Polymer Cybernetics: Enhancing Medical Implants and Tissue Connectivity

Harman Brar*

Dept. of Physics, Simon Fraser University, Burnaby, BC, Canada

(Dated: March 21, 2022)

* harman˙brar@sfu.ca

The combination of biological tissue and physical hardware is a phenomena that can potentially push the bounds of human evolution. Though the time frame of this evolution is much debated, certain precursors do exist. Cybernetic polymers are one such experimental technique that allow for the integration of biological species and physical mechanics. Polymers are instrumental in combining electronic hardware and human tissue, specifically, conjugated polymers that are both electrically and ionically active[1]. Poly(3,4-ethylenedioxythiophene) or PEDOT, is one such conductive polymer that is flexible and biocompatible[1]. When coated over microelectric material, it can be merged into human tissue to enhance medical implant functionality[2]. Figure 1 shows the chemical breakdown of PEDOT as well as it's versatility in bioelectronic use.

Conjugated polymers like PEDOT reduce the impedance experienced by implants, which increases the lifespan and efficiency of the device[1]. Human tissue is soft and has a high curvature, hence the elasticity of PEDOT allows for smooth compatibility at the implant location[2]. The Young's modulus of PEDOT is 2.6 ± 1.4 GPa, hence it is much more cohesive with tissue as compared to inorganic electric material[3]. The biggest concern with any electrode implant within neural tissue is deterioration[4]. The research behind polymers like PEDOT is to eventually allow the implants to be completely integrated inside the body. This would mean allowing the polymer to grow inside the tissue, preventing any degradation of the implant itself and maintaining function for the entirety of the patient's life[5].

When a human is given a stent implant, tissue surrounding the stent acts a layer of coating. The importance of PEDOT-like techniques arises when stent malposition occurs[4]. This is one of the main causes of heart attack with humans that undergo cardiovascular implants[4]. PEDOT-based nanocoatings have been tested to show increased cell adhesion and cytocompability with the surrounding tissue of stents[4]. Figure 2 shows a trial in which four sets of PEDOT samples were tested individually and all showed increased cell proliferation at a higher degree as compared to a control group without the polymers[4].

Atomic Force Microscopy (AFM) images within the trial showcased the contrast in roughness between the different PEDOT samples. This measurement was particularly important as it singled out potential candidates for future trials. A higher surface roughness led to higher cell adhesion and protein absorption around a stent[4]. This increased the cell response around the stent, which led to small traces of tissue regeneration[4]. Figure 3 shows the surface roughness of the polymers within the trial.

The electrical conductivity, radius of gyration and persistence length of PEDOT:PSS samples has also been experimentally tested[6]. Trials in water as well as dimethyl sulfoxide (DMSO), analyzed the changes in conductivity of these conjugated polymers as seen in Figure 4. The radius of gyration and persistence length both increased when the polymer was tested in solution as compared to water[6]. The persistence length increased from 7.8 to 10.5 Angstroms while the radius of gyration increased from 38.2 to 44.4 Angstroms[6]. This shows that the conjugated polymer chain is adaptable to different aqueous environments and can enhance chain organization[6].

Conjugate polymers like PEDOT have successfully been implanted and grown within human tissue and the hippocampus (cortex) of mice[7]. The growth within the cortex is promising as it can potentially reduce harmful side effects of implants like inflammation, scarring and neuron degradation[8]. In-vitro testing within mice showed steady electrical stimulation within neural tissue[8][9]. This stimulation was induced through electric potentials and was also able to record potential oscillations[8][9]. Figure 5 shows the fundamental approach as-well as the recorded oscillations from the implant device.

Recording electric potential within neural tissue is especially important because it allows scientists to correctly understand where mechanical and electrical misfiring occurs[9]. Parkinson's disease, paralysis and hearing loss are a few examples that can possibly be reversed through electrical stimulation from implants[7]. The electrical activity in Figure 5 was observed for five more weeks to access a longer time frame functionality. The PEDOT coating was able to successfully allow experimenters to see where electrical misfiring occurred[8]. Transience behaviour from each electrode was recorded as well as the power efficiency as a function of noise, seen in Figure 6.

