Electrospun Nylon Fibres with Integrated Polypyrrole Molecularly Imprinted Polymers for the Detection of Glucose

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Abstract:

Electrospun nylon 6,6 fibres incorporating polypyrrole (PPy) molecular imprinted polymers (MIPs) were produced for the selective detection of D-glucose using a thermal detection methodology. PPy MIPs were produced using a facile bulk synthesis approach and electrospun into intricate fibrous scaffolds giving a highly mass-producible sensing interface. The maximum incorporation of MIPs and greatest sensing performance was found to be 12.1 wt% in conjunction with the Heat-Transfer Method (HTM), a low-cost and simple thermal detection method that measures changes in the thermal resistance at the solid-liquid interface. It is demonstrated that a 12.1 % incorporation of MIPs into the electrospun fibres produces the widest working linear range with a limit of detection of 0.10 ± 0.01 mM. There were no observed change in the measured thermal resistance response to incubation with a series of structurally similar compounds, providing evidence toward the selectivity of the platform. Additionally, the sensing platform exhibited a linear working response to glucose samples in artificial sweat solutions in the biologically relevant range. This is the first report of the incorporation of MIPs into nylon 6,6 fibres for the detection of glucose and points toward the possibility of developing mass-producible electrospun fibres embedded with low-cost recognition elements of improved thermal and chemical stability for the application of wearable sensor technology.

Keywords: Electrospinning, Glucose Detection, Wearable Technology, Heat-Transfer Method (HTM), Molecularly Imprinted Polymers (MIPs).

Introduction

The development of glucose biosensors revolutionised the healthcare industry and treatment of diabetes worldwide. Type 2 diabetes mellitus is a common condition that causes increased levels of glucose in the blood and was believed to be affecting over 400 million people globally in 2015, with numbers rising still.[1] Monitoring of glucose for these patients would typically be done using a finger prick and measurement in blood, which is not optimal and can cause discomfort. However, there is recent work providing evidence for a correlation between glucose concentrations in blood and sweat, which introduce the possibility of non-invasive monitoring, with glucose concentrations in sweat ranging from 0.2 – 1.2 mM.[2] With the rapidly improving performance and decreasing size of mobile devices, wearable sensors are receiving ever-increasing attention for monitoring the health, lifestyle and surroundings of the individual.[3] Common commercially available wearables focus on the measurement of vital signs and mobility such as step counters, heart rate and temperature.

More recently, advances in non-invasive chemical sensing have allowed for the detection and monitoring of chemical markers for healthcare applications.[4] This revolution in sensing technology has allowed for the progression away from laboratory *in-vitro* testing involving blood or urine towards more non-invasive media such as sweat,[5] saliva,[6] tears[7] and interstitial fluid.[8] To achieve such wearable devices, the components need to differ from conventional rigid electronics. One such example is electronic textiles (termed e-textiles), which possess desirable properties such as flexibility, lightweight and wearability.[9] Weaving sensing fibres into textiles can overcome typical drawbacks of fragility, breathability and comfort commonly encountered with thin-film based wearable sensors.[10]

Electrospinning is a low-cost and robust methodology for the creation of fibres, with the ability to produce these in the nanometre regime.[11] It involves the application of a strong electrostatic field to a capillary connected to a polymer filled reservoir. This produces electrically charged jets of polymer solution directed toward the counter electrode, which can be a flat surface, contoured substrate or rotating drum.[12] These electrospun polymeric fibres produce intricate fibrous scaffolds with enhanced

specific sensing surface area that can increase the sensitivity and response time of polymer-based biosensors.[13]

Molecularly Imprinted Polymers (MIPs) have received increasing attention for use in biosensors due to their improved thermal and chemical stability over more commonly used biological recognition elements.[14] They are formed *via* a process in which monomers self-assemble around a target molecule, according to the exposed functionalities. The resulting polymerization process 'freezes' the monomers in place and creates specific binding sites for the target. Removal of the target then allows for the re-binding of the target molecule when exposed to it.[15]

In this paper, we describe the incorporation of MIPs, imprinted for D-glucose, into a nylon based electrospun fibre for detection in sweat using the Heat-Transfer Method (HTM) as proof-of-concept. This methodology functions through the blocking of heat when the target analyte is bound to the interface and has been utilised for the detection and monitoring of small molecules,[16] protein biomarkers[17] and microorganisms,[18] highlighting the flexibility of the technique Currently, there are multiple reports of sensor platforms for the detection of glucose in sweat, with the majority of them utilising a combination of electrochemical detection and glucose oxidase.[19] This is the first report of MIPs electrospun into nylon for the detection of glucose, which provides the opportunity for the mass production of a low-cost recognition element, that can easily be integrated in a wearable sensor platform with superior thermal and chemical stability. This work highlights the possibility of developing electrospun sensors with integrated MIPs, which could in future we used to produce wearable sensors with much longer working lifetimes.

Experimental Section

Reagents

D-glucose, fructose, galactose, L-lactic acid, nylon 6,6, pluronic P123, pyrrole, sucrose, urea, ammonium chloride, acetic acid and sodium chloride were purchased from Sigma (Gillingham, United Kingdom). Formic acid, methanol was obtained from Fisher (Loughborough, United Kingdom). For the heat-transfer measurements, phosphate buffered saline (PBS) solutions were prepared with tablets obtained from Sigma (Gillingham, United Kingdom). All aqueous solutions were prepared using deionised water of resistivity no less than 18.2 Ω cm. All reagents were used without further purification except pyrrole, which was distilled prior to use to remove any polymer from the monomeric solution.

