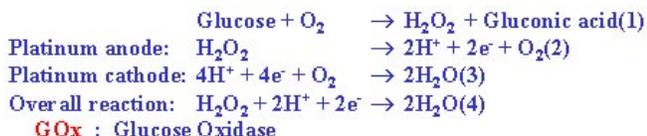


# Glucose Sensor and Glucose Control Development and Evaluation

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It is well known that glucose is a necessary nutrient for mammalian cell culture. A reliable noninvasive glucose sensor, stable over a long duration, is important for continuous real-time monitoring of glucose in bioreactors. Controlling the concentration of glucose in bioreactors alters cellular metabolism and, therefore, becomes important for in vitro cell culture. The sensor consists of a three-electrode amperometric system with a flow cell and a membrane. The glucose diffuses through the membrane and, in the presence of glucose oxidase, converts to hydrogen peroxide and gluconic acid. Generated hydrogen peroxide is measured amperometrically on a platinum working electrode at 0.7 V with the silver/silver chloride reference electrode.



The glucose sensor can continuously measure glucose present in cell culture medium in a perfused bioreactor system. The measurement is accurate within  $\pm 15$  mg/dl in the glucose range between 50 and 300 mg/dl. The glucose sensor should be calibrated once every 15 days. The sensor performed satisfactorily up to 55 days in a bioreactor cell run.

The glucose control system consists of a glucose sensor, a glucose stock solution, and the necessary hardware and software to run the system. The glucose sensor measures the glucose of the perfused culture medium in the bioreactor where mammalian cells are grown. A glucose stock solution consisting of a high glucose concentration was added to the perfused culture medium to keep the glucose within a known range. The volume of the stock solution needed for 25 mg/dl of glucose change is 2 ml for a bioreactor volume of 380 ml. It should be noted that the glucose consumption rate decreases

as the day progresses before the complete replenishment of medium. During this time, the pH of the medium decreased and the waste product concentrations increased.

