The Electronics – Biological Matter Interface.

Introduction.

The interface of *inorganic materials and biological matter* is a subject of significant current interest. The fundamental science of this area is driven both by the physics and by biology. At the same time, there are ample application opportunities, and implications on medical diagnostics; as an example many testing tools require the immobilization of biomolecules. There is also tremendous progress in instrumentation that aids the advancement of the field, ranging from imaging to protein deposition and patterning methods.

The interface between biological matter and electronic devices.

The *electronics-biological matter* interface has been identified as one of the frontiers of biophysics that will gain prominence in the next decade (an enlarged view of Fig. 1 can be found at the end of this document). Several aspects of this interface are important. First, exquisitely sensitive electronic devices that can be fabricated using CMOS or alternative, such as printed electronics technology can provide direct, real–time monitoring of biological processes. Second, local electric fields generated by the devices can influence biological processes and interactions. Third, one can use biological matter such as DNA or viruses to fabricate electronic devices with a bottom-up approach.

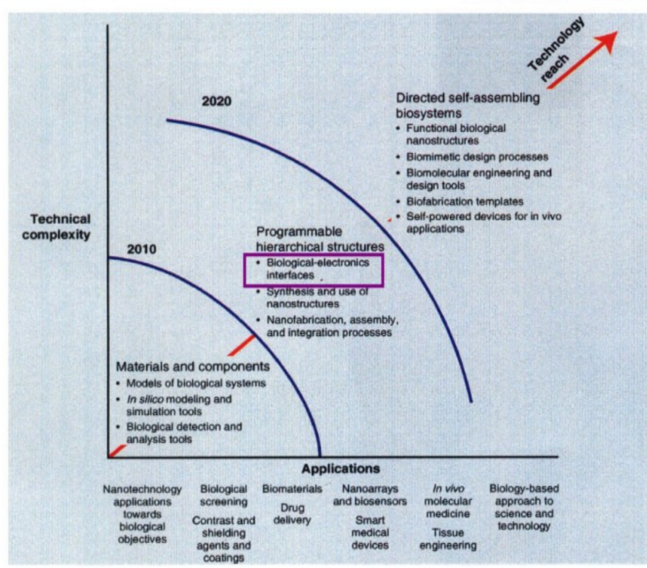

Figure 1 Nanobiotechnology: a continuum of opportunity for nanotechnology in the life sciences. Source: SRI Consulting Business Intelligence (SRIC-BC; Menlo Park, CA, USA).

The symbiosis that lies at the hart of the interface is due to the natural compatibility between bio-molecules and nano-scale inorganic materials and devices. Two observations argue for such interconnect. The first is size. Some length scales illustrate this observation: single cells have a size of approximately 1 micron, viruses are approximately 100 nanometers in size, while individual proteins are of the order of 10. The diameter of the DNA duplex is approximately 1 nanometer. Compare this with the size range for nanostructures: optical lithography based device fabrication reaches down to 100 nm, the size of a typical virus. E-beam fabrication (available at UCLA) has a current resolution limit of approximately 30 nm, and innovative printing technologies also reach this length scale. The typical cross section of fabricated semiconductor nanowires is currently on the order of 10 x 10 nanometers, the approximate size of a protein, and the diameter of single wall carbon nanotubes – naturally occurring hollow cylinders - is in the 1 nanometer range, the diameter of the DNA duplex. The second link between biology and electronic devices is electronic charge. Such charge or charge distribution of biomolecules is critical to a wide range of fundamental biological processes and applications in the biotech arena. As an example, various DNA functions such as DNA-hystone complexation are governed by localized electric dipoles. Electrophoresis, one of the fundamental tools of biotechnology, also relies on electric charges. Charge excitations, whether driven by chemical processes (oxidation) or UV light, are linked to DNA damage and to the conformational changes of various proteins.

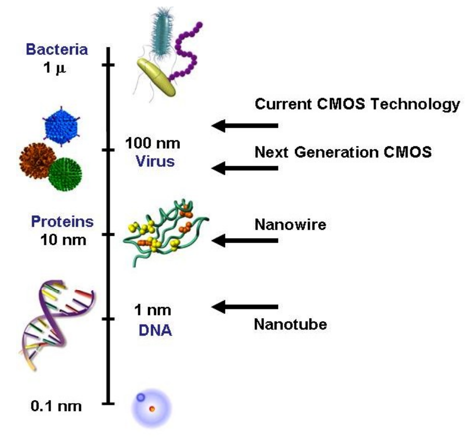

Fig.2. Size scales of biological and nano-scale matter.

Thanks to recent advances in nano-scale materials and architectures, we are now able to construct electronic circuits in which the component parts are comparable in size to biological entities, thus ensuring appropriate size compatibility between the detector and the detected species, and at the same time ensuring high sensitivity. Over the years we and also others have developed devices such as transistors that will lie at the hart of the area. The devices can be made specific to individual molecules – potentially we can vary their response to different species in a controlled way using chemical and biological functionalization.

