A Near-Infrared Fluorescence Detector for Glucose Monitoring

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Minimally-Invasive Glucose Detection

We seek to design a portable near-infrared (NIR) fluorescence detection unit that will interface with an implantable glucose sensor previously developed and published by BioTex, Inc.[1,2] The device will provide a simple, minimally-invasive alternative to current glucose monitors.

Diabetes: A Looming Epidemic

- Approximately 20 million Americans, 300 million worldwide suffer diabetes.
- Glucose levels are monitored to determine the appropriate insulin treatment.
- Most monitors involve self-administered, invasive, frequent blood withdrawals ("finger-prick" method).
- Minimally-invasive designs measure interstitial glucose.

Current Non-invasive Device Limitations

Method	How it Works	Disadvantages
Dermal Trans-phoresis	Draws interstitial glucose through skin using electrostatic charge.	• Pads last only 13 hours. • Each pad requires calibration. • Gels cause skin irritation.
Glucose Oxidase Activity	Measures glucose oxidase activity with trans-dermal implant.	• Calibration required every 12 hours. • Implant must be replaced every 3 days.

BioTex Optical FRET Sensor[1]

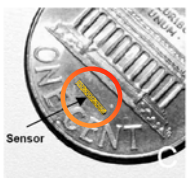

Figure 1. The BioTex sensor. (Figure courtesy of BioTex, Inc.)

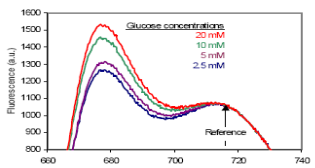

Figure 2. The BioTex sensor's typical emission spectrum. (Figure courtesy of BioTex, Inc.)

- Small, subcutaneously implantable sensor.
- The sensor is excited at 650 nm and emits a 675 nm glucose-dependent signal and a 715 nm reference signal.
- Emission of the NIR radiation occurs when fluorescence resonance energy transfer (FRET) between dyes is impaired by glucose binding.
- The fluorescence signal intensity ratio is dependent on interstitial glucose concentration.
- Allowing for real-time monitoring of glucose concentration.

Detection System

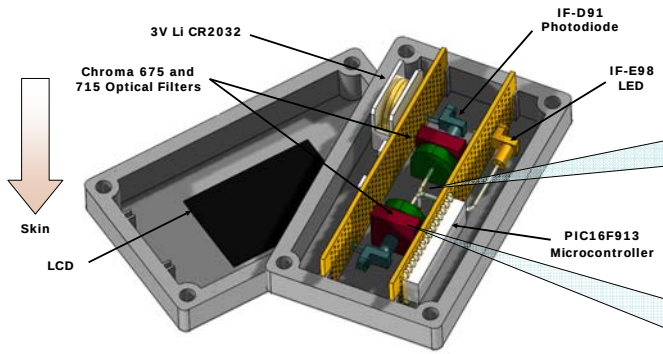

Figure 3. A CAD concept drawing of the final design for the device.

- Filtration occurs by 675 ±10 nm and 715 ±10 nm optical band-pass filters.
- Photodiode signals are electrically filtered and amplified.
- Photodiode voltages are standardized and the 675/715 ratio is determined and exported via LabView.
- The V_{RMS} generated by each emission is adjusted with respect to a PBS standard. The 675/715 ratio is displayed.

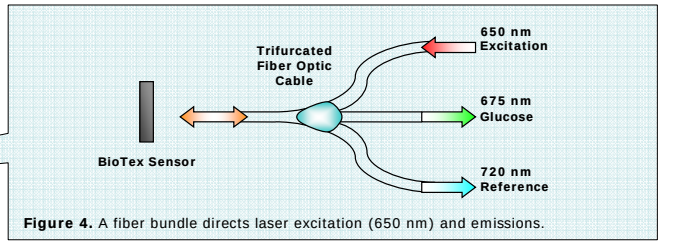

Figure 4. A fiber bundle directs laser excitation (650 nm) and emissions.

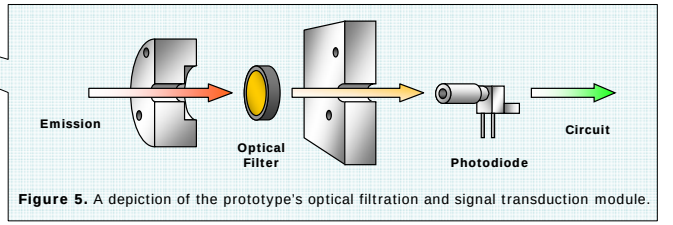

Figure 5. A depiction of the prototype's optical filtration and signal transduction module.

Figure 6. A screen capture of the current LabView GUI.

Results

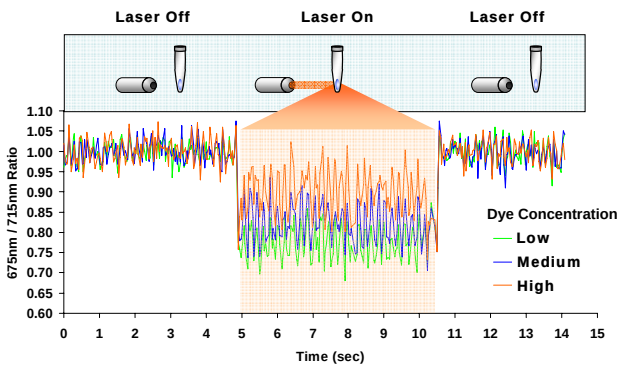

Figure 7. A647-dextran and Transfluosphere beads in 50, 400, and 800 µg/ml concentrations.

- A 5-second excitation showed immediate signal response.
- There were no significant differences between groups for the excitation laser OFF condition (ANOVA).
- There were significant differences between groups (ANOVA $p<0.0001$) for the excitation laser ON condition.
- Calculated ratios can be used to estimate dye concentration.

Conclusions

- Our current device can differentiate between fluorescence intensities of model dyes.
- Our detector is capable of measuring fluorescence at the wavelengths associated with the FRET glucose sensor.
- Increased sensitivity is needed to adequately determine dye concentrations.
- Future work includes calibration and personalization models, *in vivo* animal testing and FDA and FCC approval.

Acknowledgements

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References

[1] Ballerstadt R, Evans C, Gowda A, McNichols R. "In vivo performance evaluation of a transdermal near- infrared fluorescence resonance energy transfer affinity sensor for continuous glucose monitoring." Diabetes Technol Ther. 2006 Jun; 8(3):296-311.

[2] Ballerstadt et al., "Assay and method for analyte sensing by detecting efficiency of radiation conversion," U.S. Patent No. 7,166,458.