Menachem Elimelech

Science and Technology for Sustainable Water Supply

Traditional methods for water purification are chemical and energy intensive. Highly effective, low-cost, robust technologies for augmenting water supplies are needed, with minimal impact on the environment. Recent advances in the science and technology of water purification will be presented, focusing on desalination and water reuse technologies. Major developments in these technologies are made possible due to recent advances in materials science, nanotechnology, and the fundamental understanding of the physics/chemistry of the solid-water interface. Among the topics discussed in this presentation are the development of fouling-resistant membranes for water treatment, use of interfacial force measurements to elucidate the antifouling mechanism of water treatment membranes, highly permeable reverse osmosis membranes incorporating nanomaterials, robust systems for wastewater reuse, and novel desalination technologies that may dramatically alter the energy/water nexus. These technologies are discussed in the context of the global challenges in water supply and energy.
Desalination shocks in microstructures

Salt transport in bulk electrolytes occurs by diffusion and convection, but in microfluidic devices and porous media (“microstructures”), surface conduction and electro-osmotic flow also contribute to ionic fluxes. The classical theory assumes linear response to a small voltage, but what happens when a large voltage is applied? This talk describes some surprising nonlinear electrokinetic phenomena that result from the competition between bulk and interfacial transport in a microstructure, triggered by the removal of ions at a boundary (e.g. by electrodialysis or electrodeposition). At constant voltage, the microstructure can sustain an over-limiting current (exceeding diffusion limitation) without any hydrodynamic or chemical instability. At constant current, a “desalination shock” can propagate through the microstructure, leaving behind a macroscopic region depleted of ions and particles. These nonlinear phenomena are explored by mathematical analysis (homogenization, similarity solutions, stability, characteristics) and experiments on copper sulfate desalination in glass frits, which suggest a new approach to water desalination and purification (“shock electrodialysis”).
Computational approaches to resolving the TGF-β paradox in cancer

Transforming growth factor β (TGF-β) signaling regulates a wide range of cellular and physiologic processes including proliferation, apoptosis, differentiation, migration, angiogenesis, and immune surveillance. During the early stages of epithelial tumorigenesis, TGF-β functions as a potent tumor suppressor primarily by inhibiting cell proliferation and by inducing apoptosis. However, the level of this cytokine, TGF-β, is often significantly elevated in malignant tissues and blood from cancer patients with poor prognosis. Accordingly, in the late phases of tumor progression, the role of TGF-β appears to become one of tumor promotion, apparently supporting growth, subverting the immune system, and also facilitating epithelial to mesenchymal transition (EMT), invasion and angiogenesis. This has created the widely held perception that TGF-β is simultaneously a tumor suppressor under one condition and a tumor promoter under another. But how does a single stimulus produce multiple contradictory results? This long-standing enigma of TGF-β biology remains poorly understood because the role of TGF-β on cancer is too complex for qualitative description.

As a first step toward a quantitative explanation of such paradoxical roles of TGF-β in cancer, we have developed a dynamic model of the canonical TGF-β pathway via Smad transcription factors, the major intracellular mediators of the signaling cascades, based on reported experimental observations in the literature. By describing how an extracellular signal of the TGF-β ligand is sensed by receptors and transmitted into the nucleus through intracellular Smad proteins, the model yields quantitative insight into how TGF-β-induced responses can be modulated and regulated. The model also allows us to predict possible dynamic behavior of the Smad-mediated pathway in abnormal cells, and provides clues regarding possible mechanisms for explaining the seemingly contradictory roles of TGF-β during cancer progression. Based on the reported observations that TGF-β receptors are abnormally altered in a variety of human cancers, simulations of cancerous signaling using our model indicate that reduction in the levels of functional receptors may lead to altered TGF-β signaling behavior where tumor suppression characteristics are lost as a result of attenuated and nearly transient Smad retention in the nucleus. In particular, our dose-response results provide a potentially important characteristic of cancer, that is, cancer cells may require higher than normal levels of TGF-β in order to elicit nuclear Smad-mediated activity. These results have motivated the subsequent development of a macroscopic computational model of TGF-β regulation of prostate cell population from a control theory perspective to explain the paradoxical clinical observation that unusually high levels of TGF-β correlate with poor prognosis in prostate cancer. Our macroscopic model indicates that the observed elevated level of TGF-β is a consequence of acquired TGF-β resistance exhibited by the cancer cell, not the cause, because a putative TGF-β control system must secrete more TGF-β in a futile attempt to achieve the level of tumor suppression attainable with normal, responsive cells. If this hypothesis is validated, its most significant implication will be that the current approach of targeting TGF-β ligand therapeutically may have to be abandoned in favor of re-sensitizing the cells to the tumor suppressive effect of the TGF-β.
Dr. Kevin Dorfman

Engineering microdevices for DNA electrophoresis

If one views the typical tasks in molecular biology from a chemical engineering perspective, it becomes clear that separating DNA by size is one of the primary "unit operations" in biology labs. In recent years, there has been a concerted effort to shrink the corresponding molecular biology "plant" onto integrated lab-on-a-chip devices in order to reduce the time and material required for a given analysis. In contrast to the standard unit operations in chemical engineering (e.g., distillation columns), no design rules exist for downscaling many of the unit operations in molecular biology. Indeed, it is not obvious that simply scaling down macroscopic systems such as agarose gels will yield the best results.

We have taken a systematic, quantitative approach to understanding the transport phenomena governing new microfabricated devices for DNA electrophoresis through a combination of experiments, simulation and theory. In this presentation I will discuss our current understanding of the transport of DNA in post arrays, in particular how these systems can be understood in the context of continuous-time random walk theory. The overarching theme of the talk is that the transport phenomena in these devices often violate the conventional wisdom gained from decades of studying DNA electrophoresis in agarose gels.
Electrodes for solid oxide fuel cells and electrolyzers

Because SOFC and SOE are based on electrolytes that are oxygen-ion conductors, SOFC can operate on a wide range of fuels, including methane and other hydrocarbons. Likewise, electrolysis of CO\textsubscript{2} is feasible in an SOE. However, to allow stable operation with a wider range of feeds to the electrodes, new electrode materials must be developed. This talk will describe the methods being developed at Penn that allow the electrode composition and structure to be varied easily. Results for both fuel- and air-side electrodes will be discussed. Initial results with molten-metal anodes for direct-carbon fuel cells will also be presented.