MIP and NIP syntheses

Pyrrole particles imprinted with D-glucose were produced through oxidation in solution using $FeCl_3.6H_2O$. Briefly, Pluronic 123 (2.3 g, MW = 5,800) and D-glucose (0.1, 0.05, 0.025 and 0.125 M) were dissolved in deionized water (230 mL) at 40 ℃ for 3 h. Pyrrole (0.1 M) was distilled under vacuum, added to the solution at room temperature and stirred for 1 h. $FeCl_3.6H_2O$ (0.3 M) was then added to the solution, which was maintained at 18 ℃ and stirred for 6 h. Following this the MIPs were washed (3x) with methanol/H_2O (50/50%) to remove any pluronic and then the particles were collected. The template was removed from the polymer by refluxing with methanol/H_2O (3x, 50/50%). The particles were then collected through centrifugation and dried at 60 ℃ overnight. Non-imprinted polymers (NIPs) were made in the same way without the addition of D-glucose. FT-IR analysis of the produced MIP powder was performed on a Spectrum Two FT-IR spectrometer (Perkin Elmer, Buckinghamshire, United Kingdom).

Electrospinning of Nylon 6,6 with PPy particles

Solutions of nylon 6,6 (15 % w/v) in formic acid were prepared as the base for electrospinning solutions, to which MIPs (9.6 or 12.1 wt%) or NIPs (12.1 wt%) were added to make the solutions for the sensor platform. Electrospinning was performed on a NE300 Multinozzle Electrospinning Machine (Inovenso Ltd., Istanbul, Turkey) fitted with an IPS-12 automatic syringe pump (Inovenso Ltd., Istanbul, Turkey).

The electrospinner settings were kept constant for the production of all samples with a potential of 25 kV, drum rotation speed of 100 rpm, syringe pump injection speed of 1.4 mL min^{-1} and a needle/drum spacing of 13 cm.

Scanning Electron Microscopy

Scanning electron microscopy (SEM) images were recorded on a Supra 40VP Field Emission from Carl Zeiss Ltd (Cambridge, UK) with an average chamber vacuum of 1.3×10^{-5} mbar and average gun vacuum of 1×10^{-9} mbar. To enhance the contrast of these images, a thin layer of Au/Pd (8 V, 30 s) was sputtered onto the electrodes with a SCP7640 from Polaron (Hertfordshire, UK) prior to being places in the chamber.

Heat-Transfer Measurements with Electrospun Fibres

All thermal measurements were performed with an additively manufactured flow cell with an inner volume of 161 µL that was designed in house. This flow cell was sealed off with an O-ring and connected to the HTM set up that is described previously.[20] Electrospun polymer covered graphite substrates were pressed onto a copper block, which served as a heat sink, and which the temperature T_1 was actively maintained at 37.00 ± 0.02 °C with a Proportional-Integral-Derivative (PID) controller. The temperature in the liquid (T_2) was measured every second with a type K thermocouple (RS Components, UK) at a distance 1.7 mm above the chip surface. This allowed for the determination of the thermal resistance (R_{th}) at the solid-liquid interface, which is defined as the temperature gradient ($T_1 – T_2$) divided by the power provided to the heat source to maintain the stable temperature. The PID parameters affect the stability of the power signal, hence they have an impact upon the noise and thereby the sensitivity of the developed sensor platform. The optimal settings depend on the flow cell, electrode, temperature, and buffer composition. Previous research using this copper block and size flow cell indicated an optimal PID setting of 1, 14, 0.3 at 37± 0.02 °C.[17b] The polymer covered substrates were first stabilized for 45 min in PBS and then solutions of increasing target concentrations in PBS were injected into the flow cell with an automated NE500 programmable syringe pump from ProSense

(Oosterhout, the Netherlands). The solutions were injected at intervals of 30 min with a flow rate of 250 µL/min. The R_{th} was monitored over time (one reading per second) and determined using the average of 600 data points at each concentration. This was used to construct dose-response curves, where the limit of detection was calculated using the 3-sigma method in the linear range of the sensor. To establish the specificity of the sensor platform, identical measurements were performed with a substrate covered in electrospun fibres but including non-imprinted polypyrrole. The selectivity was evaluated by exposing the sensor to a solution containing similar molecules: fructose (1 mM), galactose (1 mM) and sucrose (1 mM), in addition to some common constituents of sweat: urea (22 mM) and L-lactate (20 mM). The performance of the sensor platform was tested in artificial sweat, comprising of ammonium chloride (327 mM), L-lactic acid (166 mM), urea (83 mM), acetic acid (42 mM) and sodium chloride (34 mM) adjusted to pH 4.7.[21]

Results and Discussion

The general procedure for the production of the electrospun biosensor is presented in Figure 1A. The production of the molecularly imprinted polypyrrole particles, presented in detail in the experimental section, was achieved using a facile mixing methodology whereby the purified pyrrole monomer and target glucose were added to a solution containing pluronic 123. The pluronic is added in concentration higher than its critical micelle concentrations (CMC), causing it to form spherical micelles.[22] These spherical micelles ensure the PPy forms spherical shape nanoparticle upon the addition of the oxidising agent.[23] The solution was continuously stirred for 3 hrs to ensure thorough mixing between the monomer and target. Upon the addition of $FeCl_3.6H_2O$ the solution immediately turned a jet black in colour indicating the formation of polypyrrole (PPy). The solution was continuously stirred for 6 hrs in order to ensure complete polymerisation, after which the template was removed from the PPy through washing with a mixture of methanol and water (1:1). The powder was collected through centrifugation as described in the experimental section to remove any excess pluronic from the solution and then manually ground down prior to use. The result of this methodology was agglomerates of PPy spherical nanoparticles, Figure S1. This powder was analysed through FT-IR, Figure 1B, confirming the formation of PPy.[24] The obtained PPy was manually ground to form a fine powder, before being suspended in formic acid along with the dissolved nylon 6,6 monomer. This solution was then electrospun onto a graphite substrate for 25 mins, to form a web of nylon 6,6 with PPy microparticles embedded within the fibres, Figure 1C. From this, graphite covered substrate 1 x 1 cm squares of the sample were cut out and used as the interface in HTM measurements.

