UNIVERSITY OF TECHNOLOGY SYDNEY

PAM Review

Subject 68412

www.uts.edu.au

Meta-study Focusing on Abiotic Cells for Human Implants

Mitchell Healey[1] and Julian Lee[2]

[1] Mitchell.P.Healey@student.uts.edu.au *

[2] Julian.J.Lee@student.uts.edu.au

*Author to whom correspondence should be addressed; Mitchell.P.Healey@student.uts.edu.au

DOI: http://dx.doi.org/10.5130/pamr.v3i0.1416

Abstract: Powering implantable devices in human body with a glucose based fuel cell (GFC) offers an alternative to non-rechargeable batteries that typically require routine invasive surgery. There are three main approaches for GFCs to oxidise glucose. Enzymatic Fuel Cells are selective and have a high reaction rate but are unstable as the proteins can denature giving the cell a short lifespan. Microbial Fuel Cells use microbes to break down glucose to produce electrons. However they possess the danger of cell leakages that can introduce the microbes to the patient and risk possible infection. Abiotic Fuel Cells employ inorganic catalysts, typically a noble metal alloy or metallic carbon to oxidise and reduce glucose and oxygen respectively. Abiotic is the safest and most stable of the three but possesses the lowest output due to the electrodes inability to target glucose specifically.

This meta-study investigates for Abiotic Glucose Fuel Cell being the most viable candidate of the three for possible use in autonomous medical devices. We will assess current abiotic fuel cells on the thermodynamic parameters of output voltage, current/current density, power density and efficiency. The kinetic parameters of internal resistance and rate at which membranes transport electrons will also be assessed. Operational parameters of lifespan and overall architecture will also be assessed to further understand the conditions and materials these cells were produced.

Keywords: Glucose; Fuel Cell; Meta-study; Enzymatic; Microbial; Abiotic; Implantable Devices

1. Introduction

As implantable medical devices (IMD) are becoming more popular and needed, there is a need to constantly make changes and improve them to encourage patients who need these medical devices to accept them. Power supply is a major factor which determines the effectiveness of an IMD. Current IMDs such as heart pacemaker, cardiac defibrillator, blood glucose monitors, and many more uses lithium battery as a power supply. These batteries are small in size and are able to produce constant voltage and current to power IMDs. However, lithium based batteries used in pacemakers have a lifetime of 6-8 years requiring patients to undergo further surgery to replace the battery, bringing great pains and financial burdens for the patient. Glucose fuel cells can utilise the human body's supply of glucose and convert them into electrical energy via the transfer of electrons. With the abundance of glucose in the body it represents an excellent energy source for powering IMDs and the potential for autonomous harvesting.

GFC's generally is composed of two half-cells, with the anode and cathode being a noble metal such as platinum or carbon variations. At the anode, glucose is oxidised to produce gluconic acid and free electrons shown in equation (1). At the cathode, oxygen is reduced with water producing hydroxide ions and an electron flow shown in equation (2). These half-cells are typically divided by a porous membrane or mediator that allows the electrons to flow. Figure 1 is an example of Abiotic Glucose Fuel Cell.

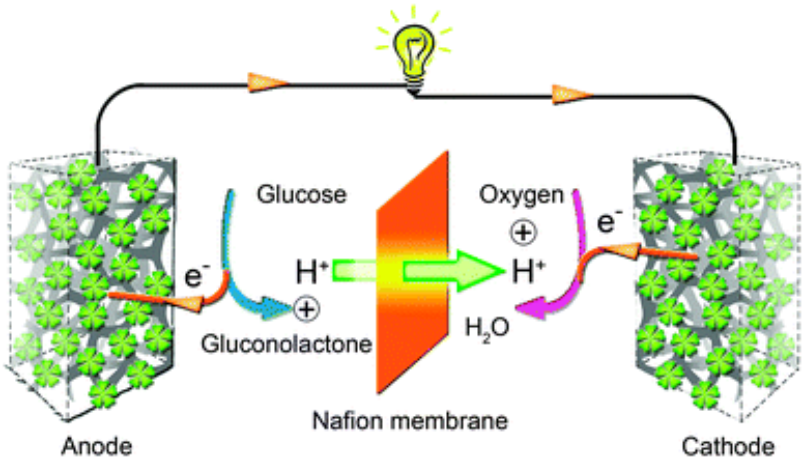

Figure 1: Illustration of basic construct of a two-chamber glucose fuel cell [7]

