CH-413 Nanobiotechnology

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Problem Set 3

Optical and Electrical Sensing, Next-Gen Sequencing

Exercise 1 – Optical sensing

Find a figure of an SPR sensorgram from a published study (peer-reviewed paper). Choose one that reports a biomolecular interaction relevant to drug discovery (e.g., small molecule–protein, antibody–antigen, etc.). Reference the paper and paste the image into your answer.

Based on the sensorgram alone, answer the following:

1. What is the research question or hypothesis that this SPR experiment aims to address? In other words: Why was this experiment done?
2. What type of data can be extracted from this experiment—kinetic rate constants (k_{on}, k_{off}), equilibrium affinity (K_D), or both?
3. Justify your answer: Refer to the *shape* and *quality* of the curves (association, dissociation, regeneration), the *range of concentrations* used, and whether the data appears to reach steady state.

Exercise 2 – Electrical sensing and NGS

Sequencing by Expansion (SBX) is a novel single-molecule sequencing approach that transforms DNA into an expanded surrogate polymer (called an *Xpandomer*) that is then sequenced using a nanopore sensor.

Paper: https://doi.org/10.1101/2025.02.19.639056

1. In your own words, describe the two major steps of SBX: (i) Xpandomer synthesis and (ii) nanopore sequencing. Use a hand-drawn or sketched diagram to illustrate the workflow. Be sure to show:
    - What happens to the original DNA strand.
    - How the Xpandomer encodes sequence information.
    - How the nanopore reads out the encoded signal.
2. Compare SBX to two other sequencing technologies:
   (a) *Illumina sequencing-by-synthesis*
   (b) *Oxford Nanopore direct DNA sequencing*

In your comparison table or discussion, consider:

- Sample prep complexity
- Read length
- Error profile and accuracy
- Signal detection modality
- Real-time capability
- Suitability for homopolymers and structured regions
- Cost and scalability potential

3. Critical thinking:
   SBX decouples biochemical synthesis from physical measurement, unlike other sequencing platforms. What advantages might this separation offer for future applications, including clinical or portable sequencing? What might be the challenges or limitations of using SBX in practice?