To determine the optimal loading of Molecularly Imprinted Polymer (MIP) in the electrospun nylon 6,6 fibres, three different compositions were produced. The imprinted PPy particles were dispersed in the monomeric nylon 6,6 solution at 0, 9.6 and 12.1 %; above this concentration of MIP particles the solutions only produced a spray, rather than full fibres due to blocking of the spinning tip. We note that higher loadings may be possible with smaller MIP particles. Electrospinning was then performed onto a carbon ink covered copper substrate at a constant flow rate and potential for 25 min. Following this, 1 x 1 cm squares of the produced fibres were cut out and placed inside the AM/3D-printed flow cell

(Figure 2A) as described above. These systems were then exposed to incremental amounts of D-glucose (0.05 – 1 mM) in PBS and the thermal resistance tracked to establish the levels of binding occurring between the fibres and target analytes, Figure 2B and 2C.

The additively manufactured flow cells were initially filled with PBS and allowed to stabilise at 37.00 ± 0.02 °C for 45 mins in order to establish a reliable baseline thermal resistance (R_{th}) measurement. All R_{th} values reported in this manuscript were calculated with its standard deviation from the average of the last 10 minutes of each injections (600 data points). In PBS the 0, 9.6 and 12.1 % fibres stabilised with R_{th} values of 2.85 ± 0.03, 2.22 ± 0.03 and 2.03 ± 0.02 °C/W respectively. This indicates that as the amount of PPy incorporated into the electrospun fibres increased, the baseline thermal resistance exhibited decreased; this agrees with literature that states PPy has a greater thermal conductivity compared with nylon 6,6.[25] Initially, for the two smallest additions of glucose there was no significant deviation from the stabilised baseline measurements for any of the three systems. Once 200 μM D-glucose was injected into to the flow cells, both systems that incorporated MIPs into the fibres exhibited an increase in their R_{th} values to 2.30 ± 0.03 °C/W for the 9.6 % MIPs and 2.31 ± 0.03 °C/W for the 12.1 % MIPs. This corresponded to an increase in the R_{th} values of 3.5 ± 1.3 % and 13.8 ± 1.1 % respectively, clearly indicating the binding of glucose to the free cavities in the MIP matrix, with a larger increase clearly observed in the presence of more MIP particles. This is corroborated by the fact that there was no significant change in the measured R_{th} values for the system incorporating 0 % MIPs, with the R_{th} staying at 2.85 ± 0.03 °C/W. This change in the R_{th} can be explained through the pore blocking model, where the heat flux through the MIP cavities is strongly reduced by the presence of the target analyte. As more cavities become blocked, a higher effect is observed.[26] For both MIP systems the increase in the measured R_{th} continued until 800 μM and 1 mM for the 9.6 and 12.1 % respectively, indicating that the higher incorporation of MIPs into the electrospun fibres increased the detection range possible for the sensor. At the peak for 9.6 % MIP incorporation, the R_{th} had stabilised at 2.54 ± 0.03 °C/W, which corresponded to an increase of 14.0 ± 1.1 %. The 12.1 % MIP system exhibited improvements over the 9.6 % system by exhibiting a larger detection range, which at its largest recorded value was 34.6 ± 1.4 % above the baseline value. As such, for the future experiments a maximum

incorporation of MIPs into the electrospun fibres was used, which in this system corresponded to 12.1 %.

Once the optimal amount of MIP particles incorporated into the electrospun fibres was found, a comparison between imprinted system and non-imprinted polymer (NIP) was explored. Two systems were electrospun using identical methodology, as described above; one incorporating 12.1 % MIP into the nylon 6,6 fibres and the other incorporating 12.1 % NIP. To perform the experiments, 1 x 1 cm squares of the produced fibres were cut out and placed inside the AM/3D-printed flow cell (Figure 3A) as described above. These systems were then exposed to incremental amounts of D-glucose (0.05 – 1 mM) in PBS and the thermal resistance tracked to establish the levels of binding occurring between the fibres and target analytes, Figure 3A and 3B.

In PBS, the MIP system stabilised at an R_{th} value of 2.04 ± 0.03 °C/W, which showed excellent agreement with the values obtained previously. Upon the addition of 0.1 mM D-glucose an increase in the R_{th} was observed to 2.09 ± 0.03 °C/W. This increase in the R_{th} continued with increasing amounts of D-glucose up to the addition of 1 mM where it stabilised at 2.74 ± 0.04 °C/W. This was followed by another addition of PBS in the absence of D-glucose, where no statistically significant increase in the R_{th} was observed; showing that the increases were a result of the D-glucose. A comparison in the change in R_{th} for both the MIP and NIP system (Figure 4B) showed that for the range of D-glucose investigated, there was an observed increase of 0.7 ± 0.03 °C/W for the electrospun nylon 6,6 with PPy MIPs; whereas for the PPy NIP system there was no statistically significant change in the measured R_{th} for the whole range of concentrations. Using the 3 sigma methodology in the dynamic linear range of the sensor platform a Limit of Detection (LoD) was calculated to be 0.10 ± 0.01 mM. This limit of detection and dynamic linear range indicated that this system could be applicable to the detection of glucose in sweat samples, as the typical concentrations range from 0.2 – 1.2 mM.[2]