PEDOT-like polymers have also been used in conjunction with biological systems like Carbon Nanotubes (CNTs)[5]. CNTs have very strong electrical and mechanical proprieties and when embedded within a polymer matrix can enhance the electrical performance of an electrode[5]. As shown in Figure 7, a polymer matrix allows for nanoparticles to stay connected with electrodes, thus leading to increased cell adhesion[5]. The flexibility of polymers such as CP polypperole and parylene C allows for the reduction in impedance of CNT implantation[5]. Though CNTs are extremely stiff (Young's modulus of 1.25TPa), it is important to note that polymer coatings can be customized[5]. Coatings can have fibrilluar surfaces to improve area roughness while chemical and electrical properties can be changed

through ionization[5].

In comparison to polymers, microelectronic materials such as silicon, iridium and gold have traditionally been used in human implanting[1]. Though these materials have the electrical capabilities required for tissue implants, they are mechanically mismatched. The elasticity of these inorganic materials, akin to The Young's modulus is much greater than soft tissue. This denotes a higher stiffness in the material. Iridium, a common microelectric material used in cancer therapy has a Youngs Modudus of 524 Gpa[11]. This is many order of magnitudes more rigid than soft tissue which has a elasticity range of 1-1000kPA[2]. Though it works well in cancer therapy, its ridigity is far less suitable in advancing implant treatments as compared to PEDOT. In comparison, the Young's modulus of PEDOT is 2.6$\pm$ 1.4 GPa[3]. Due to the higher curvature of soft human tissue, the flexibility of conjugated polymers plays a big role in their application. Scarring is another hindrance of inorganic implants[1]. When interfacing materials that send electric signals inside the body, scarring can block the signals due to the build-up of electrostatic charge[1]. Coated polymers like PEDOT can significantly reduce the impedance of electrical signals from implants, thus extending the usability of implants within human tissue[1]. Other conjugated polymers like Polypyrrole (PPY) and Polyaniline (PANI) are frequently experimented with alongside PEDOT[2]. The main advantage of furthering PEDOT research is it's mechanical and electrical stability within human tissue. PPY has a much lower persistence length and this lack of flexibility hinders its application within microelectronic implants[2]. PANI is another conjugate polymer which is derived from acidic solutions[2]. It's electrical stability is far less than PEDOT due it's rapid degradation in aqueous environments[2]. It is also important to note that PEDOT is still an experimental technique. Concerns over its long-term toxicity exist as well as the efficacy of growth in human neural tissue[2]. Though its elasticity serves well with stent implants, when placed under high strain, the electrical conductivity of PEDOT has been shown to become volatile[2]. With more research and time, experimenters can formulate a much more robust thesis.

The physics of conjugated polymers helps one understand biological systems in a comprehensive manner. Electric potentials emitted from implants can help us pinpoint neural issues that cause disease. The oscillations of these potentials and their transience behaviour can be simplified down to models like the harmonic oscillator. Energy comparisons derived from forces and power allow biologists to understand the physical efficiency of organic com-

pounds like PEDOT. We can also see how foundational measurements of persistence length, radius of gyration, conductivity and surface roughness contribute to the affects of biological systems. When combining physical mechanics with biological tissue, experimenters must understand the complications of both systems, especially when attempting to enhance medical implants. One cannot simply increase the power of implanted devices without considering the affect on surrounding tissue. Similarly, one must tailor organic polymers to become as efficient as possible while still remaining functional.

Conjugated polymers like PEDOT are still in their infancy in terms of human application. The intricacies of combining physical hardware with biological tissue result in lengthy experimental trials. The in-vitro tests of growing polymers within muscle tissue and the hippocampus show promising data for future trials[8]. Tissue regeneration and cell adhesion from various polymer samples also supports the possibility of complete integration inside the body of medical patients[4]. Though the chemical and electrical properties of PEDOT-like polymers are well suited to coating microelectrics, their long term toxicity is yet to be tested[9]. This is expected as one would have to conduct trials over a large period of time. As more researchers are able to find safe and efficient ways to combine polymer coated implants into human tissue, it is likely that we will be able transcend human biology by integrating physical systems.

