Fabrication and Characterisation of a Glucose-Sensitive Hydrogel

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Stimuli-responsive hydrogels are an attractive material for biosensing applications due to their biocompatibility, ability to incorporate a wide variety of biorecognition molecules and tuneable mechanical properties. In this study, a glucose-sensitive hydrogel has been developed based on the immobilization of glucose oxidase (GOx) within an ionisable polymer network. The catalysis of glucose to gluconic acid produces an acidic environment, thereby ionizing pendant basic groups of the network and generating charge along the polymer backbone. Electrostatic repulsion forces between adjacent ionized groups creates a large osmotic swelling force altering the hydrodynamic volume and permeability of the gel.

The sensitivity and response time of the hydrogel were optimized via weight-based swelling studies. A linear increase in swelling was observed from 1 - 20 mM glucose ($r^2 = 0.9946$), encompassing the physiological range of blood glucose levels. Additionally, novel electrochemical strategies to track the swelling response of these glucose-sensitive hydrogels were explored, including both using voltammetry of a bulk solution redox probe and non-faradaic electrochemical impedance spectroscopy (EIS).

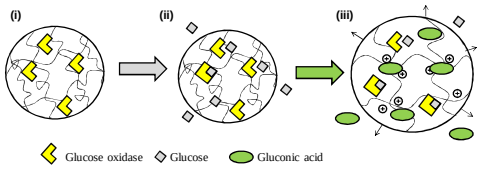

Figure 1. Schematic of the swelling mechanism: (i) Glucose oxidase immobilized within a polymer network, (ii) glucose diffusion and (iii) production of gluconic acid/network ionization.

Optimization of the Swelling Response

The swelling behaviour of the hydrogel membrane was determined gravimetrically. Hydrogel discs were weighed (W_{dry}) before immersion into glucose/gluconic acid (10 mM). At specific time intervals, the swollen discs were removed from solution, blotted dry and weighed (W_{wet}). (Swelling ratio = $(W_{wet} - W_{dry})/ W_{dry}$)

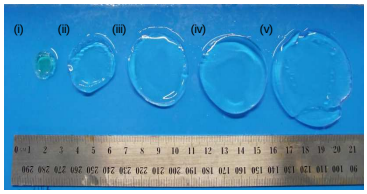

Figure 2. Swelling response of GOx hydrogels in 10 mM glucose after (i) 0 min, (ii) 100 min, (iii) 200 min, (iv) 300 min and (v) 400 min

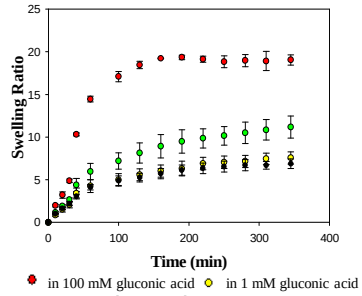

Figure 3. Swelling response of GOx hydrogel in gluconic acid. (n=3)

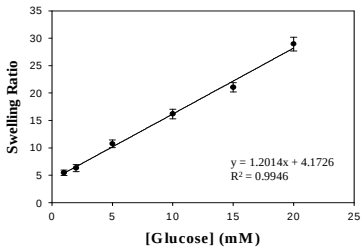

Figure 4. Calibration curve of GOx hydrogel discs after 100 min swelling time.

Use of this technique enabled facile determination of the optimum GOx loading (5 % w/w) and investigation into the incorporation of catalase, which breaks down the H_2O_2 by-product increasing the stability of GOx and the oxygen supply. Also, it was observed that providing mechanical agitation to the solution dramatically accelerated enzyme kinetics.

Characterisation of a Hydrogel-Modified Carbon Cloth Electrode

Carbon cloth was selected as a flexible, conductive electrode material that allows the hydrogel to swell without restriction and remain adhered to once swollen.

