Problem set 5
(Discussion on June 18)

Problem 1

Evaluating scientific papers. The team of Christian Drosten, a German virologist who works on Coronaviruses, published a study entitled "An analysis of SARS-CoV-2 viral load by patient age" on a preprint server on April 29, 2020. A PDF of the work is linked on the course website. This study subsequently attracted a lot of media attention in Germany, with some newspapers claiming the study was false, citing scientists that had critized the statistical analysis used. We will use it as a case study to discuss some general observations, guidelines, and suggestions on how to evaluate scientific publications.

a) In preparation for our discussion, read the preprint by Jones *et al.* that is linked on the website. You do not have to worry about technical details, it is sufficient to get an overview what was done and what key conclusions are drawn. You might find the previously used framework Problem - Significance - Approachüseful to think about how to place the current study in a wider context.

b) Look at the data in Figure 2. Do you think children have a lower viral load than adults? How would you try to determine this question from the data? Again, we don't want to worry about technical details here, I just want to you think about the question in general.

c) Do you find that the conclusions of the manuscript are justified by the data?

Problem 2

Estimates of molecular forces. In this problem, we will carry out some very simple estimates of the forces required to break interactions in biomolecular systems. A simple estimate of the force F required to break a certain interaction can be obtained by considering the characteristic energy E and the typical length scale Δx over which it acts: $E = F \cdot \Delta x$.

a) Estimate the forces required to break covalent bonds. A C-O bond has a binding energy of 84 kcal/mol; a S-S bond has an energy of 51 kcal/mol (data from `https://www.ncbi.nlm.nih.gov/books/NBK21595/`). You can assume that the bonds break over a characteristic distance of ≈ 1 Å.

b) Biological interactions are often mediated by non-covalent bonds. Non-covalent interactions tend to be weaker and longer ranged than covalent bonds. Obtain a rough estimate of the energies and rupture forces of non-covalent interactions, by assuming that they act over distances of $\approx$ 1 nm and taking into account that they are much weaker than covalent interactions but still stronger than forces due to thermal fluctuations. Hint: the thermal energy at room temperature is $k_B T \approx$ 4 pN·nm.

Problem 3

Force-extension relationship for the 1D freely-jointed chain. In class, we derived the extension response of a 3D freely-jointed chain to an external force f. In this problem, you will carry out a similar derivation, for the simpler, one-dimensional case. Consider a chain of N stiff segments of length b that always lie along the z-axis. There is a two-state variable σ that takes on the value $\sigma_i = +1$ for each segment that points "forward" in the z-direction, along the external applied force, or $\sigma_i = -1$ for segments that point "backwards", against the external force. The total extension is then given by

$$z = b \cdot \sum_{i=1}^{N} \sigma_i \tag{1}$$

Derive an expression for the average extension $\langle z \rangle$ as a function of N, b, f, and $k_B T$. *Hint:* You probably want to first write out the partition function Z. Using the partition function, you can write an expression for the ensemble average $\langle z \rangle$, which you can simplify using the "logarithm trick" used in class and familiar from stat mech courses.