldehyde can also bind to amine groups on other particles! Another challenge associated with this process is that these proteins are often quite expensive to produce, and thus it is important to not leave behind any unbound proteins. In the reports in the literature, very small amounts of these functionalized particles are made, on the order of milligrams. For these materials to be useful on a commercial scale, this process needs to be scaled up. Understanding of the kinetics and reaction equilibria involved in each step is key.

Propose a research plan for the development of a bench scale process that can be used to make approximately 100 grams per day (assume a day = 8 hours) of magnetic particles coated with a common water soluble protein, bovine serum albumin (BSA). Assume you will be using commercially available reagents. Magnetic particles can be purchased from Alfa Aesar (catalog number 39951). These magnetic particles have an average diameter of approximately 20-30 nm. BSA with a narrow molecular weight distribution (avg. MW ~ 66,000) can be purchased from Sigma-Aldrich (catalog number A8531). In the final product, there must be at least one BSA molecule attached to each particle. The end product must contain less than 1 gram of particles that have no attached BSA, and less than 0.1 grams of unbound BSA.

Some relevant questions that your research plan should address include:
A) What is the best surface modification approach for covalently attaching BSA to the particles? B) What do you think is the rate-limiting step in the overall process? What kinds of experiments could you do to estimate the rates of these reactions? C) How would you determine the average number of BSA molecules bound to per particle? D) What would be the best reactor for each step, plug flow or CSTR?

Question 3: Diffusion of a Therapeutic Protein through the Extracellular Matrix:

Proteins are increasingly being used as drugs to fight specific diseases. They can be delivered by injection, through the lungs (inhalers) and by controlled release devices. Regardless of the type of delivery, the protein must ultimately diffuse through tissue in order to target particular cells. Tissue is composed of blood vessels, cells and the interstitium, which itself is composed of interstitial fluid and the extracellular matrix (ECM). The ECM consists of various proteins and polysaccharides that provide mechanical support for the surrounding cells. One of the important transport resistances is diffusion through the ECM.

To better understand this transport resistance, you are asked to measure the diffusion coefficient of a protein drug through the ECM. Treat the ECM as if it were a continuum and not a porous material. Propose 2 or 3 techniques that could be used for this measurement. Develop the governing equations that describe the methods and from which diffusion coefficients can be obtained. Discuss the limitations of each method and recommend one for measuring the diffusion coefficient if the concentrations are very dilute (ng/ml range). If the drug binds to a component in the ECM, this interaction could influence the measurement, depending on the technique. Discuss the role of binding on the analysis of the measurements to determine the diffusion coefficient.