The complete oxidation of glucose produces 1.24V at 298 K [14] shown by equations (3) and (4). There are three main approaches to Glucose Fuel Cells (GFC); Enzymatic Fuel Cells , Microbial Fuel Cells and Abiotic Fuel Cells.

$$\text{Anode : } C_6H_{12}O_6 + 24OH^- \longrightarrow 6CO_2 + 18H_2O + 24\ e^- \quad (1)$$

$$\text{Cathode : } 6O_2 + 12H_2O + 24\ e^- \rightarrow 24OH^- \quad (2)$$

$$\text{Overall : } C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 18H_2O \quad (3)$$

$$G^\circ = -2.870 \times 106\ \text{J mol}^{-1}; U_0 = 1.24\text{V [14]} \quad (4)$$

1.1 Enzymatic Fuel Cells (EFC)

The first enzymatic biofuel cell was developed in 1964 [1] which implemented glucose oxidase (GOx). Difficulties in electron transfer and immobilisation of enzymes resulted in research favouring abiotic methods. Interest was revitalised in the 1980s as abiotic had numerous issues including poisoning of the electrodes through adsorption and a fundamental issue of incomplete oxidation.

Enzymatic GFCs have excellent biocompatibility, specific in what they oxidise, high efficiency and high reaction rates. What is blocking implementation is being able to successfully immobilise the enzymes to prevent denaturing. The most significant energy loss is in the electron transfer to the electrode. Electron transfer can occur in 2 fundamental ways. Employment of redox mediators to shuttle the electron or direct electron transfer from the enzyme active site to the electrode which requires the distance be no more than 14Å before sharp losses. [1]

1.2 Microbial Fuel Cells (MFC)

The fact that microorganisms could be used to generate electricity has been known for roughly a hundred years, but it is not until the early twentieth century that Microbial Fuel Cells are actually developed. Early MFCs required mediator chemicals such as neutral red and methylene blue to assist the transportation of electrons to the anode. However, the use of chemical mediators would cause environmental issues in the human body and increase operational costs. Most MFCs now are mediatorless, which uses specific microorganisms introduced to the body that have electrochemically active redox proteins on their outer membrane that can transfer electrons directly to the anode. Some research have also shown that MFCs could utilise existing microorganisms inside the human body to generate electricity.[2]

The major advantage of MFCs comes from the microorganism's' ability to self-regenerate. As a result, MFCs can be potentially forever lasting as the microorganisms needed to generate electricity are able to regenerate and multiply exponentially. The fact that MFCs utilise microorganisms also mean that they will be able to operate at a relatively low cost, be sustainable and have a lack of chemical waste

product. However, many current MFCs face troubles in successful containment, which leads to microbe leakage. As MFCs may require specific bacteria to operate, microbe leakage could potentially build an infectious community within the body which would cause severe damage and diseases to the body. Hence concerns are still very high even with stable containment. Implantation rejection also poses as a problem. The introduction of microbes and bacteria which the human body is not familiar with might lead to a rejection reaction by the patient. This would render the fuel cell to be useless.

1.3 Abiotic Fuel Cell (AFC)

AFCs are the most suitable candidate out of the three types as they are the most stable and pose the smallest risk to the human body. Current investigations have found that AFCs can produce very steady and usable output voltage, current and power density for extended periods of time and since they are a enclosed system with no risk of leakages, they pose no threat to the human body. However, current investigations into AFCs that we discussed have not taken size restraints into much consideration nor has there been an investigation into the effects of the membrane on the cell. We feel that these areas have strong potential for future research into AFCs in the quest for producing an AFC that can potentially power implantable devices.

2. Methods

This meta-study was conducted in order to find out if AFC technology could possibly be implemented in the human body and to see any areas future AFC research could be focused for improvement. We used Google Search on ‘Abiotic Glucose Fuel Cells’ and found 189 articles with close to 90% of the articles only being published since 2010. We chose eight articles that not only demonstrated a working glucose based fuel cell but also took different approaches to their investigation in order to cover a variety of different AFCs. From the information in the articles, we assessed each fuel cell on several parameters;

- Thermodynamic parameters were chosen as they represent a means to compare the performance each cell. The parameters we chose were output voltage, current/current density, power density and efficiency.
- Kinetic parameters of each cell were investigated to see if there was any possible shortcomings in this area of the AFCs in order to propose where any future investigations should be focused. The parameters we chose were the internal resistance of the cell and rate at which membranes transport electrons.

