Chemical sensors for continuous blood-glucose monitoring

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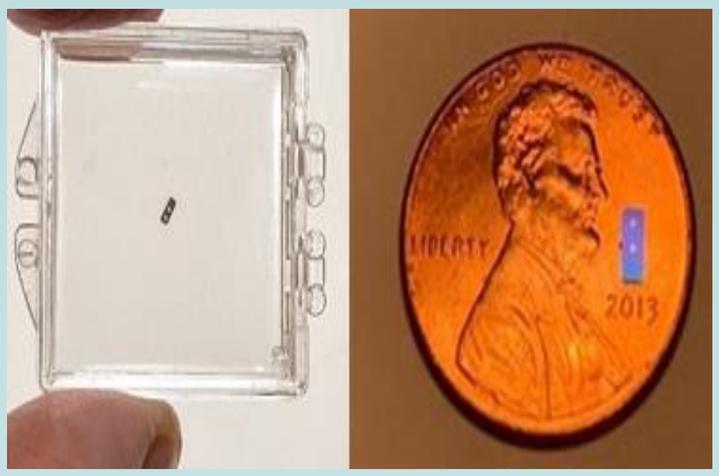
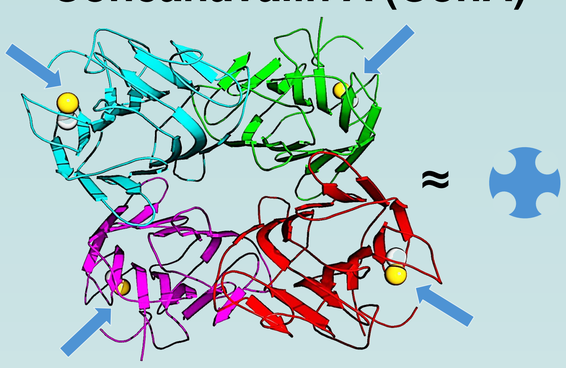
1). Background

- Lifecares Sencell technology is an implantable sensor that measures glucose levels in real time.
- It has superior accuracy and longevity to commercial continuous-glucose-measurement devices.
- It uses the binding of a glucose receptor (the lectin Concanavalin A) with a large glucose-like ligand (Dextran 40) to measure external glucose concentrations and transfer this into a measurable osmotic pressure signal.



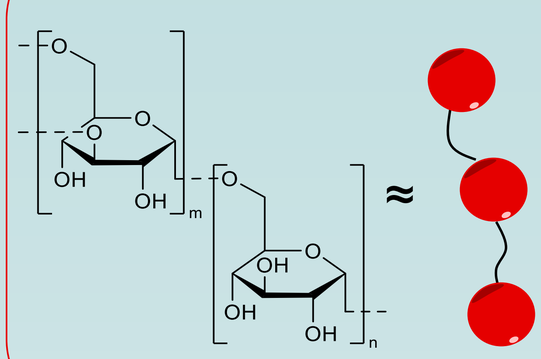
(Left) Core sensor unit and (Right) Size comparison of sensor to a coin.

Concanavalin A (ConA)

