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1D convolutional neural networks for solution of biosensor inverse problem

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OUTLINE

1. Biosensors: what are they?
2. Biosensor mathematical model.
3. Inverse biosensor problem.
4. 1D convolutional neural network.
5. Results of numerical experiments.
6. Conclusions.

Biosensors: what are they?

- **Biosensors** are devices for the detection and analysis of chemical compounds based on biochemical processes.
- **Enzyme-based amperometric biosensors** are used to find the concentration of specific substances in a medium, where these chemical constituents are enzymatically converted into products, which produce an electric current that is measured.
- **Enzymes** are biological molecules (proteins) which act as biological catalysts by accelerating chemical reactions.
- The molecules upon which enzymes may act are called **substrates**, and the enzyme converts the substrates into different molecules known as **products**.

Biosensors: how do they work?

- Each specific substrate requires its corresponding enzyme.
- For example,

Substrates	Enzyme	Products
D-Glucose + O_2	Glucose oxidase	Glucono-lactone + H_2O_2
L-Lactate + O_2	Lactate oxidase	Pyruvirate + H_2O_2

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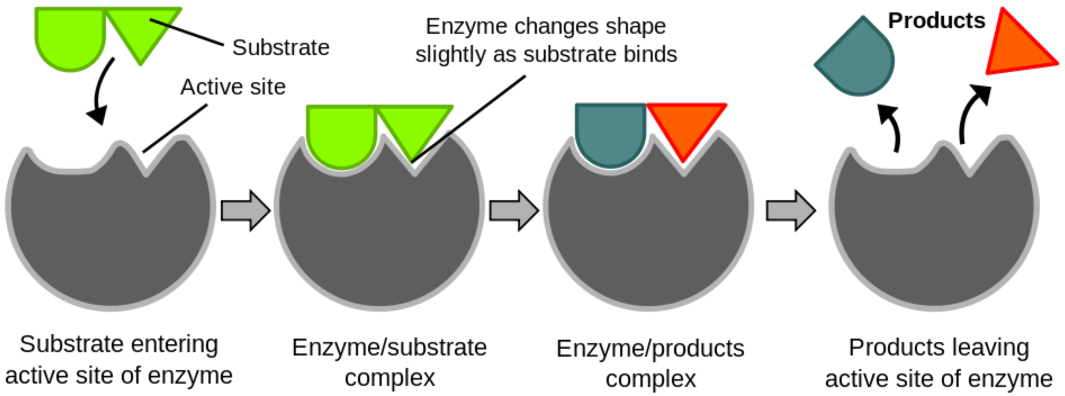


- The key is to obtain hydrogen peroxide (H_2O_2) as the reaction product.

Biosensors: how do they work?

- Hydrogen peroxide (H_2O_2) is oxidized by catalyst (for example, platinum) on electrode's surface if an electrical potential is applied:

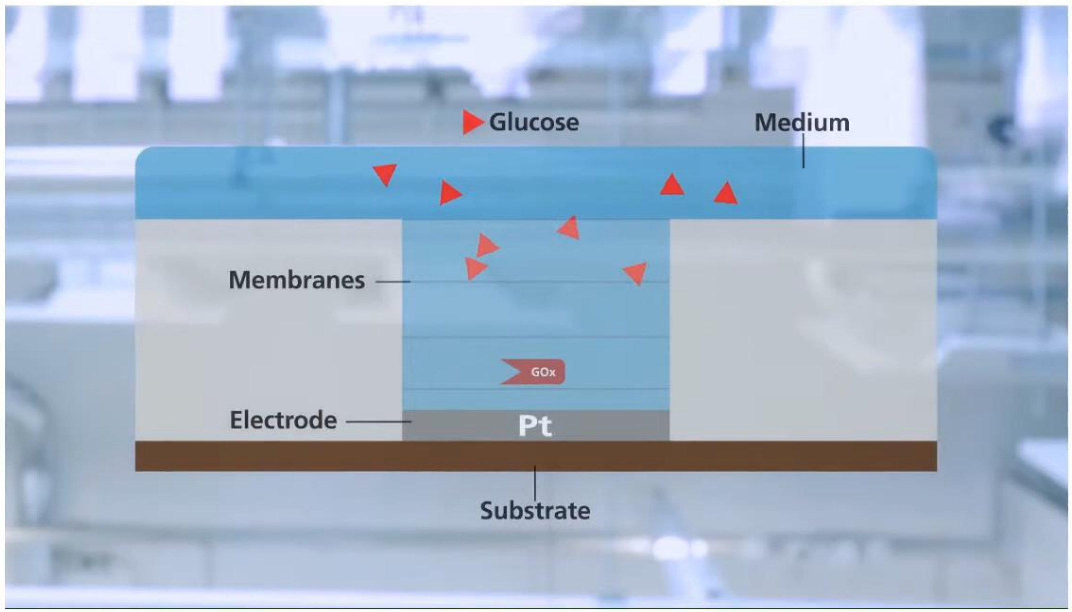
$$H_2O_2 \xrightarrow{\text{Pt: } 450\ mV} O_2 + 2H^+ + 2e^-.$$

- Two electrons are freed during each reaction. The resulting **electric current** $I(t)$ is proportional to the concentration of according substance.

Biosensors: how do they work?

Biosensors: The membrane structure

- Glucose / Glucose Oxidase reaction on the working electrode



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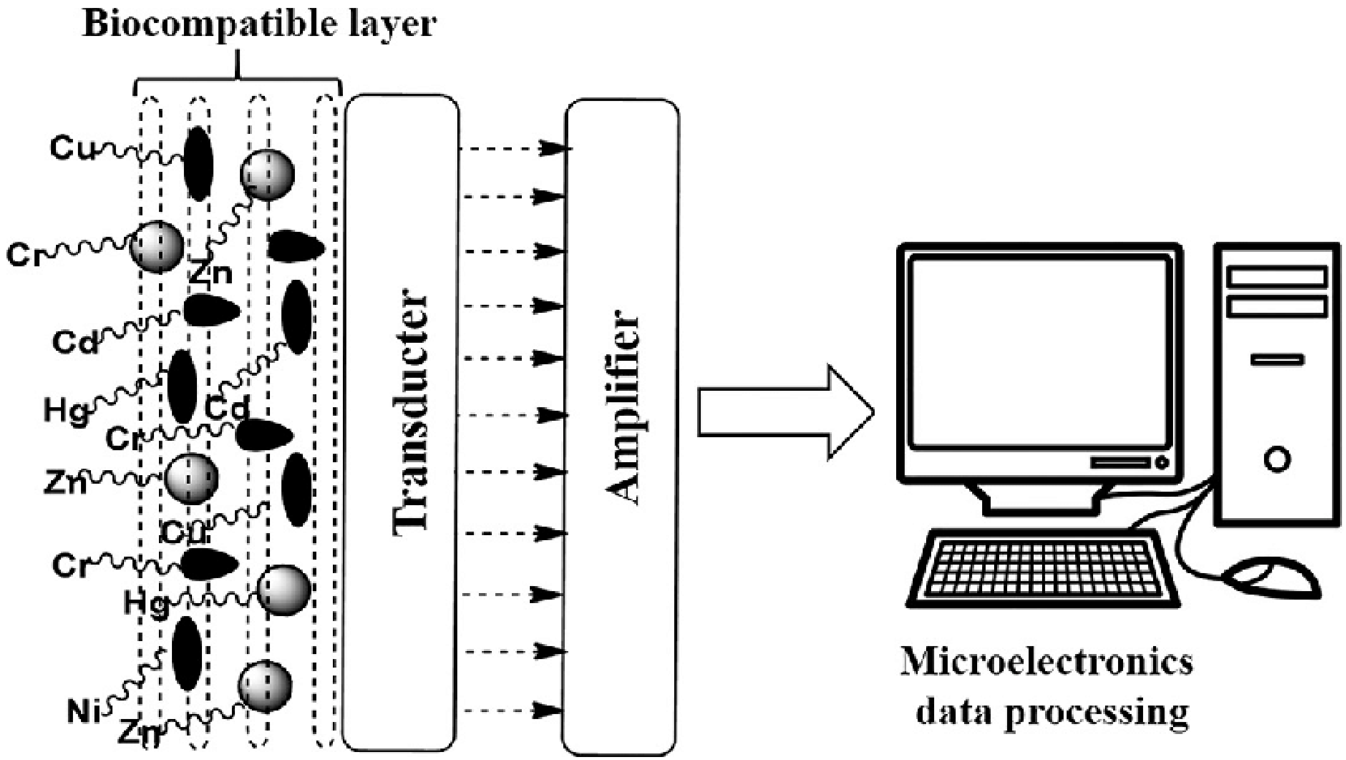
Innovative Sensor Technology: https://www.youtube.com/watch?v=WjfQ-ZHEAHg