3. Results and Discussion

3.1 Abiotic Fuel Cell Comparison Tables

Efficiency of the cell is defined at the percentage of the Gibbs Free Energy (1.24V) produced by the cell's output voltage

Table 1: Thermodynamic Parameters

Article Title	Output Voltage	Current/ Current Density	Power density	Efficiency
A membraneless single compartment abiotic glucose fuel cell [3]	Open-circuit voltage of 840mV.	Short Circuit current of 28μA,	Maximum power density of 16.2 μW/ cm^2 at a cell voltage of 495 mV	67.74%
A microfabricated low cost enzyme-free glucose fuel cell for powering low-power implantable devices [4]	Open-circuit voltage of 350mV	Sustainable power density of 1.5 μW/cm^2 at 10 μA/cm^2.	Peak power density of 2 μW/cm^2	28.22%
A potentially implantable glucose fuel cell with Raney-platinum film electrodes for improved hydrolytic and oxidative stability [5]	Average open circuit voltage of (716±21) and (698±10) mV at 3.5 and 7.0% oxygen saturation, respectively.	4.4μAcm^2 at 3.5% O_2 and 8.8μAcm^2 at 7.0% O_2	(4.4±0.2) μW/cm^2 at 7.0% oxygen saturation with 50μm wide feed holes.	At 3.5% oxygen saturation - 57.74% At 7% oxygen saturation - 56.29%
Seeking effective dyes for a mediated glucose/air alkaline battery/fuel cell [6]	Among the 19 dyes completely soluble at 50mM, MV (626 mV) and Trypan Blue (620 mV) give the highest OCV in SAAB. A subsidiary group in Table 1 comprises the remaining 17 soluble dyes whose OCVs range from 540 to 400 mV	8 mA/cm^2 at short-circuit	800 μW/cm^2 at the maximum power point.	For MV - 50.48% For Trypan Blue - 50% Remaining 17 solutions range from 32.26% to 43.55%
Enzymeless multi-sugar fuel cells with high power output based on 3D graphene–Co_3O_4 hybrid electrodes [7]	~1.1V	Co^{III} as catalyst = 231±10μA/cm^2. Co^{IV} as catalyst =469±37μA/cm^2	2.38±0.17 mW/cm^2	88.71%
Performance of a low-cost direct glucose fuel cell with an anion-exchange membrane [8]	The OCVs obtained are 0.643 V, 0.738 V 0.758 V, 0.795 V, 0.831 V, 0.833 V, and 0.834 V for 1 M, 2 M, 3 M, 4 M, 5 M, 6 M, and 7 M KOH in 1 M glucose solution, respectively.	*No current values were given.*	The maximum power densities obtained are 0.268mW/cm^2, 0.406 mW/cm^2, 0.520 mW/cm^2, 0.528 mW/cm^2, 0.549 mW/cm^2, 0.559 mW/cm^2, and 0.521mW/cm^2, respectively.	For KOH concentrations; 1M - 51.85% 2M - 59.52% 3M - 61.13% 4M - 64.11% 5M - 67.02% 6M - 67.18% 7M - 67.26%
Temperature dependence of an abiotic glucose/air alkaline fuel cell [9]	Open circuit voltages between 0.5-0.6V depending on temperature used and methyl viologen mediator. (see graphs)	Current density was varied for each temperature and compared to both voltage and power density. Methyl viologen mediator was used. (see graphs).	Power density over specified temperatures and different mediators was measured. Best result being 2.31mW/cm^2 and 2.39mW/cm^2 at 32ºC with indigo carmine and methyl viologen mediators respectively.	Between 40.32% and 48.39%
Porous Co_3O_4 hollow nanododecahedra for non-enzymatic glucose biosensor & biofuel cell[10]	There were two redox peaks. Highest anodic peak was 0.55V. Highest cathodic peak was 0.48V.	Maximum current density of 0.3mA/cm^2.	*No power density was measured.*	83.06%