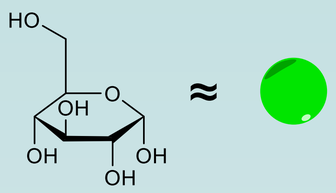


four sugar binding sites

Dextran

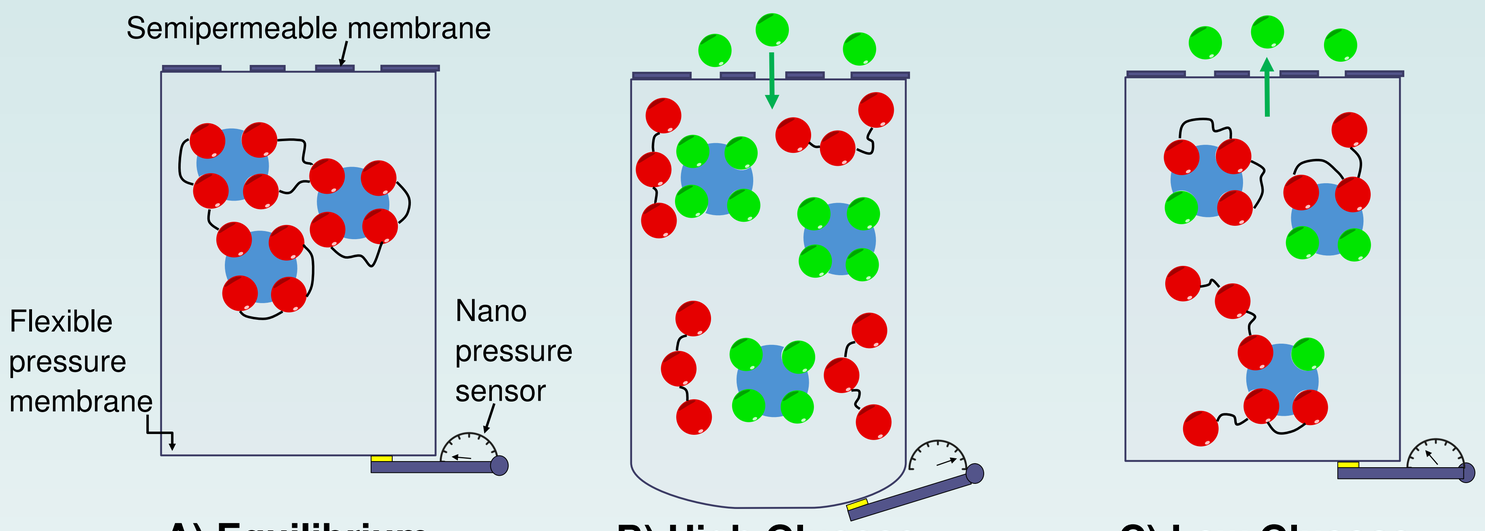


Glucose

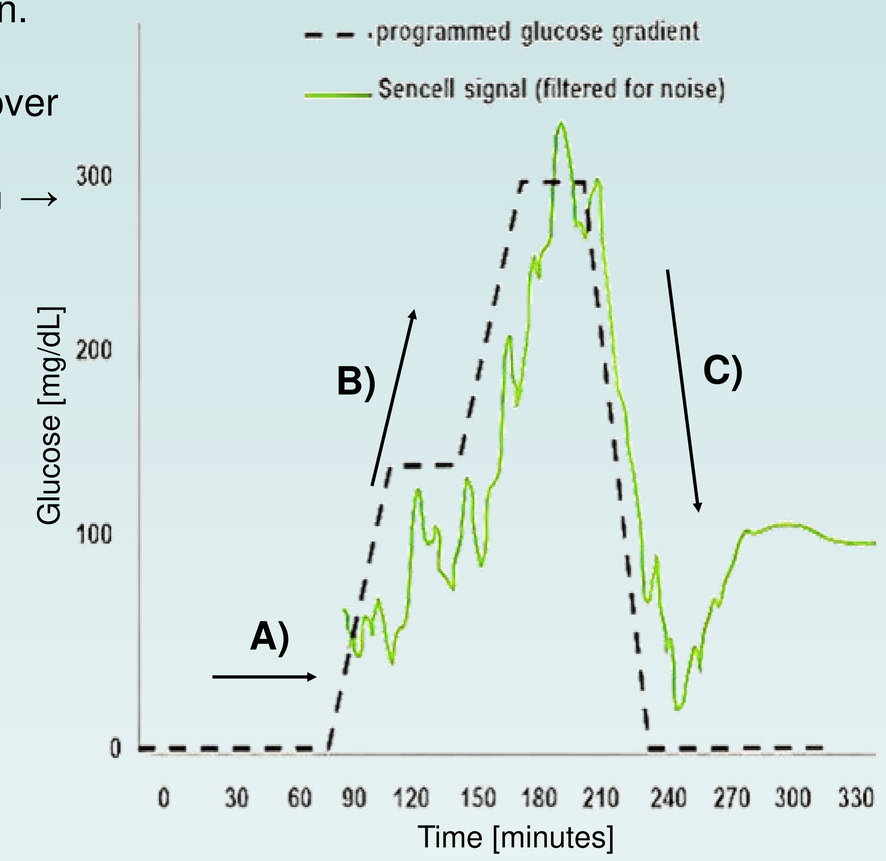


- Within the sensor is a semipermeable chamber containing a solution of ConA and Dextran.