Biosensors: 1st example

Accu-Chek Glucose Monitor Kit for Diabetic Blood Sugar Testing

Biosensors: 2nd example

Advances in protein/enzyme-based biosensors for the detection of metal contaminants in the environment. 2020, https://doi.org/10.1016/B978-0-12-814679-8.00012-1



Mathematical model of enzyme-based amperometric biosensor

$$\frac{\partial S_l}{\partial t} = D_{Se}\frac{\partial^2 S_l}{\partial x^2} - \frac{V_{max} S_l}{K_M + \sum_{k=1}^m S_k}, \quad l = 1, \dots, m, \quad 0 < x < d,\ t > 0,$$

$$\frac{\partial S_l}{\partial t} = D_{Sb}\frac{\partial^2 S_l}{\partial x^2}, \quad l = 1, \dots, m, \quad d < x < d + a,\ t > 0,$$

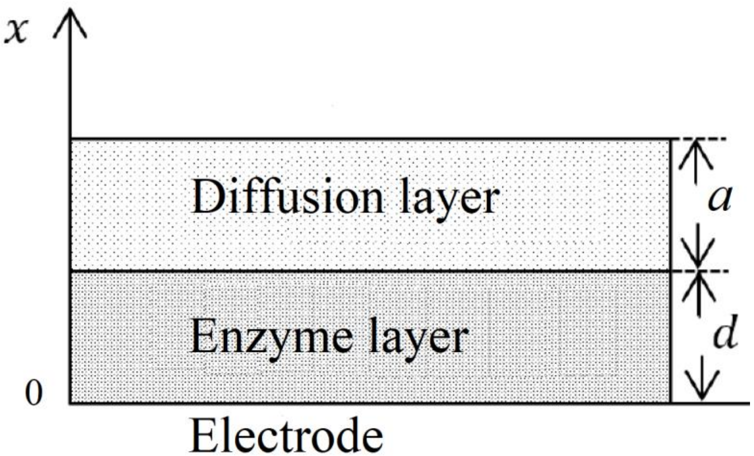
$$\frac{\partial P_l}{\partial t} = D_{Pe}\frac{\partial^2 P_l}{\partial x^2} + \frac{V_{max} S_l}{K_M + \sum_{k=1}^m S_k}, \quad l = 1, \dots, m, \quad 0 < x < d,\ t > 0,$$

$$\frac{\partial P_l}{\partial t} = D_{Pb}\frac{\partial^2 P_l}{\partial x^2}, \quad l = 1, \dots, m, \quad d < x < d + a,\ t > 0,$$

$$S_l(x, 0) = 0, \quad P_l(x, 0) = 0, \quad l = 1, \dots, m,$$

$$D_{Se}\frac{\partial S_l}{\partial x}(0, t) = 0, \quad P_l(0, t) = 0, \quad l = 1, \dots, m,$$

$$S_l(d + a, t) = s_l, \quad P_l(d + a, t) = 0, \quad l = 1, \dots, m,$$



Electric current (of virtual biosensor):