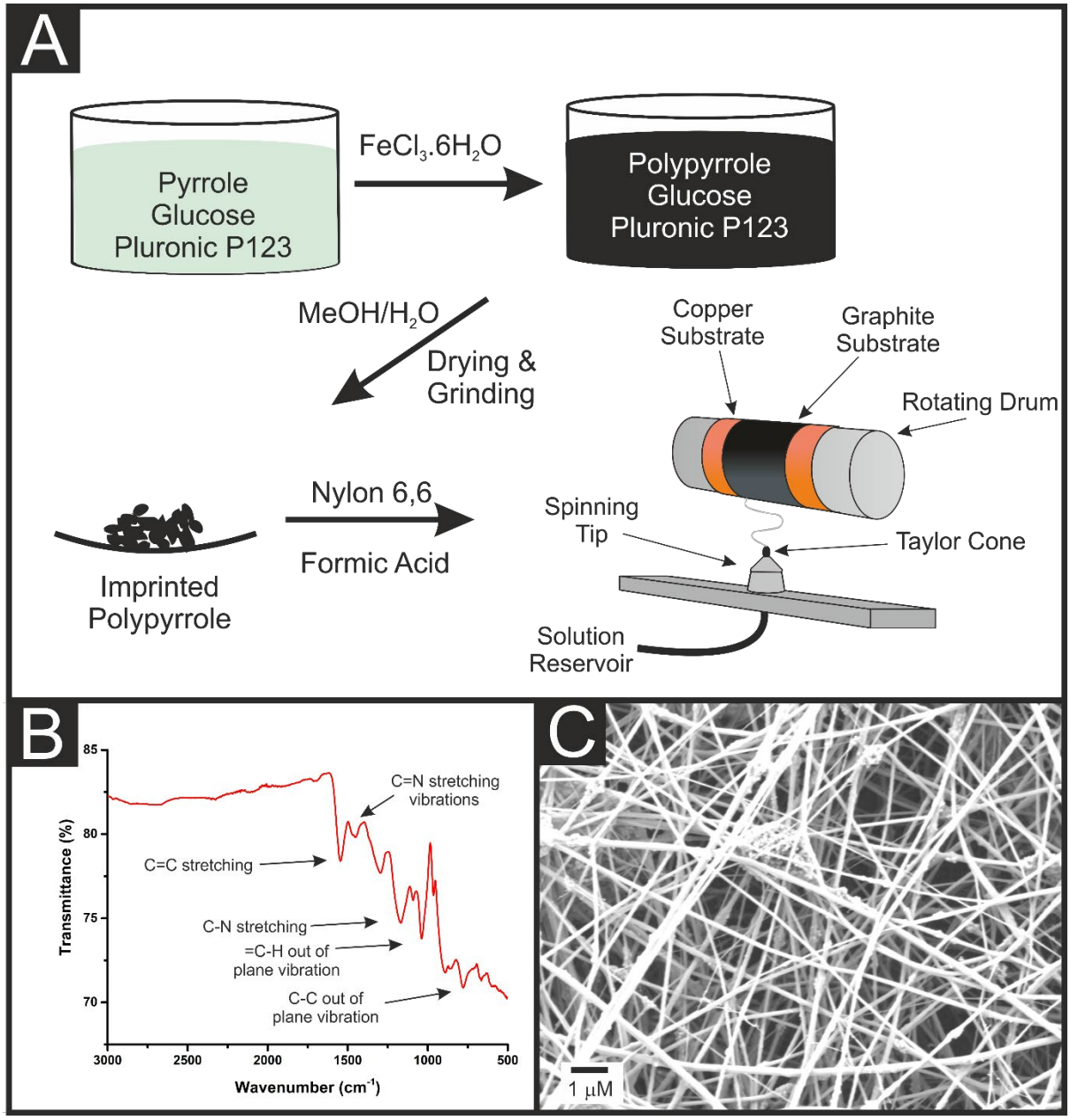
In order to test the selectivity of the sensor platform, a 1 x 1 cm square of electrospun nylon 6,6 with 12.1 % PPy MIPs in was placed inside the flow cell and different solutions of compounds with similar

functionalities or common components of sweat were injected sequentially. These included 1 mM of fructose, mannose and sucrose in addition to 20 mM of lactate and 25 mM of urea. The average change in the R_{th} observed for the addition of each of these compounds is presented in Figure 3C. This showed that there was no significant change in the R_{th} for any of the compounds tested other than D-glucose. We propose this is due to these molecules not binding to the MIP cavities as their shape and functionalities differ from glucose. These results indicate, alongside a comparison to other platforms in the literature, Table S1, that the electrospun sensor platform presented in this manuscript is selective and sensitive enough for the possible application of the detection of glucose.

Last, measurements for the detection of glucose were performed in artificial sweat solution, using a previously reported formulation.[21] The raw HTM data plot for the electrospun fibres with 12.1% incorporated MIPs is presented in Figure 4A, with the calibration plot shown in Figure 4B. This demonstrates excellent agreement with the measurements performed in PBS, with a linear regression observed up to 0.8 mM, producing an R^2 value of 0.98. Using the equation of this line of $y = 2.06x + 0.85$, the LOD for this system in artificial sweat was shown to be 0.12 ± 0.01 mM, which shows the applicability of this sensing platform toward the detection of glucose in sweat. Note that a non-exhaustive summary of previous sensors is reported within ESI Table 1 which shows the competitive nature of the sensing platform. Furthermore, note that this work demonstrates how electrospinning may be used in conjunction with molecularly imprinted polymers to provide suitable interfaces for sensing key biological biomarkers, with the potential for further development into wearable fibres for sensing.