A. At equilibrium ConA and Dextran are bound in a complex.
B. Increased glucose concentration → Selective binding of Concanavalin A to glucose over Dextran → More particles in solution → Increased osmotic pressure.
C. Decrease glucose concentration → free binding sites of ConA will bind free Dextran → Less particles in solution → Decreased osmotic pressure.[2]



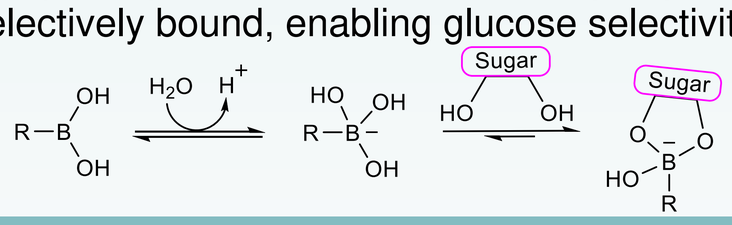
Osmotic pressure changes induced by pressure sensor by exposure to glucose[1]



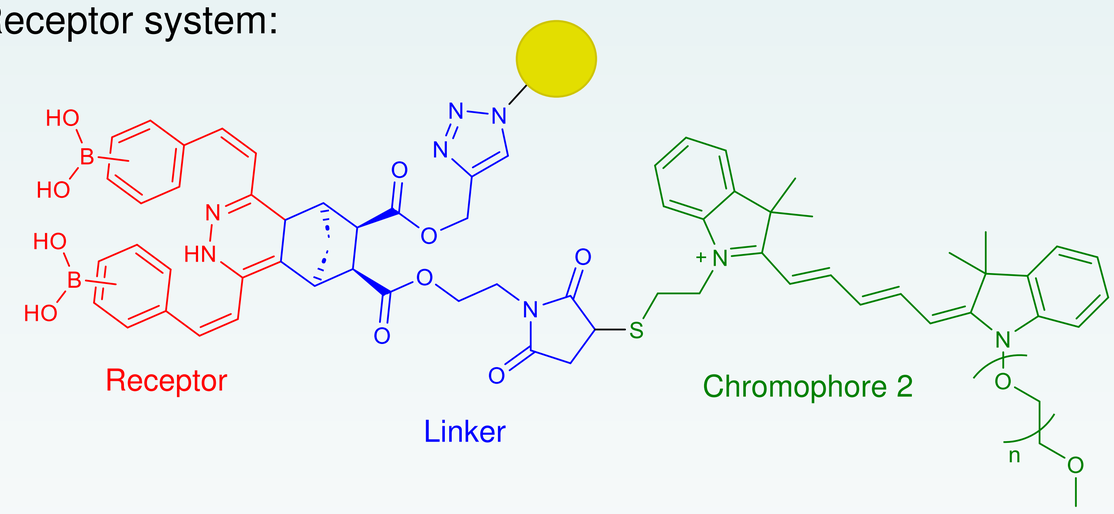
- However, ConA is cytotoxic and Dextran strands get easily entangled hindering the sensor, so an alternative system is required.

