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FEATURE ARTICLE

Coupling biology to electrochemistry—future trends and needs

F. Lisdat[1]

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The coupling of biological entities with electrodes has already quite some history and has reached a status which is not only based on phenomenological descriptions. Nowadays, we are able to effectively couple redox centres within protein molecules to electrochemical transducers. This allows the transduction of a biochemical reaction into an electrode signal with applications mainly in sensing and bioenergetics [1–8]. However, in most cases, this coupling is not direct, and shuttle molecules or side products of the reaction are used. But also for the direct coupling, significant progress has been made, and several enzymes and redox proteins can be addressed directly by electrodes [8–13]. The understanding of the functioning of developed systems is, however, in its infancy. Charge and electrostatic interactions have been mostly studied, and for small dipole molecules such as cytochrome c, the situation can be well described [14]. There is a lack of understanding for more complex enzyme molecules which brings a lot of trial and error into research.

The last decade was characterised by an explosion of new materials, which can be used to immobilise protein molecules to electrode surfaces. Particularly, material in the nanoscale appears as a valuable tool since the size dimensions which are similar to biomolecules bring new features and very often avoid inactivation processes occurring by non-biological materials in the macroscale [15–21]. Unfortunately, the literature is full of systems with several mixed materials and biomolecules, but the role of every single component is often not clear. We need more fundamental studies on the interaction of one nanomaterial with biomolecules. Here, one can not only exploit variations in the nanomaterial structure or surface, but we need to exploit more the potential of protein engineering. The recombinant preparation of proteins and mutants of the native molecule allows much better to elucidate which part of the protein surface is responsible for the surface interaction. However, also with mutants, care has to be taken that the modified protein has still the same 3D structure as the native biomolecule—a fact which is not always controlled in mutational studies.

For several nanomaterials, different shapes can be achieved by innovative preparation protocols. This is on the one hand a large "playground" to work on, and on the other hand, we do not understand which structural parameters are important for a productive interaction with a given redox biomolecule.

Thus, we need more collaborations between people from biochemical research, materials chemistry and electrochemical sciences. Here, biochemistry is not only acting as servant for electrochemistry, but one can study functional properties by electrochemistry, and thus, new information can be gained about biomolecules. Thus, electrochemistry will also develop as a tool for studying biochemical systems.

A special group of materials are polymers which have been used from early days of biosensor research as an immobilisation matrix [22]. Another role of polymers can be, however, exemplified with many enzymes and redox polymers with embedded redox centres. Here, studies show that biomolecular interaction with the polymer is influenced by the ligand shell of the metal centers and the redox potential but also the structural flexibility—mainly tested by variations in the linker length between the metal complex and the polymer backbone [23–25]. This allows the construction of defined signal chains from analyte molecules converted at the enzyme towards a current flow at the electrode. For other groups of polymers, we have much less knowledge. For example, conducting polymers seem also to be very attractive materials on electrodes since they can transport electrons through the polymeric chains [26–29]. However, only few systems with clear electron exchange between a biocatalyst and a conducting polymer have been demonstrated. The conditions for an effective reaction between an enzyme and a conducting polymer cannot simply be foreseen yet.

Polymers seem also valuable in combining different biomolecules on one electrode and thus, creating supramolecular

✉ F. Lisdat
flisdat@th-wildau.de

[1] Biosystems Technology, Institute of Life Sciences and Biomedical Technologies, Technical University of Applied Sciences Wildau, Wildau, Germany

structures. This originates from the idea to combine various features of different molecules for a new functionality of the whole system. For the arrangement of molecules, bioaffinity binding, covalent coupling, electrostatic layer-by-layer deposition or entrapment systems with different biomolecules and redox polymers can be used [30–34]. Here, one can expect significant progress since the work of enzymes in a cooperative, sequential, recycling or competitive mode follows very much biological examples. The systematic arrangement of biomolecules allows the creation of defined pathways with low diffusional distances and high conversion efficiencies. We are only at the beginning of development with some recent examples coupling enzyme reactions to photoactive protein complexes [35] or switching between different enzymes [36].

This points to another actual research direction: the combination of light-induced charge carrier generation and biocatalysis [37–39]. One could argue on the complexity of such systems, but when light activation is applied, electrons from oxidation processes can be collected at much lower electrode potential than the redox potential of the enzyme. And for reduction processes, electrons can be supplied at much higher potential. This is interesting from the energetic point of view, and thus, development will grow in this area. In addition, the light can be used as tool for multiplexing.