Table 2: Kinetics Parameters

Article Title	**Internal resistance**	**Rate at which membranes transport electrons**
A membraneless single compartment abiotic glucose fuel cell [3]	54 kΩ	No membrane used.
A microfabricated low cost enzyme-free glucose fuel cell for powering low-power implantable devices [4]	*No given value*	No membrane used.
A potentially implantable glucose fuel cell with Raney-platinum film electrodes for improved hydrolytic and oxidative stability [5]	*No given value*	*Different membrane 'feed hole' sizes were used but no rates were given. Effectiveness was shown as power and current densities.*
Seeking effective dyes for a mediated glucose/air alkaline battery/fuel cell [6]	*No given value*	*No membrane was used. Test was to see effectiveness of different electrolytes as an alternative.*
Enzymeless multi-sugar fuel cells with high power output based on 3D graphene–Co_3O_4 hybrid Electrodes [7]	Internal resistance is estimated at 214Ω.	*Nafion membrane used no rate was discussed.*
Performance of a low-cost direct glucose fuel cell with an anion-exchange membrane [8]	EXTERNAL resistance of 10-9000Ω was varied.	Resistance of membrane surface: 18Ω/cm^2
Temperature dependence of an abiotic glucose/air alkaline fuel cell [9]	Resistance of 4Ω was measured between the platinum wire and the anode.	No membrane was used. Different mediators were tested. However, it was concluded that a membrane could have been useful to slow the consumption of the mediator dye at the cathode under higher temperatures.
Porous Co_3O_4 hollow nanododecahedra for non-enzymatic glucose biosensor and biofuel cell [10]	EXTERNAL resistance of 200Ω was applied.	*Membrane was used but was not specified or its transfer rate.*

Table 3: Operational Parameters

Article Title	**lifespan**	**Overall architecture**
A membraneless single compartment abiotic glucose fuel cell [3]	Stable electrical output for 9 hours followed by a gradual decay in electrical activity.	The anode consists of an abiotic catalyst Al/Au/ZnO, in which ZnO seed layer was deposited on the surface of Al/Au substrate using hydrothermal method. The cathode is constructed from a single rod of platinum with an outer diameter of 500 mm. The abiotic glucose fuel cell was studied in phosphate buffer solution (pH 7.4) containing 5 mM glucose at a temperature of 22ºC.
A microfabricated low cost enzyme-free glucose fuel cell for powering low-power implantable devices [4]	Constant output over the first 4 hours. When stable power density of 1.5μW/cm^2 is achieved, a power drop of 0.2μW/cm^2 for the next 4 hours is observed.	All experiments were carried out under controlled conditions at physiological levels of glucose (5.0 mmol L−1) and dissolved oxygen (7% saturation) in 0.01 M phosphate buffer saline (pH 7.4) at 37□C.
A potentially implantable glucose fuel cell with Raney-platinum film electrodes for improved hydrolytic and oxidative stability [5]	*Lifespan was not measured in this investigation*	Platinum cathode and Raney-platinum film anodes. 3.5% and 7% oxygen saturation was used; best result was at 7%. Porous membrane was used and 'feed hole' size was tested at 50μm and 200μm; best result was with 50μm holes.
Seeking effective dyes for a mediated glucose/air alkaline battery/fuel cell [6]	*Lifespan was not measured in this investigation.*	2.0 mL solution, 20% methanol by volume, with 100 mM indigo carmine, 1.0 M glucose and 2.5 M sodium hydroxide at room temperature.
Enzymeless multi-sugar fuel cells with high power output based on 3D graphene–Co_3O_4 hybrid Electrodes [7]	With a constant load (100 kΩ), the output voltage can remain at a reasonably high level (~0.8 V) for long-term continuous operation (8200 s) and it can be restored to the optimal level (~1.1 V) after a recovery period	200mM glucose solution. (*No other conditions were given. Primary investigation was into the use of Co_3O_4 as a cheap and effective alternative to noble metals as electrodes.)*
Performance of a low-cost direct glucose fuel cell with an anion-exchange membrane [8]	*Lifespan was not measured as part of this investigation.*	1 M glucose in solutions with 15 mM MV and different concentrations of KOH (see voltage and power density for concentrations) at 25ºC. (DETAILED SCHEMATIC IN ARTICLE)
Temperature dependence of an abiotic glucose/air alkaline fuel cell [9]	*Lifespan was not measured as part of this investigation.*	MnO_2 cathode and carbon felt anode was used. Methyl viologen, indigo carmine, trypan blue, and hydroquinone were used as mediators and compared which was most viable. Each was tested at the pre-specified temperatures of 15, 19, 27, 32, 37, 42, and 49ºC.
PorousCo_3O_4 hollow nanododecahedra for non-enzymatic glucose biosensor and biofuel cell [10]	*A reproducible cycle of current was obtained upon 2-cycle operation within about 40hours indicating the Co_3O_4-HND was capable of producing steady electricity at milliamps level for a long time.*	Co_3O_4-HND as anode material and platinum/carbon as cathode catalyst. Glucose concentrations were varied between 2μM and 6.06mM. Room temperature was used.

