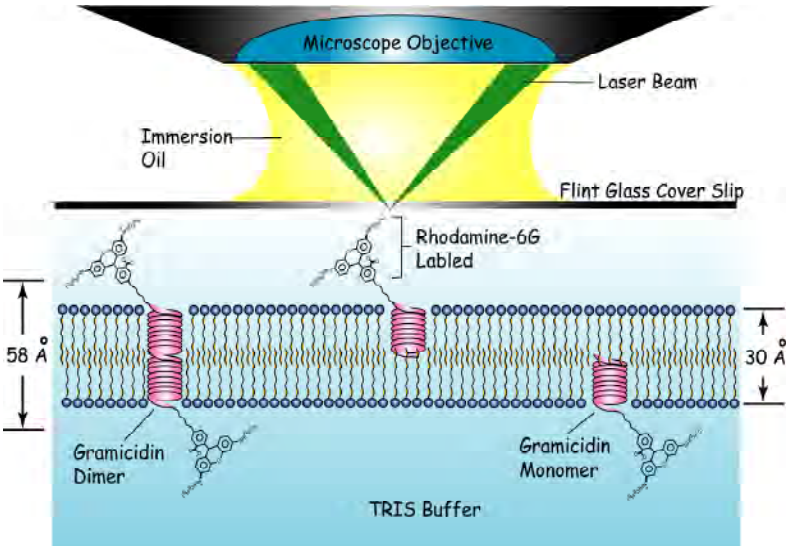
Bioscience and Technology
Biomimetics



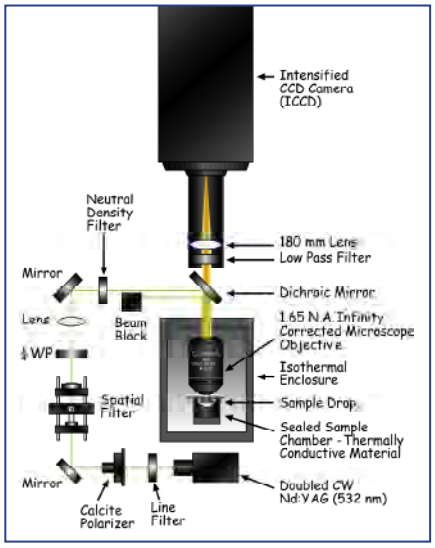


Figure 1. Experimental apparatus for optical studies of transmembrane proteins.

Transmembrane protein function evaluated in biomimetic environments

Sandia researchers are overcoming the difficulties associated with studying transmembrane protein function in the complex environment of a living cell, and creating a body of knowledge that could benefit drug development, medical treatments, and biosensing technologies.

Despite decades of intensive research in the transmembrane protein structure-function relationship field, not a lot is known about it. Today, Sandia researchers are developing artificial biomimetic structures into which we can incorporate transmembrane proteins, eliminating the complications of the cell and cell membrane, and allowing us to isolate individual proteins for study while retaining their native structure and function. We also are adapting optical and electrochemical techniques to probe the structure and function.

Our initial work focused on the thermodynamics of gramicidin ion channel formation in supported lipid bilayers (Fig. 1), investigated through single molecule fluorescence imaging. More recently, lipid-coated nanoporous silica beads (Fig. 2) have shown promise as convenient platforms for the study of transmembrane proteins (Fig. 3). We find that the proteins can be correctly oriented in these artificial substrates, that they have near-native diffusion characteristics, retain their function in this biomimetic environment, and the beads are the most stable biomimetic platform reported to date. We now have the ability to perform optical fluorescence and electrochemical patch clamp studies, isolating a single protein on these microspheres.

Ultimately, our goal is to produce new solid-supported lipid bilayer platforms in which single transmembrane proteins can be simultaneously interrogated with electrochemical and optical probes. Early prototypes of this device are shown in Fig. 4. Single molecule spectroscopic measurements, in combination with electrical detection, offer a unique opportunity for obtaining a dynamic view of structural/functional relationships on transmembrane proteins.

The potential impact of combined optical and electrochemical measurements goes well beyond the study of basic biophysical mechanisms and can provide the ultimate in biodetection schemes: using the specificity of biochemical interactions, the sensitivity of single molecule fluorescence detection, and the enormous electrochemical amplification afforded by the opening of a membrane channel.

See reverse side for contacts.