Conclusions

MIPs for the detection of glucose have been developed using a facile bulk synthesis methodology using $FeCl_3.6H_2O$ to polymerise pyrrole monomers in the presences of the template. These MIPs were then incorporated into a solution of nylon 6,6 in formic acid and electrospun into a web of fibres, impregnated with MIPs, onto a graphite substrate. The maximum incorporation of MIPs into the electrospun platform was found to be 12.1 %, noting that above this, a spray was formed rather than the desired fibres. The 12.1 % MIP incorporated fibres were found to give rise to the largest analytical response in the presence of glucose in PBS solutions, providing the widest linear working range (0.1 – 1 mM), with a limit of detection equal to 0.10 ± 0.01 mM. As a control, the performance of the 12.1 % incorporated MIP platforms were tested against a system with 12.1 incorporated non-imprinted polymers, which indicated no change in the measured thermal resistance in the presence of glucose. The selectivity of the MIPs were also tested against possible interferents of similar chemical compositions in sucrose, galactose, fructose and L-lactate, where there was again no change in the measured thermal resistance. Finally, the electrospun MIP platform is demonstrated to detect glucose in an artificial sweat solution, exhibiting a LOD of 0.12 ± 0.01 mM and a linear working range between 0 – 0.8 mM demonstrating that the proposed sensing platform was suitable for measurements of glucose concentrations present in sweat samples in the biologically relevant range. The ability to incorporate MIPs into electrospun fibres to produce functioning sensor platforms provides evidence toward the possibility of using this technology for the development of wearable sensor platforms in the future through the use of functionalised fibres; our future work is directed towards this.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Pyrrole
Glucose
Pluronic P123
FeCl3.6H2O
Polypyrrole
Glucose
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Copper
Substrate
Graphite
Substrate
Rotating Drum
Nylon 6,6
Formic Acid
Imprinted
Polypyrrole
Spinning
Tip
Taylor Cone
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Reservoir
B
Transmittance (%)
85
80
75
70
3000
2500
2000
1500
1000
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Wavenumber (cm-1)
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C-N stretching
=C-H out of
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plane vibration
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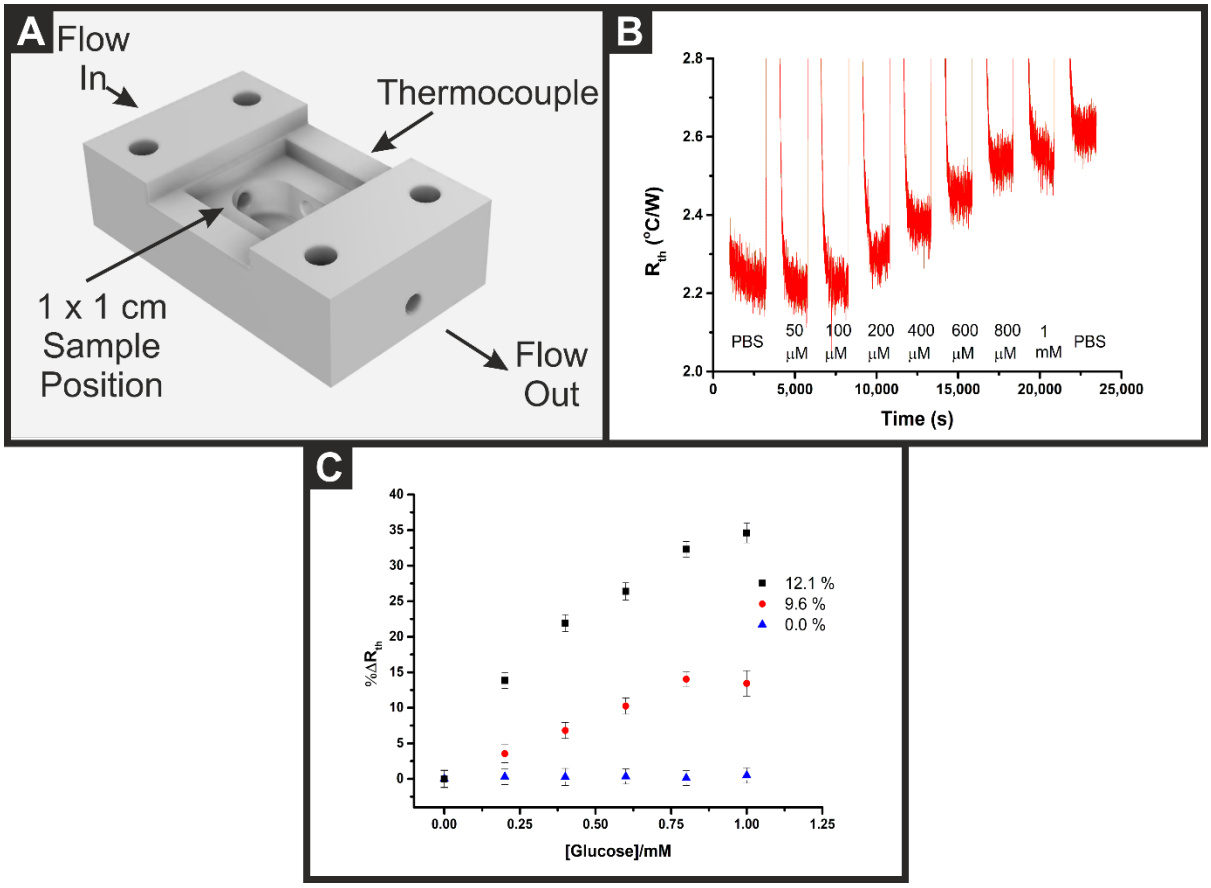
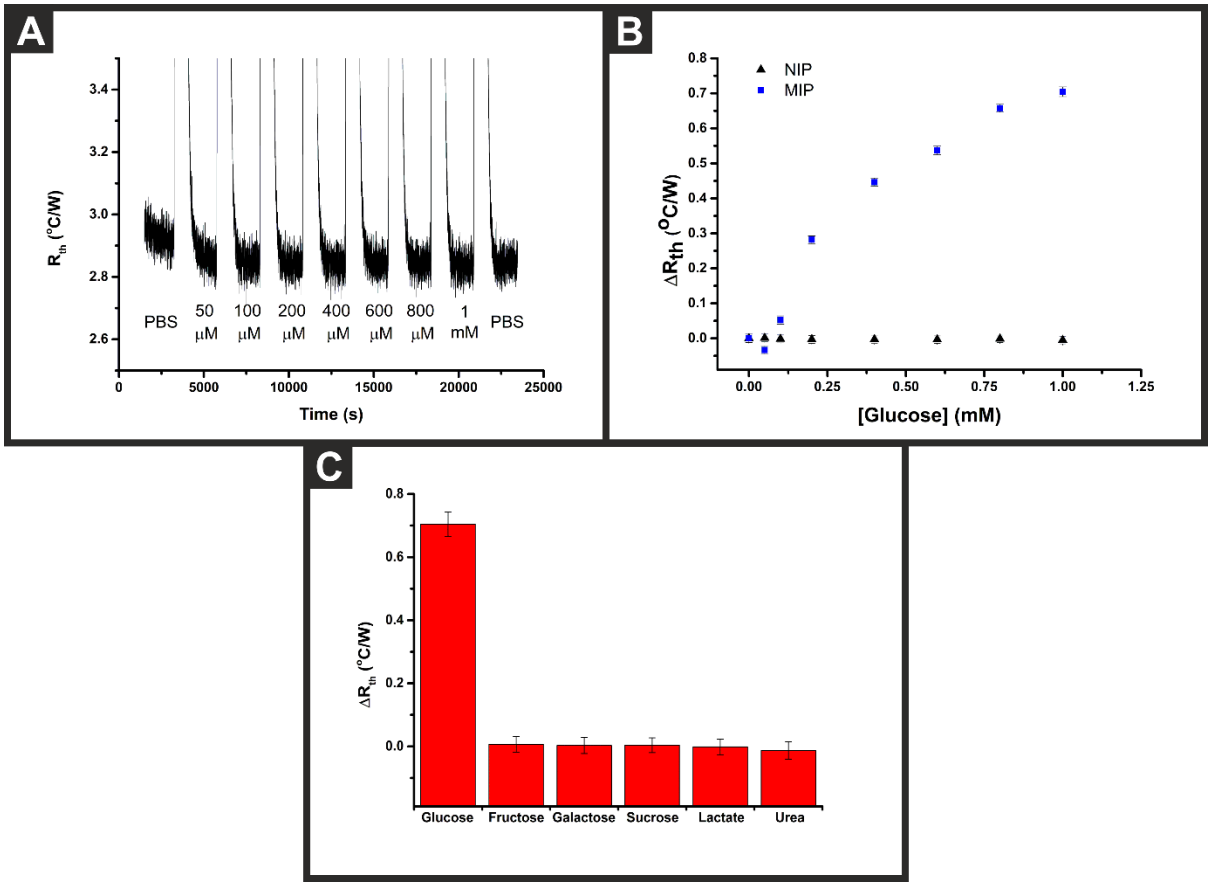