REFERENCES

[1] American Chemical Society. (2020). Cyborg technology could enable new diagnostics, merger of humans and AI. *Phys.org*. https://phys.org/news/2020-08-cyborg-technology-enable-diagnostics-merger.html

[2] Mehrali, M., Bagherifard, S., Akbari, M., Thakur, A., Mirani, B., Mohammad, M., Hasany, M., Orive, G., Das, P., Emneus, J., Andreson, T., Pirouz, A. (2018). Blending Electronics with the Human Body: A Pathway toward a Cybernetic Future. *Wiley Online Library*. https://doi.org/10.1002/advs.201700931

[3] Qu, J., Ouyang, L., Kuo, C., Martin, D. (2015). Stiffness, strength and adhesion characterization of electrochemically deposited conjugated polymer films. *National Library of Medicine*. https://doi.org/10.1016/j.actbio.2015.11.018

[4] Karagkiozaki, V., Karagiannidis, P., Gioti, M., Kavatzikidou, P., Georgiou, D., Georgaraki, E., Logothetidis, S. (2013). Bioelectronics meets nanomedicine for cardiovascular implants: PEDOT-based nanocoatings for tissue regeneration. *Biochimica et Biophysica Acta* , 1830(9). https://doi.org/10.1016/j.bbagen.2012.12.019

[5] Robles, U., Woolley, A., Warren, L., Nigell, L., Green, R. (2014). Organic electrode coatings for next-generation neural interfaces. *Frontiers in Neuroengineering*. https://doi.org/10.3389/fneng.2014.00015

[6] Choudhury, P., Bagchi, D., Sangeeth, S., Menon, R. (2011). Modified conformation and physical properties in conducting polymers due to varying conjugation and solvent interactions. *Arxiv.org*. https://arxiv.org/pdf/1009.3768.pdf

[7] Singer, E. (2008). Growing Neural Implants. *MIT Technology Review*. https://www.technologyreview.com/2008/07/16/96851/growing-neural-implants/

[8] Ferlauto, L., Vagni, P., Fanelli, A., Genvieve, E., Monsorno, K., Chiara, R., Ghezzi, D. (2021). All-polymeric transient neural probe for prolonged in-vivo electrophysiological recordings. *Biomaterial*, 274. https://doi.org/10.1016/j.biomaterials.2021.120889

[9] Vajrala1, V., Saunier, V., Nowak, L., Flahaut, E., Bergaud, C., Maziz, A. (2021). Nanofibrous PEDOT-Carbon Composite on Flexible Probes for Soft Neural Interfacing. *Frontiers in Bioengineering and Biotechnology*. https://doi.org/10.3389/fbioe.2021.780197

[10] Yusoff, A., Salimi, M. (2018). Superparamagnetic nanoparticles for drug delivery. *Science Direct* https://www.sciencedirect.com/topics/materials-science/polymer-matrix

[11] AZO Materials. (2022). *Iridium (Ir) - Properties, Applications*. https://www.azom.com/article.aspx?ArticleID=9092

[12] Boehler, C., Aqrawe, Z., Asplund, M. (2019). Applications of PEDOT in bioelectronic medicine. *Future Medicine*, 2(2). https://doi.org/10.2217/bem-2019-0014

