CIMIT MEETING SUMMARY 7/6/2004

The meeting was devoted to the first lectures in the tutorial series on: “Biomaterials: The Next Generation”. Robert Langer, PhD, MIT gave an overview entitled “ New Materials and Tissue Engineering”. Many of the materials used in tissue engineering initially were used in very different commercial applications and are often not optimum for clinical use; for example, silicone breast implants are based on a material used as a lubricant. Dr. Langer decided to design materials from first principles, based on the required properties. For drug delivery, polymers undergoing surface erosion are needed to achieve controllable delivery rates. A hydrophobic polymer with water-labile bonds would be a candidate and led to the investigation of anhydrides. By making a polymer of two different monomers the dissolution rate could be controlled by varying the monomer ratio. This drug delivery system was then applied to the treatment of recurrent glioblastoma multiforme, an especially aggressive brain tumor. Polymer wafers were loaded with the chemotherapy drug BCNU (gliadel) and used to line the surgical cavity remaining after tumor resection. The local delivery avoided the high systemic toxicity of the BCNU. Clinical trials showed an increase in survival and in 1997 FDA approval was obtained. The next step in drug delivery was to make “smart” systems capable of delivering one or more drugs upon command by internal sensors or external signals. Silicon chips with multiple drug-containing wells were fabricated; gold films were used to cover the wells. Applying a potential to the gold film caused its dissolution and released the drug. The next application of biodegradable polymers was as scaffolds for tissue engineered (TE) organs. Polymers with lysine side chains were used to allow cells to adhere during in vitro tissue culture and TE cartilage has been demonstrated. Polymers of potential use in minimally-invasive surgery have been developed; by making structures of two polymers with different transition temperatures it is possible to have the structure change shape as a function of temperature. An example was a polymer whose shape changed from linear to coiled as the temperature was varied.

Jennifer West, PhD, Rice University, spoke on “ Metal Nanoshells: Diagnostic and Therapeutic Applications of Nanotechnology”. Metal nanoshells are a new class of nanomaterials with highly tunable optical properties; they consist of a dielectric core nanoparticle that is coated with an ultrathin metal shell. By varying the ratio of the thickness of the shell to the diameter of the core the peak of the extinction spectrum can be shifted, moving to the red as the shell becomes thinner. The ratio of absorption to scattering can be adjusted by varying the diameter of the shell. Most biomedical applications involve shifting the extinction peak into the NIR window of tissue absorption. The shells have been used to thermally destroy tumor, using heating by an 820-nm diode laser source. A mouse tumor model was used and MRI was used to determine that the tissue temperature reached 55ºC, the denaturation temperature. Survival to > 8 months was found. For combined imaging and treatment of tissue nanoshells with equal absorption and scattering were made and used to demonstrate cell imaging in dark field microscopy as well as cell killing. Nanoshell heating has been used to assist tissue welding, with the shells at the tissue interface. Nanoshells have also been used to photothermally control drug delivery by embedding them in a drug-laden thermally-responsive polymer; NIR heating collapses the polymer and releases the drug.