Operational parameters were also investigated in order to gain a better understanding of the cells and if there are any factors corroborating with the thermodynamic and kinetic parameters investigated. For this we looked into the lifespan of the cell before outputs diminished and the overall architecture of the cell such as the temperature, types of anodes and cathodes used, oxygen and glucose concentrations and any other factors that may have been investigated in the study.

3.2 Required Outputs for Current Implantable Devices

In order for AFCs to be implanted in a body and function properly, they will need to meet the minimum power requirements of current IMDs. The two most used IMD right now are cardiac pacemakers and cardiac defibrillators.[11]

Cardiac pacemakers

Current pacemakers require a minimum power of 25 μW and an open circuit voltage (OCV) of 2.8 V to operate.[12]

Cardiac defibrillators

Cardiac defibrillators require a larger minimum power than pacemakers, generally between 50-100 μW. [13]

3.3 Size Considerations

The best and most effective AFC that we found was the one produced by Chen et al., 2013[7], which produced an open circuit voltage of 1.1 V and power density of 2.38±0.17 mW/cm^2. The power density produced by this cell is more than enough to power a cardiac pacemaker or defibrillator, however it does not have enough open circuit voltage and its size makes it impossible to be implanted in a human body, as seen in figure 2.

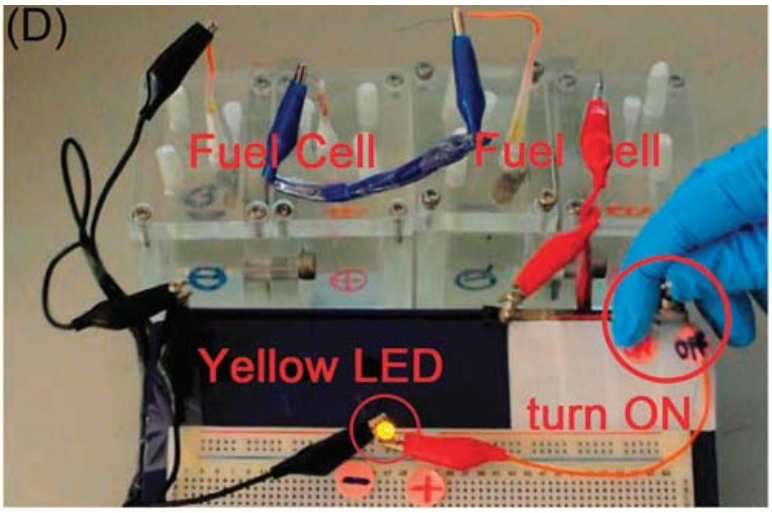

Figure 2: Actual size of Chen et al., 2013 fuel cell. Hand to scale.[7]

The AFC as researched by Kerzenmacher et al., 2011[5] produced an average open circuit voltage of 716±21 mV and a power density of 4.4±0.2 µW/cm^2. This fuel cell is the most probable to be implanted in a body in terms of its size, as shown in figure 3. It does not have enough OCV nor power density to power an IMD. However, as these cells are only in the micrometre range in terms of size, more of these cells could be connected in a series circuit inside the body. This would amplify the cell's OCV and power density to meet the power requirements for IMDs.

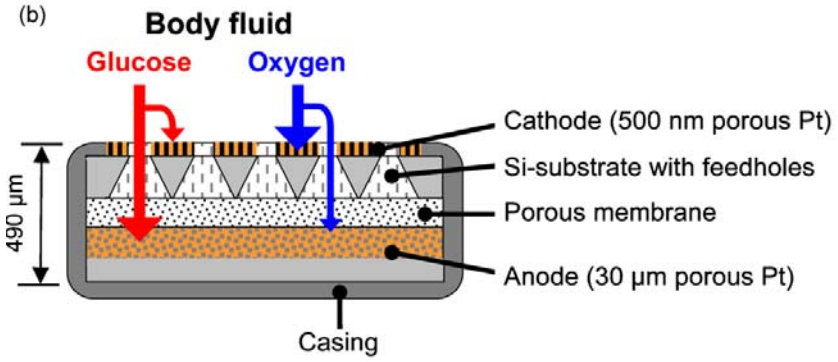

Figure 3:Size of fuel cell proposed by Kerzenmacher et al., 2011[5].

