Biosensing for Human Health

Today we learned about how biosensors work where molecular recognition between a bioreceptor and a target allows detection. The following questions will help you to interpret the data that you get out of a biosensing experiment.

1. Let's first do a problem involving the classical glucose electrochemical biosensor. A glucose biosensor operates by detecting hydrogen peroxide H_2O_2 produced during the enzymatic oxidation of glucose. The generation of H_2O_2 is measured at the Platinum electrode, which has a standard reduction potential of +0.695 V for the reaction: $\mathbf{H_2O_2 \Rightarrow 2H^+ + O_2 + 2e^-}$

   a) Based on this reduction potential, is this reaction spontaneous? Why or why not?

   b) The glucose sensor generates a current of 10 μA during the measurement. Calculate how many moles of H_2O_2 are oxidized per second.

      Here is **Faraday's law of electrolysis** for you to use: $n = \frac{I}{zF}$

   c) What factors could influence the efficiency of the platinum electrode in oxidizing H_2O_2?

   d) Blood contains other electroactive molecules like ascorbic acid and uric acid. How could these interfere with the sensor? Propose one strategy to minimize these interferences.

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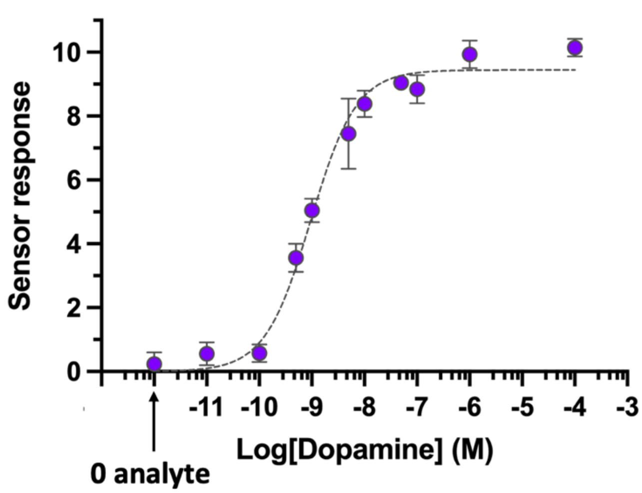
2. To monitor concentration flux of neurochemicals such as dopamine in the brain, the physiologically relevant range is 10 nM (1×10^{-8} M) to 1 μM (1×10^{-6} M). We want to see whether a newly isolated dopamine antibody is an optimal bioreceptor to monitor the change in dopamine concentrations in the brain. To test this new dopamine antibody, we functionalized these receptors to the sensing substrate of a device (*e.g.,* surface plasmon resonance). When dopamine was added to the solution, the signal change was plotted as a function of dopamine concentration (see table, SD = standard deviation, error bar) and shown in Figure 1.



Concentration (M)	Mean	SD
0	0.234	0.363
1×10^{-11}	0.557	0.361
1×10^{-10}	0.576	0.279
5×10^{-10}	3.559	0.439
1×10^{-9}	5.046	0.369
5×10^{-9}	7.452	1.105
1×10^{-8}	8.379	0.412
5×10^{-8}	9.039	0.191
1×10^{-7}	8.838	0.439
1×10^{-6}	9.933	0.430
1×10^{-4}	10.142	0.276

Figure 1. *Biosensor signal change dependence on dopamine (target) concentration when dopamine-specific antibodies (bioreceptors) are functionalized on the surface.*

a) What is the limit of detection (LOD, lowest detectable concentration) of this dopamine sensor? Note the equation for the LOD:

$$LOD = \frac{3\sigma_{S_0}}{\frac{dS}{dc}}$$

You can approximate the slope as 5 x 10^9 (you can check this by plotting the curve linearly rather than logarithmically)

b) What is the sensitive detection regime for this sensor for dopamine? In other words, what concentration range of dopamine can we differentiate with this sensor?

c) What is the approximate dissociation constant (K_d value) of the interaction between dopamine and the dopamine antibodies based on this sensing curve?

d) Now that you know the K_d of the dopamine aptamer (1 nM), we conduct an experiment where we add 600 pM of dopamine in buffer to the sensor surface. Using the law of mass action, calculate the expected fractional occupied receptor density ($\boldsymbol{\phi}$) in equilibrium. You can assume the free dopamine concentration is unchanged due to the reaction ($[A] = [A_0]$).

e) Would this biosensor be useful for monitoring dopamine flux in the brain microenvironment? The physiologically relevant range in humans is 1 nM (10^{-9} M) to 1 µM (10^{-6} M).

Key Takeaways from this Exercise:

- Seeing the real-world applications of biosensors for human health (glucose for diabetes, neurotransmitters for brain chemical dynamics).
- Understanding how amperometric biosensors like the glucose sensor work by monitoring the generation of H_2O_2 based on enzymatic activity.
- Getting a grasp on reduction potentials and predicting the spontaneity of a reaction (whether an operating potential is necessary or if the reaction is spontaneous).
- Understanding the key metrics for evaluating biosensor performance such as the LOD, sensitivity, dissociation constant, fractional receptor occupancy