Figure 2. A) Schematic of the Additively Manufactured flow cell used throughout this manuscript. **B)** Raw data HTM plot of thermal resistance (R_{th}) for the detection of D-glucose (0.05 – 1 mM) in PBS using electrospun nylon 6,6 with 9.6 % incorporated PPy MIPs. **C)** Plot of the % increase in the R_{th} for the addition of glucose to flow cells containing electrospun nylon 6,6 incorporating different amounts of PPy MIPs (0, 9.6 and 12.1 %).


A
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PBS
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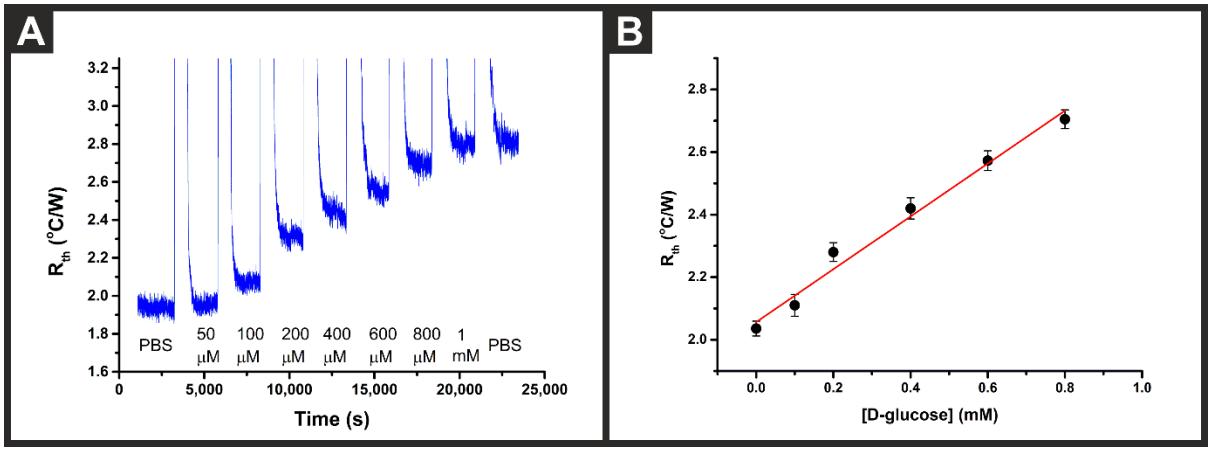
Glucose
Fructose
Galactose
Sucrose
Lactate
Urea


A
B
R_{th} (°C/W)
Time (s)
PBS
50 μM
100 μM
200 μM
400 μM
600 μM
800 μM
1 mM
PBS
[D-glucose] (mM)