Since the outputs of these cells alone cannot power cardiac pacemakers or defibrillators, it is important that investigations are conducted into how these cells operate when connected up in series. For AFCs to be implemented, we must first know if this is not only feasible, but if they output the appropriate power densities and OCVs in order to power these devices, while also remaining within a reasonable size to be implanted in the human body.

3.4 Mediators vs. Membranes

In the eight cells we investigated, we found a trend of cells using membranes on average produced higher output voltages than those using some form of mediator (*shown in Figure 4).*

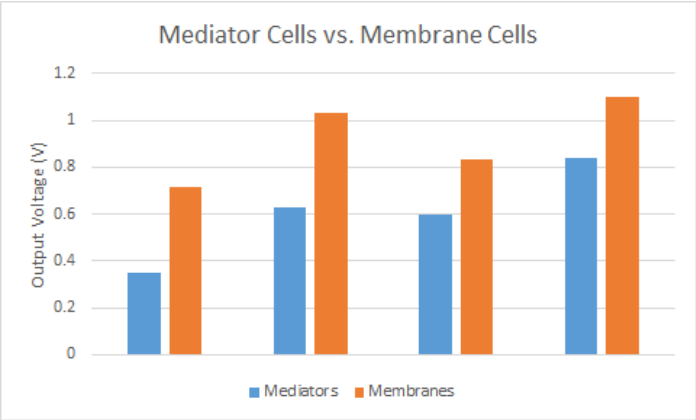

Figure 4: Comparison of Output Voltages and cells using Mediators and Membranes. (Cells from left to right; [4], [5], [6], [10], [9], [8], [3], [7])

In our table 2 we attempted to assess the rate at which membranes were transferring electrons in the AFCs that used membranes to separate the electrodes. The cell produced by Yang et al., 2015[8] was the only article that mentioned a resistance per area for the membrane they had used ($18\Omega/cm^2$). Others had mentioned that a *Nafion*™ membrane was used, but did not mention specifically which one was used so we were unable to retrieve any characteristics for the membranes.

The article by Eustis et al., 2013[6] tested how different mediator dyes could be used as an electrolyte in the cell and which was the most effective for power and voltage outputs. In our research we found only Kerzenmacher et al., 2011[5] attempted to test the effect of the membrane on the cell by changing the size of the *'feed holes'* in the membrane. The *'feed hole'* sizes of 50μm and 200μm were tested and it was found that increasing the *'feed hole'* size led to a small increase voltage potential at the anode but a relatively large decrease in voltage potential at the cathode. It was concluded from the study that *'the application of smaller feed holes is feasible.'* However this was only a minor investigation as part of the study done by Kerzenmacher et al., 2011[5]. We propose that considering that the *'feed hole'* size in the cell membrane seem to have a profound effect on the overall cell performance, this would be a fruitful area for future investigations into AFCs as our results have demonstrated a positive influence of the membrane on the AFCs investigated. In particular the questions how does the resistance per area of the membrane affect the AFCs outputs, and does the material of the membrane affect the output of the AFCs.

3.5 Temperature Range

For AFCs to be used within the human body, they must be able to operate under the conditions associated with those present in the body. It is paramount that these cells can produce a sufficient amount of power across the entire core body temperature range to not run the risk of failing should the patient experience a high fever or cold. Normal body temperature range is between 36.5°C and 37.5°C, minimum body temperature or hypothermia is anything less than 35°C and maximum body temperature being 41.5°C or hyperpyrexia.[15] Since it is possible for the human body to experience these temperatures, it is important that these cells are able to not only operate but produce a sufficient output to power the device.

In our investigation into these eight cells, only Orton et al.,[9] investigated a range of temperatures on the cell the produced. The findings are shown in figure 5 with dotted lines added to indicate the minimum and maximum possible body temperatures.