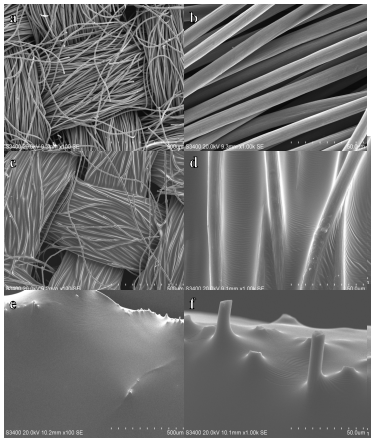

Figure 6. SEM images of (a)-(b) bare electrode, (c)-(d)1 dip-coat of hydrogel and (e)-(f) 5 dip-coats of hydrogel.

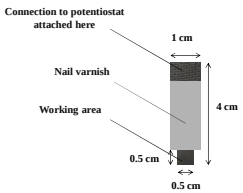

Figure 5. Schematic of carbon cloth electrode.

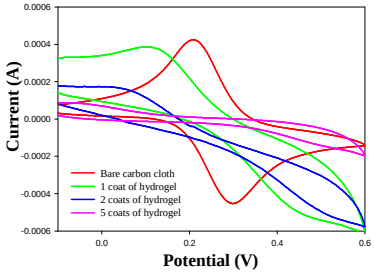

Figure 7. Cyclic voltammograms of different hydrogel loadings in 2 mM ferri/ferrocyanide in 1 M KCl .

Electrochemical Characterisation

The non-electrical swelling signals were converted into measurable electrical signals using electrochemical transduction. Tracking of the swelling response with glucose concentration was achieved with voltammetry of a bulk solution redox probe and non-faradaic EIS.

(i) Voltammetry

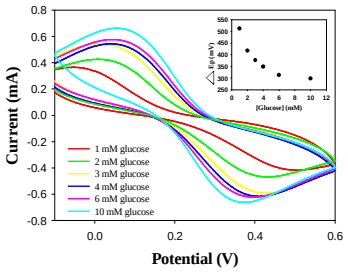

Figure 8. Cyclic voltammograms of GOx hydrogel in 2 mM ferri/ferrocyanide (in 1 M KCl) after exposure to glucose concentrations for 24 hr. Inset represents the relationship between ΔEp and glucose concentration.

Bulk solution Fe^{2+}/Fe^{3+} reversibility and peak current improved with increasing glucose concentration. Enhanced diffusional properties are attributed to the increased porosity in the hydrogel network, resulting in lower electric resistance.

(ii) EIS

Impedance decreased with increasing glucose concentration across the whole frequency range, with maximum changes in magnitude observable at lower frequencies (*Figure 9*).

The presence of the hydrogel produced a kinetic barrier at the surface of the carbon cloth, perturbing interfacial electron transfer. The resistance to electron transfer decreased with glucose concentration due to network expansion *(Figure 10).*

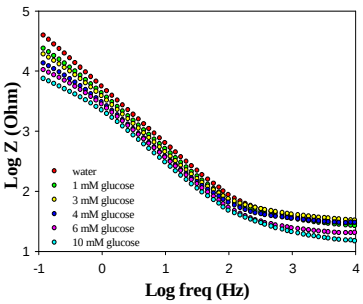

Figure 9. Bode plot of GOx hydrogel after swelling in glucose for 24 hr (in 10 mM PBS).

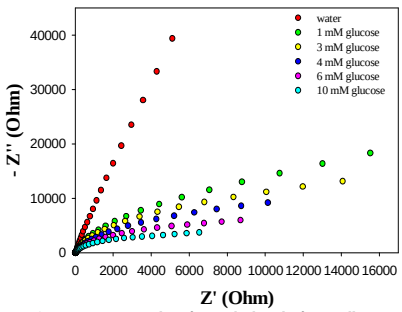

Figure 10. Nyquist plot of GOx hydrogel after swelling in glucose for 24 hr (in 10 mM PBS)

Conclusion

An effective enzyme-based hydrogel capable of glucose detection has been illustrated. Sensitivity of the gel to physiological blood glucose levels was optimised via swelling studies. Use of a flexible electrode material enabled electrochemical characterisation. Successful tracking of the swelling response electrochemically was achieved using both indirect (voltammetry) and direct (non-faradaic EIS) methods of analysis.

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