FIGURES

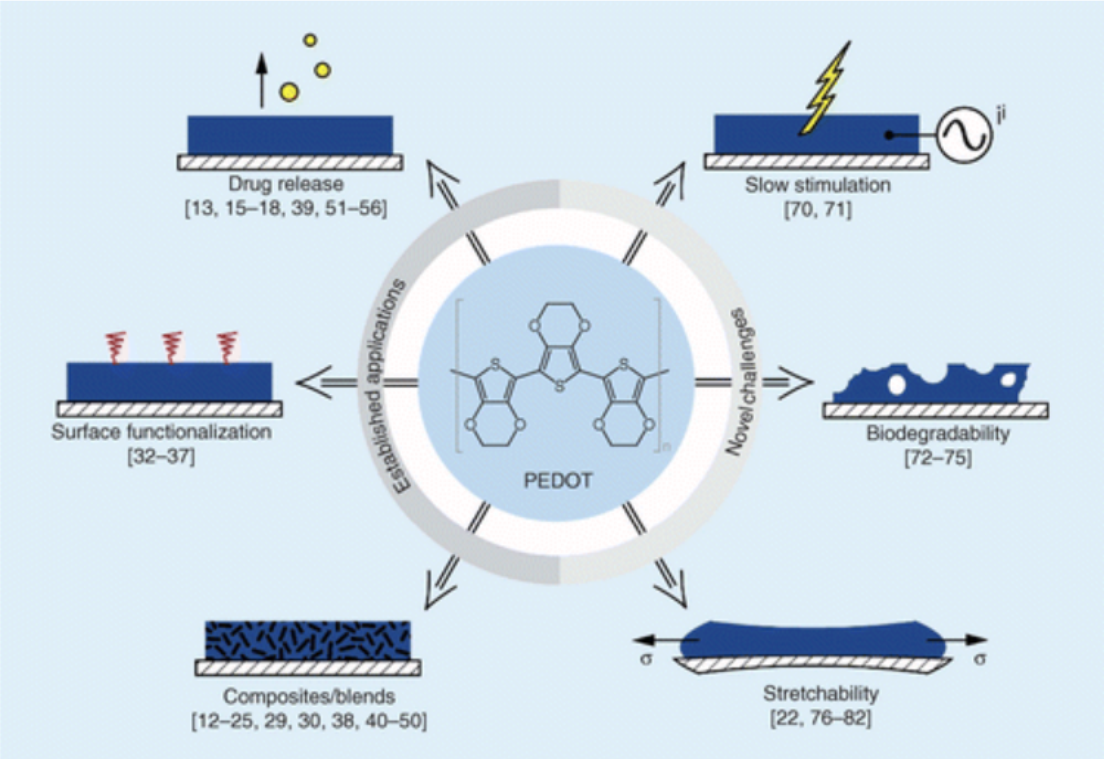

FIG. 1. Chemical breakdown of poly(3,4-ethylenedioxythiophene). Figure adapted from (Boehler et al.,2019)[12]