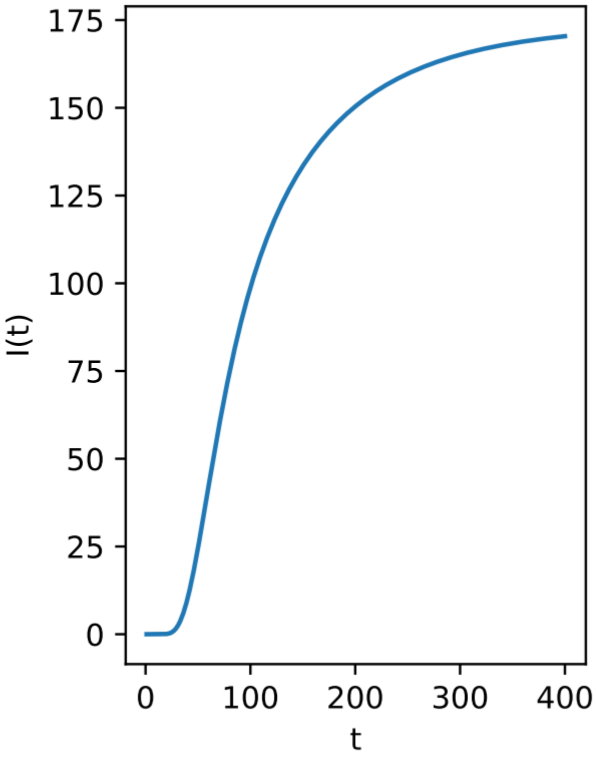
$$I(t_k) = \sum_{l=1}^m c_l D_{Pe}\frac{\partial P_l}{\partial x}(0, t_k), \quad 0 < t_1 < \dots < t_K = T$$

Biosensor's operational modes

Batch mode:

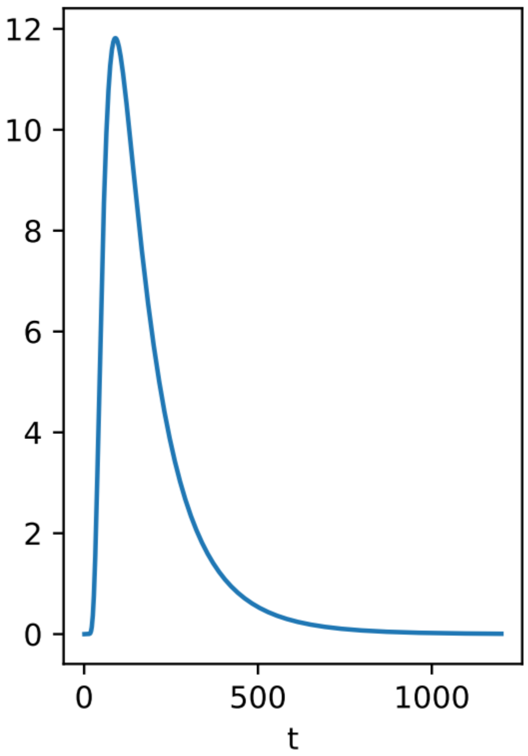
$S_l(d+a,t) = C_l = const,$

$l = 1, .., m.$



Flow injection mode:

$$S_l(d+a,t) = \begin{cases} C_l, \ t \le t_f, \\ 0, \ t > t_f, \end{cases} \quad l = 1, .., m.$$