Proposed activities

We propose to exploit directly this platform, and our focus will be the interface between biological matter and active electronic devices, with resistors, field effect transistors (FETs) and electrochemical, double layer capacitors, as the devices that will be interfaced with biological matter is an additional aspect that has been experimented with and solved by us. Direct electronic monitoring in a liquid, such as buffer and serum environment will have the most impact on the field. Reproducible electronic devices are essential, in particular where control experiments have to be performed.

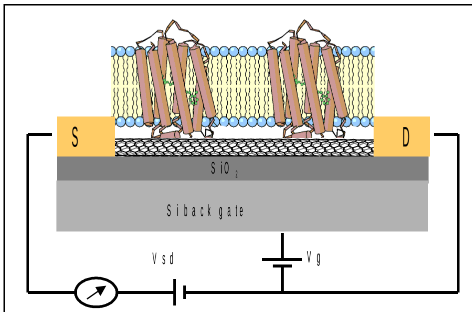

Fig 3.Integration of nano-scale transistors with cell membranes.

The following areas are selected examples of what this field may encompass.

Monitoring/influencing biological interactions*.* Ligand-receptor, antibody-antigen binding, monitoring enzymatic interactions.

Cellectronics: integration of cells and electronic devices both for monitoring and driving cellular functions – their response to drugs and other environmental factors.

Integration of nerve cells and active electronic devices, for complex memory systems.

Bio-inspired monitoring functions: artificial vision, hearing and the like.

Application opportunities

An example of the current opportunities is the direct conversion of bio-molecular processes such as an antibody-cancer marker interaction. With appropriate – biotech driven – immobilization schemes a PSA detection chip has been developed with sensitivity that can provide Point-of-Care identification of prostate cancer.

The exploration of such applications will continue, but novel opportunities will also arise. For example protein chips, utilizing direct conversion of biological presence to an electronic signal, artificial eyes, etc will be developed, together with platforms that lead to novel, electric field driven biological interactions

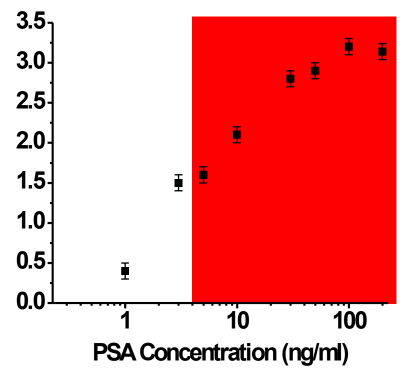

Fig.4. PSA detection using nano-scale electronic devices. The red area indicates the need for prostate cancer testing.

UCLA Physics Presence

Several faculty members are pursuing pioneering research that is or related to this area. **Professor Zocchi** has developed sensitive tools to monitor biological functions on surfaces. **Professor Miao** is developing imaging tools that, in combination with the devices can lead to new tools. **Professor Bozovic** is working on the mechanism if hearing, and there are ample integration opportunities with electronic devices. My own group has developed a variety of devices and conducted a fair number of experiments including the first integration between a cell membrane and an electronic device. The excellent theory group, with its strong solid state physics background and expertise in charge interactions and conformational changes of bio-molecules is eminently suited to contribute to this area and play an important role.

Relations to other programs at UCLA

The proposed area can, potentially have strong relations to other activities at UCLA. The association with **CNSI** is obvious. The area is also related to **bio-imaging,** and can be part of this large effort at UCLA. The **UCLA Nanofabrication Facility** would be used for many of the device fabrication activities. Finally there is a natural programmatic association with the **Medical School.**

Publications

The publications and patent applications below (from my own group) are a small cross section of what the initial research in the area may encompass.

Alexander Star, Jean-Christophe P. Gabriel, Keith Bradley, and George Grüner, "Electronic Detection of specific Protein Binding Using Nanotube FET Devices", Nano Lett. ***3****, 459-463 (2003)*

Bradley, K., Briman, M., Star, A., Grüner, G., "Charge Transfer from Adsorbed Proteins", Nano Lett. ***4****, 253-256 (2004)*

*A. Star, V. Joshi, T.-R. Han, M. V. P. Altoé, G. Grüner, J. F. Stoddart, "The electronic detection of the enzymatic degradation of starch****",*** *Org. Lett.* ***6****, 2089 – 2092 (2004)*

K. Bradley, A. Davis, J-C. P. Gabriel, and G. Grüner, "Integration of Cell Membranes and Nanotube Transistors", Nano Lett ***5****, 841-845 (2005)*

G. Grüner "Carbon Nanotube Transistors for Biosensing Applications", Analytical and Bioanalytical Chemistry ***384****, 322-335 (2006)*