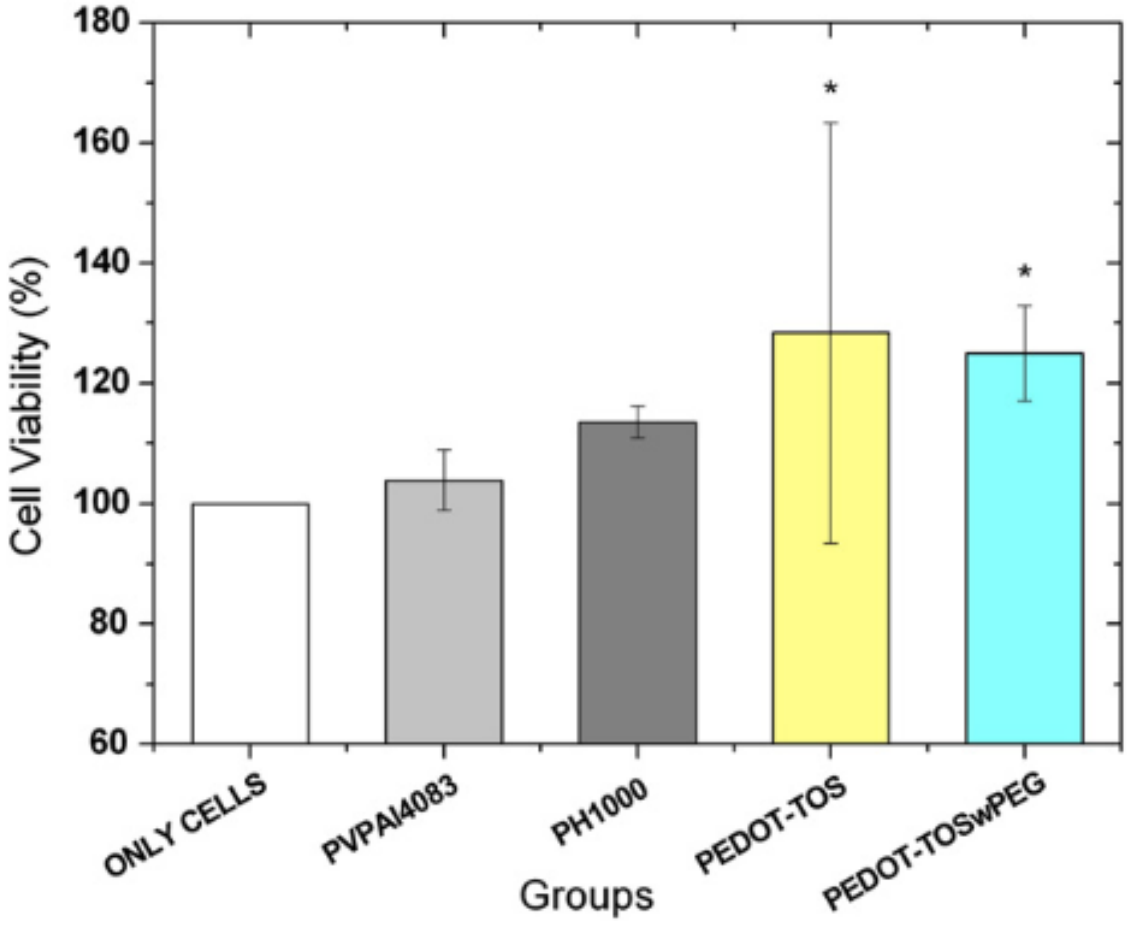

FIG. 2. Cell vitality induced by each polymer. Figure adapted from (Karagkiozak et al.,2013)[4]