Inverse biosensor problem

- We assume that we can only observe only the net current of all products – we have no information on separate currents for each product.
- Given the biosensor electrical current signal $I(t)$, determine the substrate concentrations
$$\vec{C} = (C_1, C_2, \ldots, C_m).$$
- In this work, we solve the inverse problem for $m = 3$.
- To simulate the influence of noise, we use two different types:
  - Additive: $I_{mn}(t_i, C) = I(t_i, C) + \sigma X$
  - Multiplicative: $I_{mn}(t_i, C) = I(t_i, C)\,(1 + \sigma X)$

Results of numerical experiments

Train domain: $$D = \left\{ 3.2\left(1 - \frac{k}{N-1}\right) + \frac{k}{N-1}12.8 : k = \overline{0, N-1} \right\}$$

Error: $$\frac{|a_i(I) - c_i|}{|c_i|} \times 100\%, \ i = \overline{1, m},$$

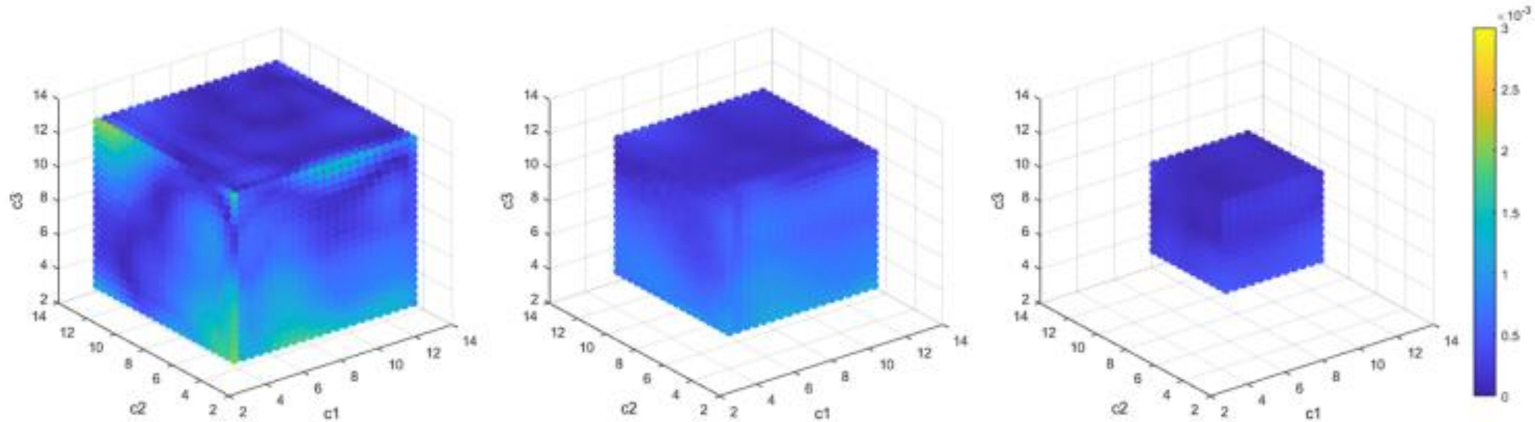


Figure 3: Biosensor error distribution. Left - original cube, middle - 3 outer layers removed, right - 6 layers removed

Results with FNN (PCA)

- Batch mode, Additive noise:

σ	Epochs	PCs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	3200	4	0.078	1.899	0.038	0.214
0	3200	80	0.050	1.093	0.039	0.269
0.01	2000	4	16.89	154.69	7.77	50.15
0.01	3200	80	1.04	9.88	0.92	6.64
0.02	3200	80	1.87	18.50	1.69	12.16
0.03	3200	80	2.66	26.62	2.38	17.52
0.04	3200	80	3.36	35.72	3.09	22.17
0.05	3200	80	4.08	39.75	3.77	26.50
0.10	3000	4	16.88	156.21	7.82	50.35
0.10	1000	80	8.12	107.02	7.20	52.22
0.20	450	80	12.54	163.91	8.77	74.70
0.40	3000	4	16.95	155.54	7.90	49.74
0.40	477	80	15.24	207.84	9.59	77.95

