

2nd Annual National Academies Keck *Futures Initiative* Conference
*Designing Nanostructures at the Interface
between Biomedical and Physical Systems*
Arnold & Mabel Beckman Center, Irvine, California
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Building a Cell-Chip Interface to Sense Response to Drug Leads and Toxins
Focus Group Description

Background

The responses of biological systems to drugs or toxins are typically measured at supracellular levels, ranging from tissue cultures to whole organisms. Some measurements have become possible at the level of single cells by the use of fluorescent indicators (e.g., fluorescent protein indicators of gene expression, calcium concentration, or receptor binding and internalization). A number of assay systems of these kinds have been commercialized (Ref 1). The further development of cellular scale detection, and the development of models of cellular scale responses, would contribute greatly to the discovery of new pharmaceuticals and protective agents.

The Problem

Some issues relating to the development of cellular scale detection methods and models include the following:

- Some biopolymers are present in small numbers in the cell, so that noise due to small sample sizes should be considered (Ref 2).
- Electronic detection of bioactive molecules by nanoscale systems such as carbon nanotubes is currently being explored (Ref 3). A useful on-line lecture by G. Gruener is available at <http://cyclotron.aps.org/weblectures/biology2004/20040201-umwlc0001-002/real/index.htm>.
- Optical nanosensors for use in single cells are also currently being explored (Ref 4).
- What other ideas might be worth considering? Inverted receptors, with normal cytoplasmic readout side available outside the cell for signal transduction? Functionalized viral capsids or other structures that might be endocytosed?

Initial References

- 1- Commercial technologies: example from BioImage - http://www.bioimage.com/pdf/Science_and_Tech%20v2.pdf
- 2 - J. Paulsson, Summing up the Noise in Gene Networks. *Nature*, 2004. 427, p. 415-418.
- 3 - A. Star, J. P. Gabriel, K. Bradley, G. Gruener, Electronic Detection of Specific Protein Binding Using Nanotube FET Devices. *Nano Letters*, 2004. 3, p. 459-463.
- 4 - P.M. Kasili, J.M. Song, T. Vo-Dinh, Optical Sensor for the Detection of Caspase-9 Activity in a Single Cell. *Journal of the American Chemical Society*, 2004. 126, p. 2799-2806.