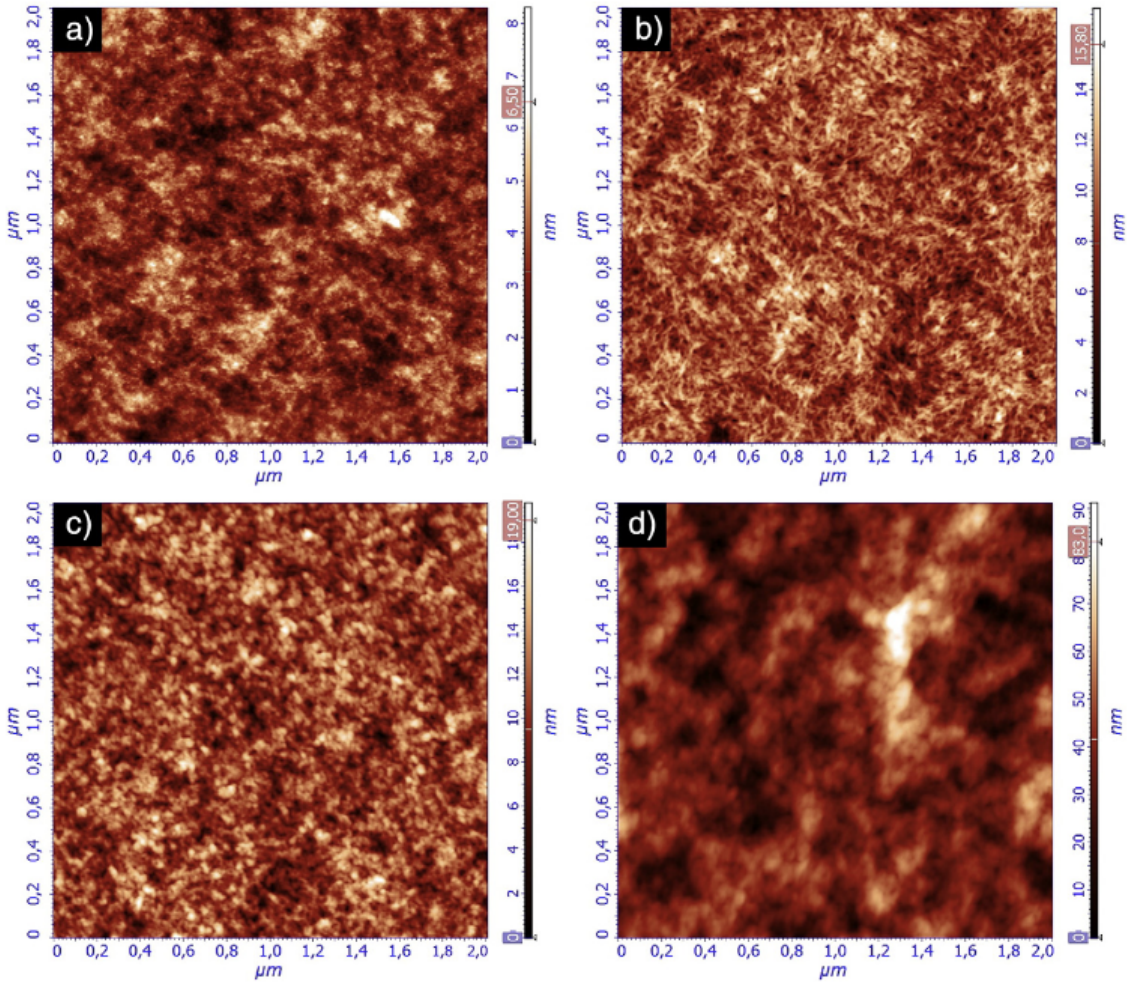

FIG. 3. AFM images for four different conjugate polymer samples. (a) PVPAI4083 with R_q = 0.8 nm, (b) PH1000 with $R_q = 1.9$ nm, (c) PEDOT:TOS with $R_q = 2.5$ nm and (d) PEDOT:TOS-PEG with $R_q = 11.7$ nm. Figure adapted from (Karagkiozak et al.,2013)[4]

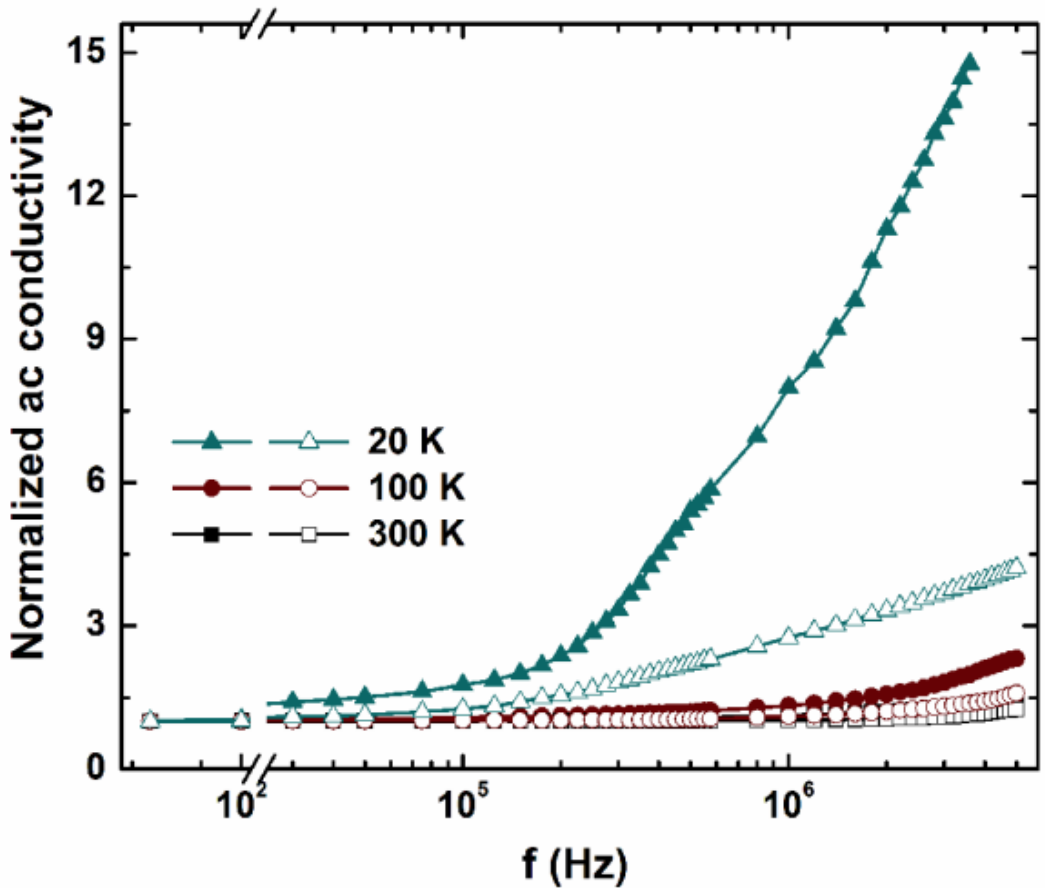

FIG. 4. AC conductivity of PEDOT-PSS in water. The closed symbols represent water and the open symbols represent DMSO. Data recorded at various temperatures. Figure adapted from (Choudury et al.,2011)[6]