Another field of electrochemical research has seen some dramatic development in the last decade. It is based on the coupling of even more complex biological structures to electrodes—whole cells. Here, one needs to realise that only little can be transferred from isolated biomolecules to living structures on the surface. Application seems attractive in wastewater treatments and thus bioenergetics, but also in sensing—particularly for environmentally relevant substances [40–43]. The living character has to be taken in consideration by conditions and the supply of nutrients, but it also allows much better stability of a biofilm on an electrode compared with an enzyme layer. However, there is a lack in understanding of such systems, and thus, again collaboration of experts from different fields such as microbiology, bioprocess technology, biochemistry and electrochemistry is necessary.

The deepening of understanding biomolecular interactions with surfaces and materials will also help to come to more systems which will find application in an everyday life situation. Presently, this can be mainly seen in simple detection systems which can be coupled to digital read out units and which are directed to biomarkers, toxins, but also viruses and bacteria. But there is also room for other fields such as synthesis of special chemicals and energy conversion.

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References

1. Turner APF (2013) Biosensors: sense and sensibility. Chem Soc Rev 42(8):3184–3196
2. Habermuller L, Mosbach M, Schuhmann W (2000) Electron-transfer mechanisms in amperometric biosensors. Fresenius J Anal Chem 366(6–7):560–568
3. Yanez-Sedeno P, Campuzano S, Pingarron JM (2019) Pushing the limits of electrochemistry toward challenging applications in clinical diagnosis, prognosis, and therapeutic action. Chem Commun 55(18):2563–2592
4. Zhou M, Wang J (2012) Biofuel cells for self-powered electrochemical biosensing and logic biosensing: a review. Electroanalysis 24(2):197–209
5. Leech D, Kavanagh P, Schuhmann W (2012) Enzymatic fuel cells: recent progress. Electrochim Acta 84:223–234
6. Cosnier S, Le Goff A, Holzinger M (2014) Towards glucose biofuel cells implanted in human body for powering artificial organs: review. Electrochem Commun 38:19–23
7. Lisdat F, Schäfer D (2008) The use of electrochemical impedance spectroscopy for biosensing. Anal Bioanal Chem 391(5):1555–1567
8. Jenner LP, Butt JN (2018) Electrochemistry of surface-confined enzymes: inspiration, insight and opportunity for sustainable biotechnology. Current Opinion In Electrochemistry 8:81–88
9. Adachi T, Kitazumi Y, Shirai O, Kano K (2020) Direct electron transfer-type bioelectrocatalysis of redox enzymes at nanostructured electrodes. Catalysts 10(2) Article Number:236
10. Bollella P, Gorton L (2018) Enzyme based amperometric biosensors. Current Opinion In Electrochemistry 10:157–173
11. Leger C, Bertrand P (2008) Direct electrochemistry of redox enzymes as a tool for mechanistic studies. Chem Rev 108(7):2379–2438
12. Cracknell JA, Vincent KA, Armstrong FA (2008) Enzymes as working or inspirational electrocatalysts for fuel cells and electrolysis. Chem Rev 108(7):2439–2461
13. Ludwig R, Harreither W, Tasca F, Gorton L (2010) Cellobiose dehydrogenase: a versatile catalyst for electrochemical applications. Chemphyschem 11(13):2674–2697
14. Fedurco M (2000) Redox reactions of heme-containing metalloproteins: dynamic effects of self-assembled monolayers on thermodynamics and kinetics of cytochrome c electron-transfer reactions. Coord Chem Rev 209(1):263–331
15. Yang WR, Thordarson P, Gooding JJ, Ringer SP, Braet F (2007) Carbon nanotubes for biological and biomedical applications. Nanotechnology 18(41) Article Number: 412001
16. Guo SJ, Dong SJ (2009) Biomolecule-nanoparticle hybrids for electrochemical biosensors. TrAC Trends Anal Chem 28(1):96–109
17. Pingarron JM, Yanez-Sedeno P, Gonzalez-Cortes A (2008) Gold nanoparticle-based electrochemical biosensors. Electrochim Acta 53(19):5848–5866

