Extracellular and Intracellular Glucose Sensors for Monitoring Glucose Metabolism

Liqiang Zhang, Fengyu Su, Sean Buizer, Yanqing Tian, and Deirdre R. Meldrum
Center for Biosignatures Discovery Automation, Biodesign Institute, Arizona State University, Tempe, AZ 85287

Statement of Purpose: Glucose metabolism is one of the most important aspects of cell metabolism. It is not only the main energy source for cells, but it provides the necessary biomasses for cell proliferation. Monitoring glucose metabolism of cells reflects cell responses to stimuli and proliferative states including the unregulated cell divisions in tumors. Based on the sensing moiety (GS-COOH) shown in Figure 1, two glucose sensors, i.e. extracellular sensor and intracellular sensor, have been developed by our group to monitor the cellular glucose uptake and the change of glucose levels in live cells.

Methods: Sensor film for extracellular glucose was prepared through two steps (Figure 1). The first step is to prepare a film with amino-groups on the surface (Film-NH2). The second step is to graft the GS-NHS onto the amino-containing film to form glucose sensor film. A sensing probe for oxygen (OS) was also polymerized into the film making the sensor capable of simultaneously monitoring the consumption of cellular oxygen and glucose.

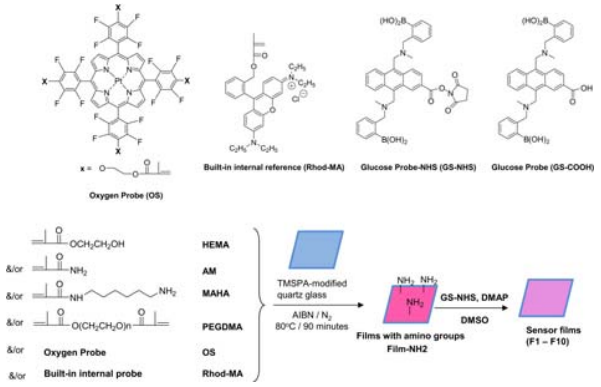

Figure 1. Chemicals and schematic drawing for the preparation of extracellular sensor.

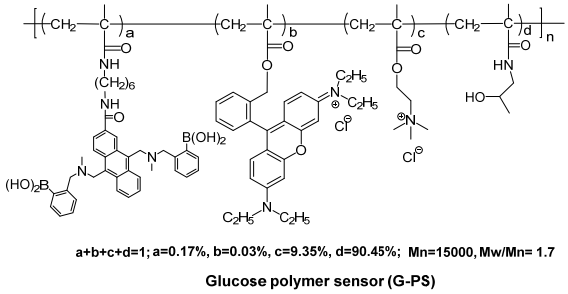

Figure 2. Chemical structure of a polymeric intracellular glucose sensor (G-PS).

The chemical structure of the intracellular glucose sensor was given in Figure 2. The polymer possesses positive charges to ensure its high efficiency for cellular uptake.

Results: The extracellular sensors were titrated in PBS buffer, which showed excellent responses to glucose (Figure 3A) as well as to oxygen (Figure 3B). The sensor was also demonstrated to be suitable for simultaneously

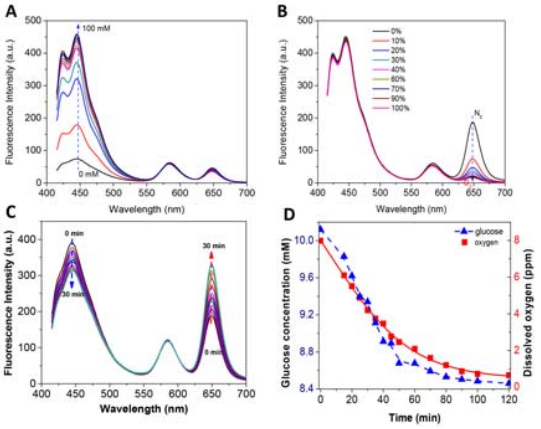

Figure 3. Responses of an extracellular dual sensor to glucose (A) and oxygen (B). C shows the emission spectral changes during the growth of bacteria (B. Subtilis). D gives the glucose and oxygen uptake assay by mammalian cells (HeLa cell).

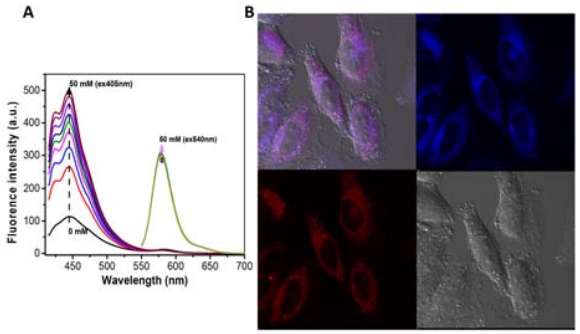

Figure 4. A: glucose responses in PBS buffer excited at 390 nm and 540 nm, respectively. B: images of HeLa cells after 16 hour internalization with the G-PS.

monitoring glucose and oxygen for bacterial and mammalian cells. The changes of glucose and oxygen levels can be detected dynamically (Figure 3C and 3D).

G-PS shows a good response to glucose and cell permeability with low cytotoxicity (Figure 4). With an internal built-in reference fluorescent probe in G-PS, ratiometric approach can be applied for intracellular glucose concentration determination with high accuracy.

Conclusions: We have developed glucose sensors which are suitable for monitoring intracellular and/or extracellular glucoses metabolism. Integrated with microfabrication and microscopy, these sensors are expected to be used in high throughput scanning for single cell metabolism understanding.

References:

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