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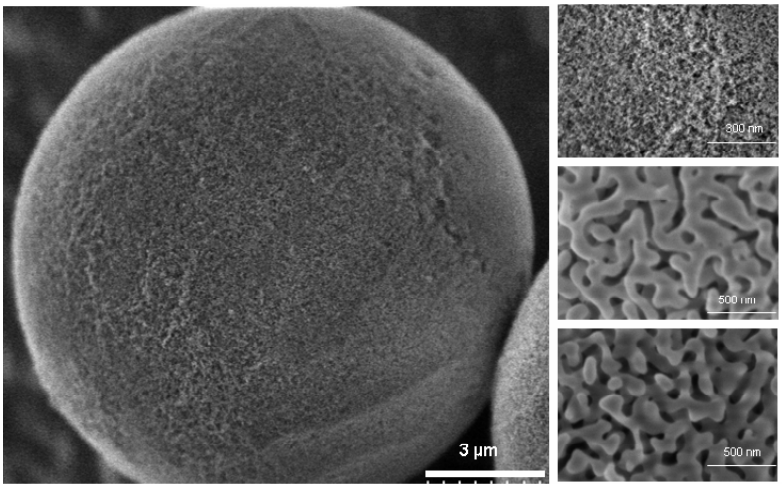

Figure 2. SEM images of nanoporous silica microspheres. Left: 10,000x image of a 10 µm bead with 10 nm pores. Right, descending vertically: 100,000x images of beads with 10 nm, 50 nm, and 100 nm pores.

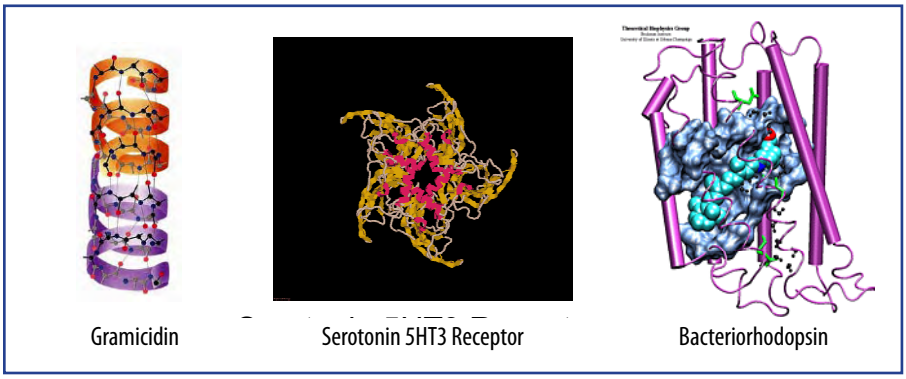

Figure 3. Transmembrane proteins under study.

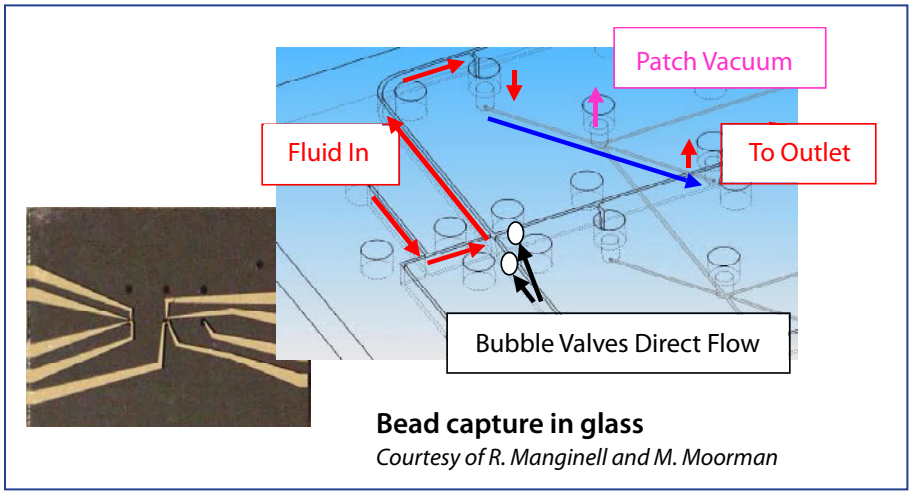

Figure 4. Prototype development of a microfluidic instrument for simultaneous optical and electrochemical measurements on a single transmembrane protein.

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