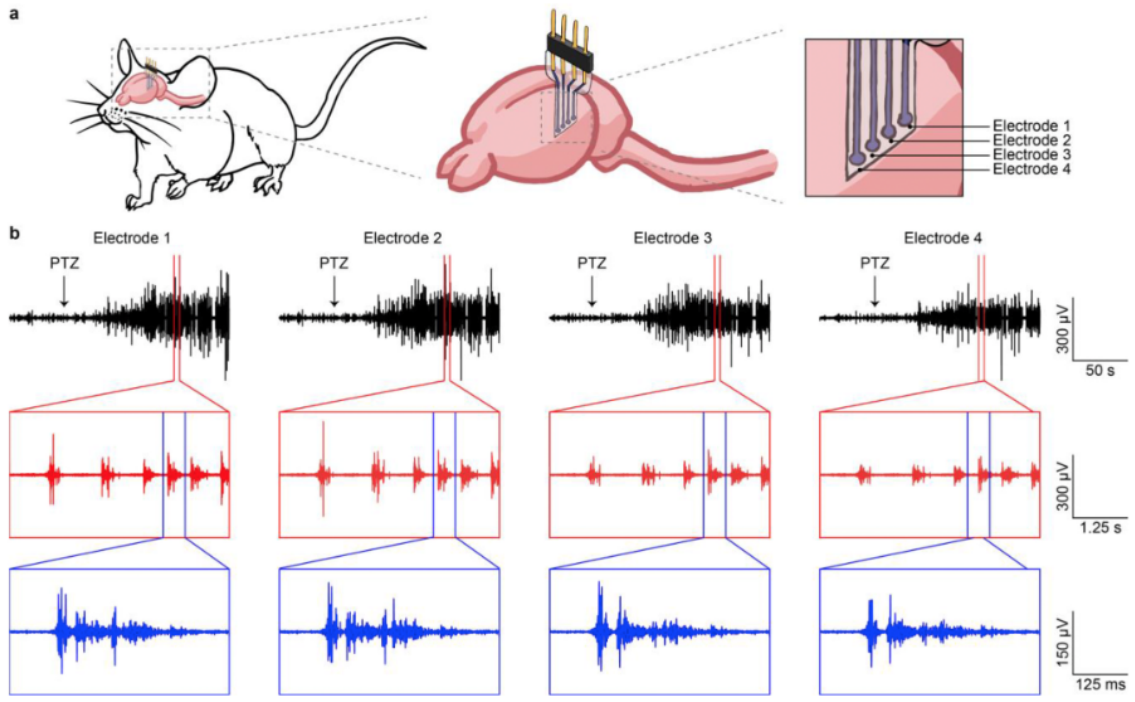

FIG. 5. (a) Diagram of neural probe placement with electrodes. (b) Oscillation recordings from each electrode. The red images and blue images showcase the enlargement of the electrical activity. Figure adapted from (Ferlauto et al., 2021)[8]

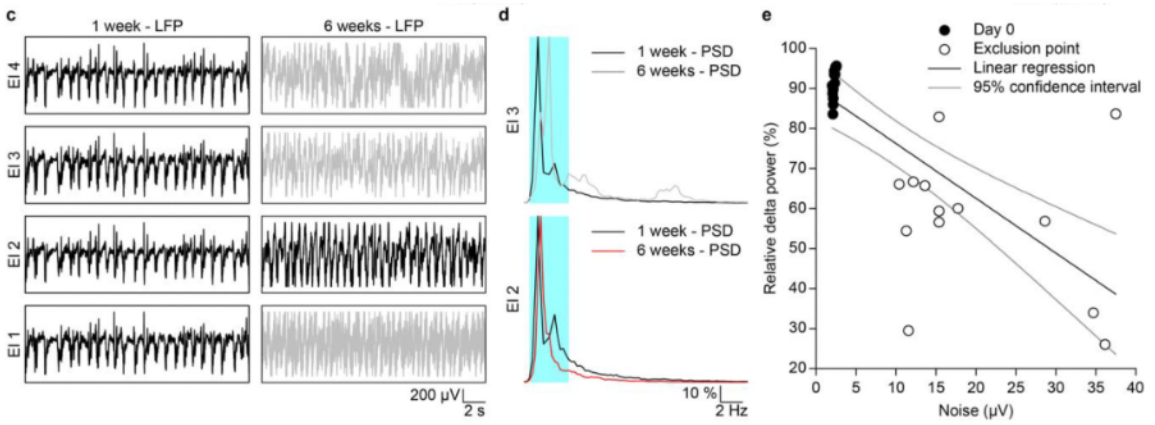

FIG. 6. (a) Diagram of neural probe placement with electrodes. (b) Oscillation recordings from each electrode. The red images and blue images showcase the enlargement of the electrical activity. Figure adapted from (Ferlauto et al., 2021)[9]