References

1. Zimmet, P.; Alberti, K. G.; Magliano, D. J.; Bennett, P. H., Diabetes mellitus statistics on prevalence and mortality: facts and fallacies. *Nature Reviews Endocrinology* **2016,** *12* (10), 616.
2. (a) Sakaguchi, K.; Hirota, Y.; Hashimoto, N.; Ogawa, W.; Hamaguchi, T.; Matsuo, T.; Miyagawa, J.-I.; Namba, M.; Sato, T.; Okada, S., Evaluation of a minimally invasive system for measuring glucose area under the curve during oral glucose tolerance tests: usefulness of sweat monitoring for precise measurement. *Journal of diabetes science and technology* **2013,** *7* (3), 678-688; (b) Moyer, J.; Wilson, D.; Finkelshtein, I.; Wong, B.; Potts, R., Correlation between sweat glucose and blood glucose in subjects with diabetes. *Diabetes technology & therapeutics* **2012,** *14* (5), 398-402; (c) Makaram, P.; Owens, D.; Aceros, J., Trends in nanomaterial-based non-invasive diabetes sensing technologies. *Diagnostics* **2014,** *4* (2), 27-46.
3. (a) Cima, M. J., Next-generation wearable electronics. *Nature biotechnology* **2014,** *32* (7), 642-643; (b) Bandodkar, A. J.; Wang, J., Non-invasive wearable electrochemical sensors: a review. *Trends in biotechnology* **2014,** *32* (7), 363-371; (c) Amjadi, M.; Kyung, K. U.; Park, I.; Sitti, M., Stretchable, skin-mountable, and wearable strain sensors and their potential applications: a review. *Advanced Functional Materials* **2016,** *26* (11), 1678-1698.
4. (a) Yeo, J. C.; Lim, C. T., Emerging flexible and wearable physical sensing platforms for healthcare and biomedical applications. *Microsystems & Nanoengineering* **2016,** *2* (1), 1-19; (b) Tricoli, A.; Nasiri, N.; De, S., Wearable and miniaturized sensor technologies for personalized and preventive medicine. *Advanced Functional Materials* **2017,** *27* (15), 1605271; (c) Kim, J.; Campbell, A. S.; de Ávila, B. E.-F.; Wang, J., Wearable biosensors for healthcare monitoring. *Nature biotechnology* **2019,** *37* (4), 389-406.
5. Bariya, M.; Nyein, H. Y. Y.; Javey, A., Wearable sweat sensors. *Nature Electronics* **2018,** *1* (3), 160-171.
6. Kim, J.; Imani, S.; de Araujo, W. R.; Warchall, J.; Valdés-Ramírez, G.; Paixão, T. R.; Mercier, P. P.; Wang, J., Wearable salivary uric acid mouthguard biosensor with integrated wireless electronics. *Biosensors and Bioelectronics* **2015,** *74*, 1061-1068.
7. Yao, H.; Shum, A. J.; Cowan, M.; Lähdesmäki, I.; Parviz, B. A., A contact lens with embedded sensor for monitoring tear glucose level. *Biosensors and Bioelectronics* **2011,** *26* (7), 3290-3296.
8. Sempionatto, J. R.; Jeerapan, I.; Krishnan, S.; Wang, J., Wearable Chemical Sensors: Emerging Systems for On-Body Analytical Chemistry. *Analytical Chemistry* **2019,** *92* (1), 378-396.
9. Heo, J. S.; Eom, J.; Kim, Y. H.; Park, S. K., Recent progress of textile-based wearable electronics: a comprehensive review of materials, devices, and applications. *Small* **2018,** *14* (3), 1703034.
10. Wang, L.; Wang, L.; Zhang, Y.; Pan, J.; Li, S.; Sun, X.; Zhang, B.; Peng, H., Weaving sensing fibers into electrochemical fabric for real-time health monitoring. *Advanced Functional Materials* **2018,** *28* (42), 1804456.
11. (a) Grafahrend, D.; Heffels, K.-H.; Beer, M. V.; Gasteier, P.; Möller, M.; Boehm, G.; Dalton, P. D.; Groll, J., Degradable polyester scaffolds with controlled surface chemistry combining minimal protein adsorption with specific bioactivation. *Nature materials* **2011,** *10* (1), 67-73; (b) Akbari, M.; Tamayol, A.; Bagherifard, S.; Serex, L.; Mostafalu, P.; Faramarzi, N.; Mohammadi, M. H.; Khademhosseini, A., Textile technologies and tissue engineering: a path toward organ weaving. *Advanced healthcare materials* **2016,** *5* (7), 751-766.
12. Bognitzki, M.; Czado, W.; Frese, T.; Schaper, A.; Hellwig, M.; Steinhart, M.; Greiner, A.; Wendorff, J. H., Nanostructured fibers via electrospinning. *Advanced materials* **2001,** *13* (1), 70-72.
13. (a) Wang, X.; Kim, Y.-G.; Drew, C.; Ku, B.-C.; Kumar, J.; Samuelson, L. A., Electrostatic assembly of conjugated polymer thin layers on electrospun nanofibrous membranes for biosensors. *Nano Letters* **2004,** *4* (2), 331-334; (b) Saetia, K.; Schnorr, J. M.; Mannarino, M. M.; Kim, S. Y.; Rutledge, G. C.; Swager, T. M.; Hammond, P. T., Spray-Layer-by-Layer Carbon Nanotube/Electrospun Fiber Electrodes for Flexible Chemiresistive Sensor Applications. *Advanced Functional Materials* **2014,** *24* (4), 492-502; (c) Chinnappan, A.; Baskar, C.; Baskar, S.; Ratheesh, G.; Ramakrishna, S., An

