**Gen 575 Spring 2025**

**Problem Set 3**

*Due by 11:59 pm May 22, 2024 to maccoss [at] uw.edu*

**Name:**

**Problem 1 (35 points)**

* 1. **(10 points)** After a year of working on trying to detect your favorite analyte using some old instrument, your PI just bought the latest greatest platform. The instrument has just been installed and they ask you to quickly design an experiment to assess whether you can detect said analyte. In your own words, describe below in a few sentences how you will prove that your analyte is detectable with the new instrument. A high-level description is sufficient:
  2. **(10 points)** The experiment above worked great, and you can definitely detect your favorite analyte. Your PI is now working on a grant proposal and wants to be able to report the signal-to-noise of the analyte measured in a specific sample matrix they are interested in. In your own words, describe below in a few sentences, one possible way to report the signal-to-noise. Justify your reasoning for using this method.
  3. **(15 points)** After thinking about the signal-to-noise experiment a bit more, you wanted to see if the new instrument is “shot noise” limited. In your own words, describe a simple experiment to assess whether most of the noise is shot noise or if most of the noise is constant regardless of the signal (e.g. Johnson noise).

**Problem 2 (25 points)** Your lab just got a new grant to add plasma proteomics measurements to part of a multi-omics effort with 1000s of samples. You are trying to decide between Somoscan, O-link, and an LC-MS assay at the local proteomics core lab. Before spending your entire budget on your samples, you decide to prepare a pilot set of samples that you can send to the three services before sending your valuable samples. You want to assess 1) what proteins will be measured with each, 2) how similar the results are between platforms, 3) how precise the measurements are, and 4) whether known quantitative changes are accurately reflected by the respective technologies. Your PI says you are limited to 10 samples for this pilot. What 10 samples would you prepare and send to each of the three services?

**Problem 3 (40 points)**

* 1. **(25 points)** You’ve been hired as a consultant by QuantumSi (<https://www.quantum-si.com/>). They are working on some new single molecule peptide sequencing technology based on affinity reagents that recognized specific N-terminal amino acids, combined with amino peptidases (<https://www.science.org/doi/10.1126/science.abo7651>). They are hoping to be able to image 1,000,000 peptide molecules per sample with the hopes of being able to handle analysis of model organisms like *S. cerevisiae*. Using what you’ve learned this quarter how large of a flow cell will they need to use? Why?
  2. **(15 points)** There are ~10 billion protein molecules in each HeLa cell. If you wanted to acquire 100 billion peptide reads to have a chance of covering the dynamic range of the HeLa proteome, is this practical using a method based on spatially separated single molecules? Why or why not?