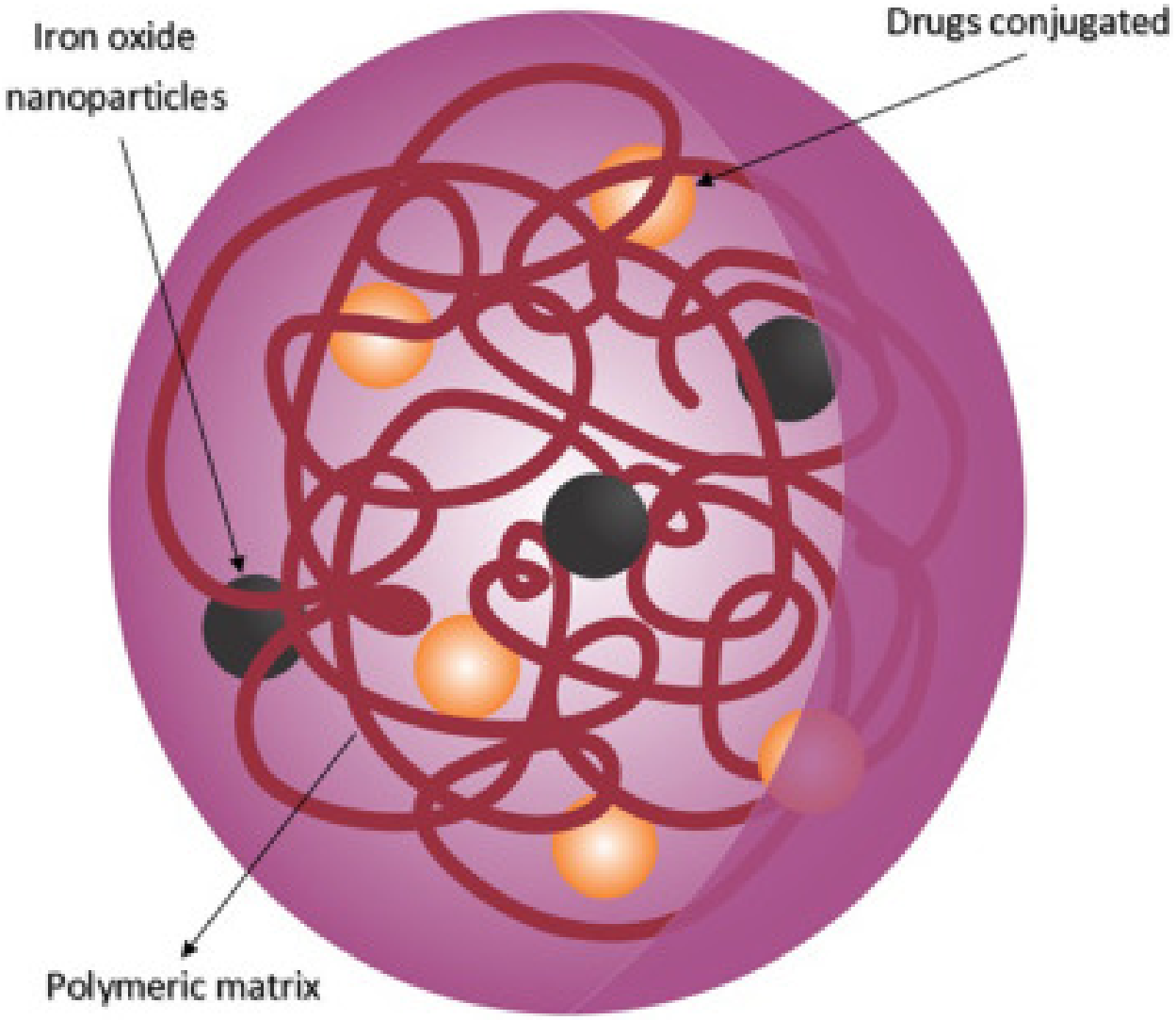

FIG. 7. Polymer matrix with a conjugation of drugs and nanoparticles. Figure adapted from (Yusoff et al., 2018)[10]