David S.Hecht, Robert J. A. Ramirez, Mikhail Briman, Erika Artukovic, Kelly S.Chichak, J. Fraser Stoddart, George Grüner, "Bioinspired detection of light using a porphyrin-sensitized single-wall nanotube field effect transistor", Nano Letters, ***6****, 2031-2036 (2006)*

M. Briman, E. Artukovic, L. Zheng, D. Chia, L. Goodglick, G. Grüner, "Direct Electronic Detection of Prostate-Specific Antigen in Serum", Small ***3****, 758–762 (2007*

G. Grüner: "Electronic Sensing of Biomolecular Processes", US Patent Application 10/431963

M. Briman and G. Grüner: "Analyte Identification Using Electronic Devices," Patent Application PCT/US2005/040295

G. Grüner and M. Briman: "Nanowire Network electrolyte Capacitor Nanosensor," UCLA, Provisional Patent Application.UCLA 2006 – 454- 1.

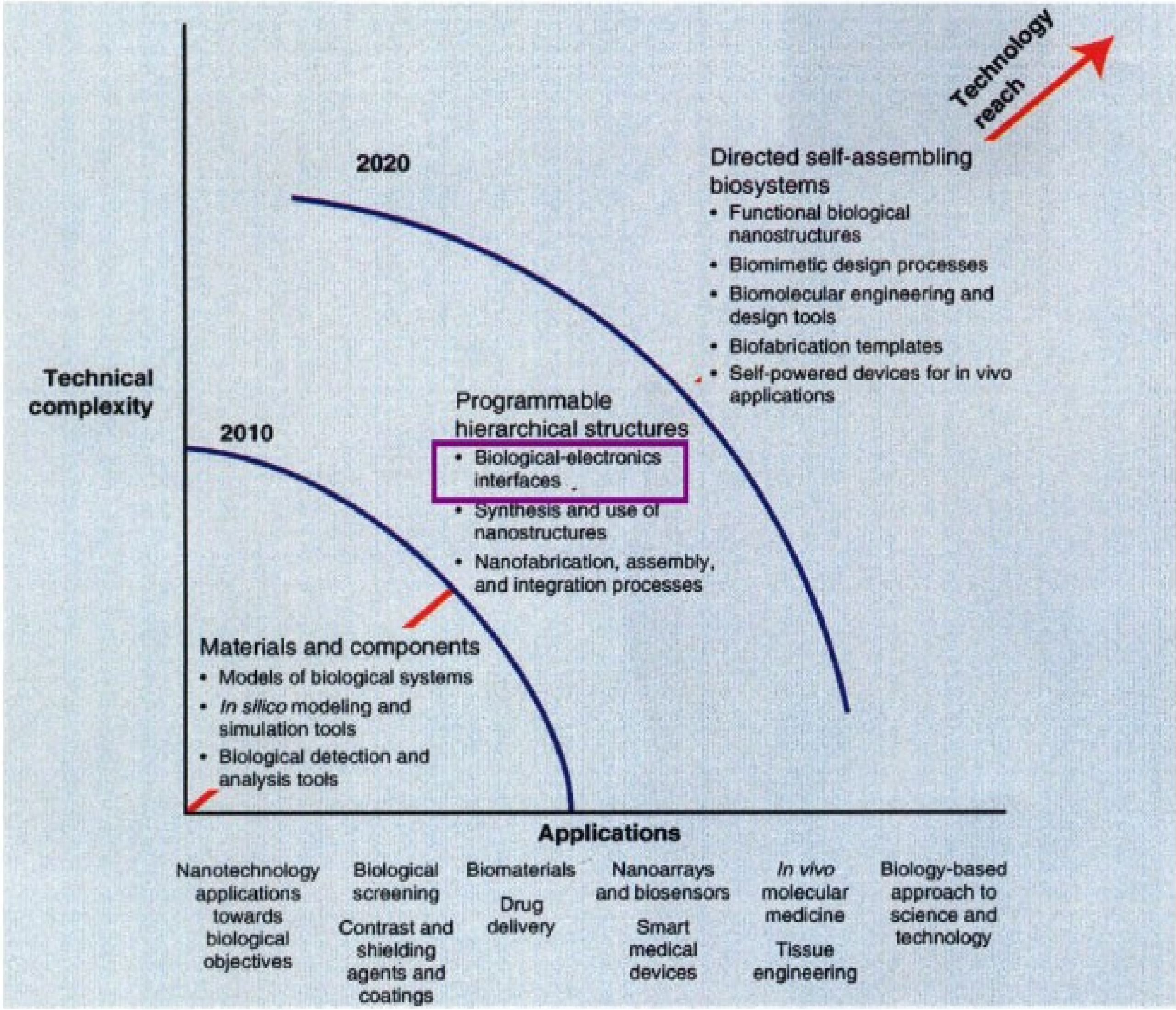

Figure 1 Nanobiotechnology: a continuum of opportunity for nanotechnology in the life sciences. Source: SRI Consulting Business Intelligence (SRIC-BC; Menlo Park, CA, USA).