overview of electrospun nanofibers and their application in energy storage, sensors and wearable/flexible electronics. *Journal of Materials Chemistry C* **2017,** *5* (48), 12657-12673.
14. Crapnell, R. D.; Dempsey-Hibbert, N. C.; Peeters, M.; Tridente, A.; Banks, C. E., Molecularly imprinted polymer based electrochemical biosensors: Overcoming the challenges of detecting vital biomarkers and speeding up diagnosis. *Talanta Open* **2020**, 100018.
15. Haupt, K.; Mosbach, K., Molecularly imprinted polymers and their use in biomimetic sensors. *Chemical reviews* **2000,** *100* (7), 2495-2504.
16. (a) Betlem, K.; Mahmood, I.; Seixas, R.; Sadiki, I.; Raimbault, R.; Foster, C.; Crapnell, R.; Tedesco, S.; Banks, C.; Gruber, J., Evaluating the temperature dependence of heat-transfer based detection: A case study with caffeine and Molecularly Imprinted Polymers as synthetic receptors. *Chemical Engineering Journal* **2019,** *359*, 505-517; (b) Jamieson, O.; Soares, T. C.; Faria, B. A. d.; Hudson, A.; Mecozzi, F.; Rowley-Neale, S. J.; Banks, C. E.; Gruber, J.; Novakovic, K.; Peeters, M., Screen Printed Electrode Based Detection Systems for the Antibiotic Amoxicillin in Aqueous Samples Utilising Molecularly Imprinted Polymers as Synthetic Receptors. *Chemosensors* **2020,** *8* (1), 5.
17. (a) Betlem, K.; Canfarotta, F.; Raumbault, R.; Banks, C.; Eersels, K.; van Grinsven, B.; Cleij, T.; Crapnell, R.; Hudson, A.; Peeters, M., Thermistors coated with molecularly imprinted nanoparticles for the electrical detection of peptides and proteins. *Analyst* **2020,** *145* (16), 5419-5424; (b) Crapnell, R.; Canfarotta, F.; Czulak, J.; Johnson, R.; Betlem, K.; Mecozzi, F.; Down, M. P.; Eersels, K.; van Grinsven, B.; Cleij, T. J.; Law, R.; Banks, C. E.; Peeters, M., Thermal Detection of Cardiac Biomarkers H-FABP and ST2 Using a Molecularly Imprinted Nanoparticle-Based Multiplex Sensor Platform. *ACS sensors* **2019**; (c) Crapnell, R. D.; Jesadabundit, W.; García-Miranda Ferrari, A.; Dempsey-Hibbert, N. C.; Peeters, M.; Tridente, A.; Chailapakul, O.; Banks, C. E., Toward the Rapid Diagnosis of Sepsis: Detecting Interleukin-6 in Blood Plasma Using Functionalized Screen-Printed Electrodes with a Thermal Detection Methodology. *Analytical Chemistry* **2021,** *93* (14), 5931-5938.
18. (a) Betlem, K.; Kaur, A.; Hudson, A. D.; Crapnell, R. D.; Hurst, G.; Singla, P.; Zubko, M.; Tedesco, S.; Banks, C. E.; Whitehead, K.; Peeters, M., Heat-Transfer Method: A Thermal Analysis Technique for the Real-Time Monitoring of Staphylococcus aureus Growth in Buffered Solutions and Digestate Samples. *ACS Applied Bio Materials* **2019,** *2* (9), 3790-3798; (b) Jamieson, O.; Betlem, K.; Mansouri, N.; Crapnell, R.; Vieira, F.; Hudson, A.; Banks, C.; Liauw, C.; Gruber, J.; Zubko, M., Electropolymerised molecularly imprinted polymers for the heat-transfer based detection of microorganisms: A proof-of-concept study using yeast. *Thermal Science and Engineering Progress* **2021**, 100956.
19. (a) Senthamizhan, A.; Balusamy, B.; Uyar, T., Glucose sensors based on electrospun nanofibers: a review. *Analytical and bioanalytical chemistry* **2016,** *408* (5), 1285-1306; (b) Kim, J.; Campbell, A. S.; Wang, J., Wearable non-invasive epidermal glucose sensors: A review. *Talanta* **2018,** *177*, 163-170.
20. van Grinsven, B.; Vanden Bon, N.; Strauven, H.; Grieten, L.; Murib, M.; Jiménez Monroy, K. L.; Janssens, S. D.; Haenen, K.; Schöning, M. J.; Vermeeren, V.; Ameloot, M.; Michiels, L.; Thoelen, R.; De Ceuninck, W.; Wagner, P., Heat-Transfer Resistance at Solid–Liquid Interfaces: A Tool for the Detection of Single-Nucleotide Polymorphisms in DNA. *ACS Nano* **2012,** *6* (3), 2712-2721.
21. Brunet, B. R.; Barnes, A. J.; Scheidweiler, K. B.; Mura, P.; Huestis, M. A., Development and validation of a solid-phase extraction gas chromatography–mass spectrometry method for the simultaneous quantification of methadone, heroin, cocaine and metabolites in sweat. *Analytical and bioanalytical chemistry* **2008,** *392* (1-2), 115-127.
22. Petrov, P.; Yuan, J.; Yoncheva, K.; Müller, A. H.; Tsvetanov, C. B., Wormlike morphology formation and stabilization of “Pluronic P123” micelles by solubilization of pentaerythritol tetraacrylate. *The journal of physical chemistry B* **2008,** *112* (30), 8879-8883.
23. Zhang, X.; Zhang, J.; Song, W.; Liu, Z., Controllable synthesis of conducting polypyrrole nanostructures. *The Journal of Physical Chemistry B* **2006,** *110* (3), 1158-1165.
24. Umer, A.; Liaqat, F.; Mahmood, A., MoO3 Nanobelts Embedded Polypyrrole/SIS Copolymer Blends for Improved Electro-Mechanical Dual Applications. *Polymers* **2020,** *12* (2), 353.

25. (a) Lunn, B.; Unsworth, J.; Booth, N.; Innis, P., Determination of the thermal conductivity of polypyrrole over the temperature range 280–335 K. *Journal of materials science* **1993,** *28* (18), 5092-5098; (b) King, J. A.; Tucker, K. W.; Vogt, B. D.; Weber, E. H.; Quan, C., Electrically and thermally conductive nylon 6, 6. *Polymer Composites* **1999,** *20* (5), 643-654.
26. Van Grinsven, B.; Eersels, K.; Peeters, M.; Losada-Pérez, P.; Vandenryt, T.; Cleij, T. J.; Wagner, P., The heat-transfer method: a versatile low-cost, label-free, fast, and user-friendly readout platform for biosensor applications. *ACS applied materials & interfaces* **2014,** *6* (16), 13309-13318.

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