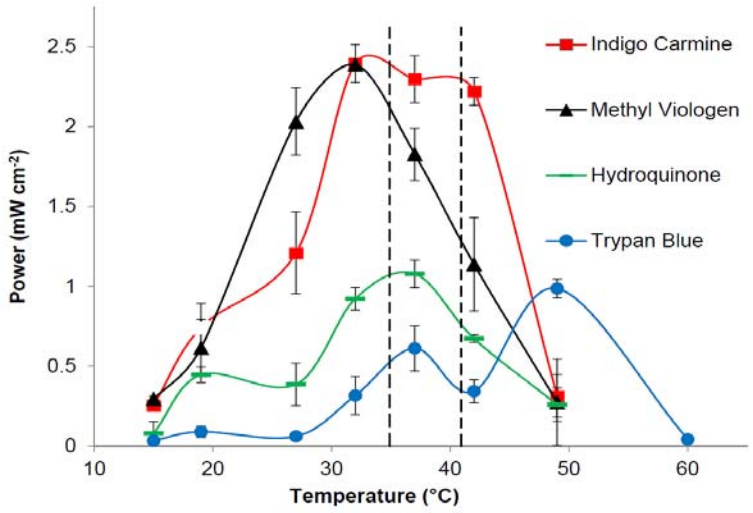

Figure 5: Graph taken from Orton et al., 2015[9] showing temperature effect on power output in different mediator dyes. Dotted lines added at 35°C and 41.5°C indicating body temperature range.

Out of the four mediator dyes tested, methyl viologen that has both a high and steady output in this range. However no further information was presented on methyl viologen as more focused was placed on indigo carmine as it had produced the highest output value in the study. It is important to note that lines for each mediator are indicators and that the error bars suggest possible smaller or bigger drops in power in that temperature range.

In our investigation, we found that many of the AFCs were tested at room temperatures of 22-25°C [3, 8, 10] which is well outside of the estimated core body temperature range. Some took the human biological conditions into consideration testing at 37°C [4] but the full range was not tested so there would be no guarantee that these cells would produce the same outputs if the patient were to experience hypothermic or hyperpyrexic conditions. Orton et al.,[9] was the only study we found that investigated a temperature range but was only done on the effects of mediator based cells. Since membrane based cells have shown serious promise compared to mediators, investigations need to be done into how a range of temperatures can affect the outputs of a membrane based AFC.

4. Conclusion

To conclude, it was found that Abiotic Glucose Fuel Cells are the most viable method for producing a fuel cell for implantable devices. This is due to it being far more stable than Enzymatic Fuel Cells and posing no potential risk to the patient as Microbial Fuel Cells do.

After investigating a variety of articles on AFCs, we chose eight articles that not only produced a working AFC but investigated different approaches to the cell in an attempt to find a cell for possible implementation or areas for future AFC investigations. This meta-study investigated these cells and compared them on thermodynamic and kinetic properties. A few avenues for future investigations into AFCs that could have serious potential for developing a cell that could be implanted in the human body were found.

The cell produced by Kerzenmacher et al.,[5] showed the most promise for implementation as it produced a high power density and open circuit voltage and was an appropriate size for implantable

use. However its outputs are too low to power typical implanted medical devices such as cardiac pacemakers and defibrillators. Investigations into how these cells operate when a few are combined in series is paramount to find if they can produce the appropriate outputs while remaining small enough to be implanted in the body.

After comparing cells that used a mediator or membrane to separate the anodic and cathodic half cells, it was found that AFCs containing membranes on average, produced higher output voltages compared to mediator based AFCs. However, no investigations into how the resistance per area or the material of the membrane affects the output of the cell. This would be a potentially fruitful area for future investigations into AFCs.

Finally, it was found that only Orton et al.,[9] had investigated how a range of temperatures affect the output voltage and power density of the cell. Although this investigation was only done on a variety of mediator dyes. Again no such investigation was done on a membrane based cell. This meta-study determined that any future AFC that is intended for implantation in the human body must produce the appropriate output voltages and power densities in the hypothermic to hyperoxic body temperature range of 35°C to 41.5°C.

Acknowledgments

We would like to acknowledge Jurgen Schulte for his constant help throughout this meta-study and the staff at the University of Technology Sydney Library for their help during the research of this paper.

References

[1] A. T. Yahiro, S. M. Lee, D. O. Kimble, Biochim. Biophys. Acta, Spec. Sect. Biophys. 1964, 88 , 375–383.