2). Sugar sensors using boronic acids

- Boronic acids react with the *cis*-1,2 and 1,3-diols found in sugar motifs to form a cyclic ester.
- This reaction is reversible making them ideal for continuous glucose measurement systems.
- By adjusting the position of boronic acid groups, specific sugars can be selectively bound, enabling glucose selectivity.[3]



Receptor system:



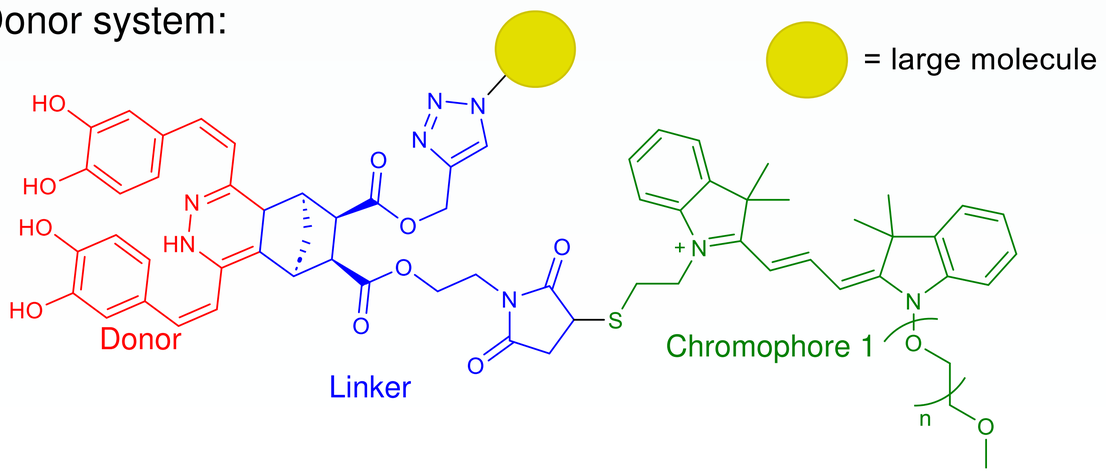
- The donor and receptor will bind at equilibrium and should be close enough to form a FRET pair.
- Upon glucose addition, the receptor selectively binds and displaces the donor molecule, raising osmotic pressure and disabling FRET emission.

3). Aims and Synthetic Plan

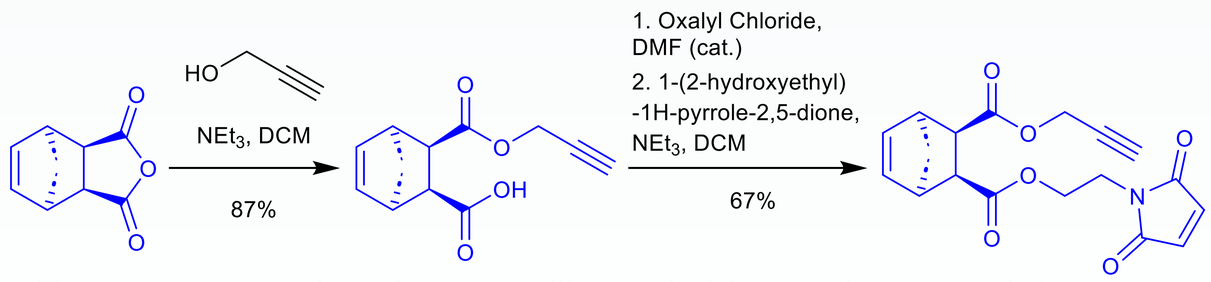
- To create a synthetic system that can replicate/improve upon the results of Sencell technology using boronic acids as a sugar sensor
- To implement a fluorescence resonance energy transfer (FRET) pair into the design.

Sensor design:

- Two different scaffolds will be built, one using boronic acids as a 'receptor' system and another with diols to act as a 'donor' system.
- Donor system:



4) Current progress – Linker synthesis



- Two-step procedure from readily available starting materials.
- Allows for a convergent synthesis of the complex scaffolds in a one pot procedure using orthogonal click reactions.

5) Associations and References

[a] University of Bath, [b] Lifecare Chemistry

1 A. Pfützner, B. Tencer, B. Stamm, M. Mehta, P. Sharma, R. Gilyazev, H. Jensch, N. Thomé and M. Huth, *Sensors*, 2023, **23**, 4541.

2 O. Krushinitskaya, PhD thesis, Vestfold University College, 2012.

3 Y. Egawa, R. Miki and T. Seki, *Materials*, 2014, **7**, 1201–1220.