18. Zhu CZ, Yang GH, Li H, Du D, Lin YH (2015) Electrochemical sensors and biosensors based on nanomaterials and nanostructures. Anal Chem 87(1):230–249
19. Artiles MS, Rout CS, Fisher TS (2011) Graphene-based hybrid materials and devices for biosensing. Adv Drug Deliv Rev 63(14–15):1352–1360
20. Xu JH, Wang YZ, Hu SS (2017) Nanocomposites of graphene and graphene oxides: synthesis, molecular functionalization and application in electrochemical sensors and biosensors, A review. Microchimica Acta 184(1):1–44
21. Willner I, Baron R, Willner B (2007) Integrated nanoparticle-biomolecule systems for biosensing and bioelectronics. Biosens Bioelectron 22(9–10):1841–1852
22. Sassolas A, Blum LJ, Leca-Bouvier BD (2012) Immobilization strategies to develop enzymatic biosensors. Biotechnol Adv 30(3):489–511
23. Ruff A (2017) Redox polymers in bioelectrochemistry: common playgrounds and novel concepts. Curr Opin Electrochem 5(1):66–73
24. Heller A (2006) Electron-conducting redox hydrogels: design, characteristics and synthesis. Curr Opin Chem Biol 10(6):664–672
25. Yuan M, Minteer SD (2019) Redox polymers in electrochemical systems: From methods of mediation to energy storage. Current Opinion in Electrochemistry 15:1–6
26. Bartlett PN, Birkin PR (1993) The application of conducting polymers in biosensors. Synth Met 61(1-2):15–21
27. Guimard NK, Gomez N, Schmidt CE (2007) Conducting polymers in biomedical engineering. Prog Polym Sc 32(8-9):876–921
28. Kaur G, Adhikari R, Cass P, Bown M, Gunatillake P (2015) Electrically conductive polymers and composites for biomedical applications. RSC Adv 5(47):37553–37567
29. Tomczykowa M, Plonska-Brzezinska ME (2019) Conducting polymers, hydrogels and their composites: preparation, properties and bioapplications. Polymers 11(2):350
30. Lisdat F, Dronov R, Möhwald H, Scheller FW, Kurth DG (2009) Self-assembly of electro-active protein architectures on electrodes for the construction of biomimetic single chains. Chem Commun 3: 274–283
31. Wheeldon I, Minteer SD, Banta S, Barton SC, Atanassov P, Sigman M Substrate channelling as an approach to cascade reactions. Nat Chem 8(4):299–309
32. Feifel SC, Kapp A, Lisdat F (2014) Protein multilayer architectures on electrodes for analyte detection, Biosensor Based on Aptamers and Enzymes, Series: Advances in Biochemical Engineering / Biotechnology, Vol. 140, 253–298, Springer
33. Lisdat F (2017) Trends in the layer-by layer assembly of redox proteins and enzymes in bioelectrochemistry. Curr Opin Electrochem 5(1):165–172
34. Zhao S, Caruso F, Dähne L, Decher G, De Geest BG, Fan J, Feliu N, Gogotsi Y, Hammond PT, Hersam MC, Khademhosseini A, Kotov N, Leporatti S, Li Y, Lisdat F, Liz-Marzán LM, Moya S, Mulvaney P, Rogach AL, Roy S, Shchukin DG, Skirtach AG, Stevens MM, Sukhorukov GB, Weiss PS, Yue Z, Zhu D, Parak WJ (2019) The future of layer-by-layer assembly: a tribute to ACS nano associate editor Helmuth Möhwald. ACS Nano 13(6):6151–6169
35. Tapia C, Milton RD, Pankratova G, Minteer SD, Akerlund HE, Leech D, De Lacey AL, Pita M, Gorton L (2017) Wiring of photosystem I and hydrogenase on an electrode for photoelectrochemical H-2 production by using redox polymers for relatively positive onset potential. Chemelectrochem 4(1):90–95
36. Feifel SC, Kapp A, Ludwig R, Lisdat F (2014) Nanobiomolecular Multiprotein Clusters on Electrodes for the Formation of a Switchable Cascadic Reaction Scheme. Angewandte Chemie International Edition 53(22):5676–5679
37. Yue Z, Lisdat F, Parak W, Hickey S, Tu L, Sabir N, Dorfs D, Bigall N (2013) Quantum dot based photoelectrochemical sensors for chemical and biological detection. ACS Appl Mater Interfaces 5(8):2800–2814
38. Lee SH, Choi DS, Kuk SK, Park CB (2018) Photobiocatalysis: activating redox enzymes by direct or indirect transfer of photoinduced electrons. Angewandte Chemie-International Edition 57(27): 7958–7985
39. Utterback JK, Ruzicka JL, Keller HR, Pellows LM, Dukovic G (2020) Electron transfer from semiconductor nanocrystals to redox enzymes. Annu Rev Phys Chem 71:335–359
40. Logan BE, Wallack MJ, Kim KY, He WH, Feng YJ, Saikaly PE (2015) Assessment of microbial fuel cell configurations and power densities. Environ Sci Technol Lett 2(8):206–214
41. Shi L, Dong HL, Reguera G, Beyenal H, Lu AH, Liu J, Yu HQ, Fredrickson JK (2016) Extracellular electron transfer mechanisms between microorganisms and minerals. Nat Rev Microbiol 14(10): 651–662
42. Pankratova G, Gorton L (2017) Electrochemical communication between living cells and conductive surfaces. Current Opinion In Electrochemistry 5(1):193–202
43. Logan BE, Hamelers B, Rozendal RA, Schroeder U, Keller J, Freguia S, Aelterman P, Verstraete W, Rabaey K (2006) Microbial fuel cells: methodology and technology. Environ Sci Technol 40(17):5181–5192