[2] Han, Y; Yu, C; Liu, H, 2010. A microbial fuel cell as power supply for implantable medical devices. *Biosensors and Bioelectronics*, 25, pp. 2156-2160. doi: http://dx.doi.org/10.1016/j.bios.2010.02.014

[3] Slaughter, G. and Sunday, J. (2014) 'A membraneless single compartment abiotic glucose fuel cell', *Journal of Power Sources*, 261, pp. 332–336. doi: 10.1016/j.jpowsour.2014.03.090. doi: http://dx.doi.org/10.1016/j.jpowsour.2014.03.090

[4] Oncescu, V. and Erickson, D. (2011) 'A microfabricated low cost enzyme-free glucose fuel cell for powering low-power implantable devices', *Journal of Power Sources*, 196(22), pp. 9169–9175. doi: 10.1016/j.jpowsour.2011.06.100. doi: http://dx.doi.org/10.1016/j.jpowsour.2011.06.100

[5] Kerzenmacher, S., Kräling, U., Metz, T., Zengerle, R. and von Stetten, F. (2010) 'A potentially implantable glucose fuel cell with Raney-platinum film electrodes for improved hydrolytic and oxidative stability', *Journal of Power Sources*, 196(3), pp. 1264–1272. doi: 10.1016/j.jpowsour.2010.08.019. doi: http://dx.doi.org/10.1016/j.jpowsour.2010.08.019

[6] Eustis, R., Tsang, T.M., Yang, B., Scott, D. and Liaw, B.Y. (2013) 'Seeking effective dyes for a mediated glucose–air alkaline battery/fuel cell', *Journal of Power Sources*, 248, pp. 1133–1140. doi: http://dx.doi.org/10.1016/j.jpowsour.2013.10.022

[7] Chen, Y., Prasad, K. P., Wang, X., Pang, H., Yan, R., Than, A., et al. (2013). Enzymeless multi-sugar fuel cells with high power output based on 3D graphene-Co3O4 hybrid electrodes. *Physical Chemistry Chemical Physics; Phys.Chem.Chem.Phys.*, *15*(23), 9170-9176. doi: http://dx.doi.org/10.1039/c3cp51410b

[8] Yang, Y.-L., Liu, X.-H., Hao, M.-Q. and Zhang, P.-P. (2015) 'Performance of a low-cost direct glucose fuel cell with an anion-exchange membrane', *International Journal of Hydrogen Energy*, 40(34), pp. 10979–10984. doi: http://dx.doi.org/10.1016/j.ijhydene.2015.05.192

[9] Orton, D. and Scott, D. (2015) 'Temperature dependence of an abiotic glucose/air alkaline fuel cell', *Journal of Power Sources*, 295, pp. 92–98. doi: http://dx.doi.org/10.1016/j.jpowsour.2015.06.120

[10] Zhang, E., Xie, Y., Ci, S., Jia, J. and Wen, Z. (2016) 'Porous CoO hollow nanododecahedra for nonenzymatic glucose biosensor and biofuel cell', *Biosensors and Bioelectronics*, 81, pp. 46–53. doi: http://dx.doi.org/10.1016/j.bios.2016.02.027

[11] 24/7 Wall St.. 2016. *The Eleven Most Implanted Medical Devices In America - 24/7 Wall St.*. [ONLINE]
Available at http://247wallst.com/healthcare-economy/2011/07/18/the-eleven-most-implanted-medical-devices-in-america/. [Accessed 16 May 2016].

[12] Mallela, V.S., Ilankumaran, V. and Rao, N.S. (2004) 'Trends in cardiac pacemaker batteries', *Indian Pacing Electrophysiology Journal*, 4(4), pp. 201–212.

[13] Thakor, N.V. (no date) *Pacemakers and Defibrillators.Pdf*. Available at: http://faculty.ksu.edu.sa/MFALREZ/EBooks%20Library/ECG%20and%20Cardiac/Pacemakers%20and%20Defibrillators.pdf (Accessed: 16 May 2016).

[14] Kerzenmacher, S., Ducrée, J., Zengerle, R. and von Stetten, F. (2008) 'Energy harvesting by implantable abiotically catalyzed glucose fuel cells', *Journal of Power Sources*, 182(1), pp. 1–17. doi: http://dx.doi.org/10.1016/j.jpowsour.2008.03.031

[15] World™2016 Disabled (2004) *Human body temperature: Fever - normal - low readings*. Available at: http://www.disabled-world.com/calculators-charts/degrees.php (Accessed: 24 May 2016).