Results with FNN (PCA)

- Flow injection mode, Additive noise:

σ	Epochs	PCs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	2200	4	0.030	0.273	0.021	0.068
0	3200	80	0.039	0.443	0.022	0.108
0.01	2200	4	2.52	35.42	2.43	23.97
0.01	1000	80	2.70	38.95	2.59	26.24
0.02	1200	4	3.49	49.56	3.53	34.92
0.03	1500	4	4.27	62.90	4.41	43.62
0.04	2000	4	4.98	76.12	5.15	52.20
0.05	2000	4	5.61	86.36	5.81	60.08
0.10	2000	4	8.37	139.32	7.38	76.99
0.10	260	80	9.41	148.92	8.66	81.60
0.20	2000	4	13.54	175.08	7.55	75.60
0.40	2000	4	15.03	161.68	7.76	49.77
0.40	150	80	16.64	198.22	10.35	80.29

Results with convolutional network

- Batch mode, Additive noise:

σ	Config	Epochs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	1	990	0.392	4.420	0.261	1.812
0.01	1	936	2.09	25.75	1.69	13.70
0.05	1	979	5.01	72.97	4.50	38.08

- Flow injection mode, Additive noise:

σ	Config	Epochs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	3	340	0.095	0.945	0.111	0.470
0.01	5	277	1.25	17.35	1.16	12.19
0.05	5	393	3.25	52.10	3.07	38.97
0.10	7	200	6.03	101.26	5.48	65.81
0.40	7	200	12.74	182.75	8.24	88.29

Results with FNN (PCA)

- Batch mode, Multiplicative noise:

σ	Epochs	PCs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	3200	4	0.078	1.899	0.038	0.214
0	3200	80	0.050	1.093	0.039	0.269
0.01	2200	4	5.34	82.11	5.17	42.39
0.01	1000	80	5.52	78.93	5.12	41.08
0.02	2200	4	9.64	128.39	8.88	71.27
0.02	700	80	9.61	136.20	8.50	67.72
0.03	2200	4	12.03	141.35	9.41	79.48
0.04	2200	4	13.48	155.49	9.51	86.14
0.05	2200	4	14.52	156.96	9.22	83.86

Results with FNN (PCA)

- Flow injection mode, Multiplicative noise:

σ	Epochs	PCs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	2200	4	0.030	0.273	0.021	0.068
0	3200	80	0.039	0.443	0.022	0.108
0.01	2000	4	0.14	1.25	0.11	0.58
0.01	400	80	0.22	2.23	0.16	0.83
0.02	2000	6	0.23	2.11	0.21	1.17
0.03	2000	4	0.36	3.18	0.31	1.78
0.04	2000	4	0.47	4.09	0.41	2.41
0.05	2000	4	0.58	5.02	0.52	3.02
0.10	2000	4	1.11	9.34	1.03	5.88
0.20	2000	4	2.19	19.75	2.06	11.49
0.40	2000	4	4.15	41.12	4.11	22.91
0.80	2000	4	7.67	75.68	7.98	45.23

Results with convolutional network

- Batch mode, Multiplicative noise:

σ	Config	Epochs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	1	990	0.392	4.420	0.261	1.812
0.01	2	459	6.13	82.67	6.01	45.89
0.05	2	131	14.83	180.28	9.80	94.08

- Flow injection mode, Multiplicative noise:

σ	Config	Epochs	$E_{ts,a}$	$E_{ts,m}$	$E_{rc,a}$	$E_{rc,m}$
0	3	340	0.095	0.945	0.111	0.470
0.01	4	335	0.26	2.25	0.19	1.40
0.05	3	312	0.64	6.81	0.59	3.99
0.10	5	200	1.25	10.00	1.16	7.26
0.40	5	240	4.19	34.23	3.97	24.33
0.80	4	308	6.01	51.47	5.91	37.86

Thank you for your attention!