Summary Report of Surface Interaction Simulation

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at the Goh Lab, April 2020-2021

**Note: Presentation slide decks in the folder contain visuals and quick notes that can help with further understandings **

Overview

1. Background
2. Goal
3. Advancements in the Simulation Model
4. Next Steps

Background

- Investigate bacteria-surface interactions from nanoscale distances which assumes electrostatic attraction and repulsion
    - The interaction energy is calculated from $U_E = k\frac{q_1 q_2}{r}$ (assuming k=1)
- Simulation of cylindrical bacteria finding the lowest energy configuration on a charged surface
- The bacteria are primarily composed of negative charges on the surface due to the phospholipid bilayer
    - However, there are positive domains on the surface (ex. transmembrane proteins)
- Key Takeaways from Literature:
    - Strongest interactions are between matching domains, but are unlikely
        - Shen, L.; Zhu, J. Heterogeneous surfaces to repel proteins. https://www.sciencedirect.com/science/article/abs/pii/S000186861530004X#:~:text=In%20general%2C%20representative%20heterogeneous%20surfaces,topographic%20surfaces%20with%20different%20feature (accessed Apr 22, 2021).
    - “On a series of E. coli, Zita and Hermansson [211] found that the number of positively charged surface structures per cell surface was only a fraction of the number of negatively charged surfaces structures, but that nevertheless the presence of positive surface charges was more influential upon adhesion of the strains to activated sludge flocs than the presence of negative surface charges.”
        - Bos, R.; van der Mei, H. C.; Busscher, H. J. Physico-chemistry of initial microbial adhesive interactions – its mechanisms and methods for study.

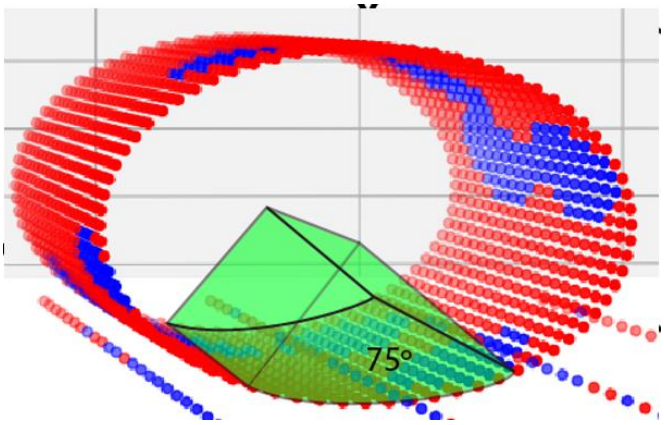
https://academic.oup.com/femsre/article/23/2/179/524397 (accessed Apr 22, 2021).

Goal

1. Show that patchiness/domain size affects the configuration of the bacteria
    a. In other words, a mostly negative bacteria will not necessarily bind to the most positive surface.
2. How does a mostly negative bacteria interact with a net neutral surface which has domains randomly dispersed on the surface?

Advancements in the Simulation Model

1. 3D Model
    - Bacteria:
        - Cylindrical
        - Mostly negative
        - Positive domains
        - Represented by dots on a Cartesian coordinate grid
        - Elevated 1 relative nm above the surface
    - Surface:
        - Flat
        - Gradient (100% positive/0% negative to 0%positive/100%negative)
        - No domains
        - Represented by dots on a Cartesian coordinate grid
    - Interaction:
        - Interaction is only affected by points directly above and below
        - r (distance from point on surface to point on bacteria) changes
        - There is a select area on the bacteria that interacts with the surface (shown in the picture below)



    - **PROBLEMS**:
        - Calculation Errors – The line of points on the bacteria closest to the surface are the most significant contributors to the interaction energy because of the nm distance. The rest of the bacteria would have much

larger r's because the bacteria is on the µm-scale. The final effect of this is that the domain size doesn't make any difference.
    - Time Efficiency – The number of interactions coupled by the amount of rotations and translations made each simulation cost 8+ hrs.
    - Scaling – The density of points on the surface was too low compared to the bacteria. Thus, any point on the bacteria would interact only with one line of points on the surface. (As seen in the picture above)
2. Matrix Model
    - We noticed that what we really want to test is whether domain size matters, and creating a 3D environment introduced many variables that are difficult to control
    - Solution? Simplification of the model!
    - Bacteria:
        - Flat
        - 100 x 100 points
        - An array of domain sizes
        - 80% negative / 20% positive
    - Surface:
        - Flat
        - 10000 x 10000 points
        - Matching domain sizes to the bacteria
        - Gradient surface (100% positive/0% negative to 0%positive/100%negative)
    - **Conclusions:**
        - The matrix environment had much **better efficiency**, running 200 simulations within 3-4hrs.
        - The environment was more **malleable**, I could tweak many parameters easily
        - The next step was to **design an experiment**
3. Net Zero Surface
    - Data is located in the same folder in the Excel files
        - Constant_Net_Zero_Bacteria (changing surface domain size)
        - Constant_Net_Zero_Surface (changing bacteria domain size)
    - Surface:
        - Net Zero Charge surface (50% negative / 50% positive)
    - To answer the research question, I changed the domain sizes:
        - Changing surface domain size, keeping the same domain size on the bacteria
            - The results suggested that larger domain sizes yield lower energy. However, this contradicts with my hypothesis which is matching domain sizes should yield lowest energy.

        a. The unaccounted variable is that the density of larger domains better matches the bacteria (this is because of the concentration mismatch between surface and bacteria)
    - Changing bacteria domain size, keeping the same domain size on the surface (we changed the concentration to match but in opposite charges)
        - Better replicates real-life scenario since we cannot design the bacteria, but we can design the surface.
        - **Conclusions**: The results agreed with the hypothesis. The lowest energy is created by having matching domain sizes and concentrations (but in opposite charges)

Next Steps

- From the simplest model, add layers of complexity without sacrificing the integrity of a simple model
    - Features: topography, hydrophobic and hydrophilic interactions
- Incorporate the findings from a simulation into a physical experiment, and continue to modify the simulation with accordance to how the physical experiment behaves
    - i.e. bridging the theoretical/simulated environment and the physical environment
- Good luck!

Questions

If you have any concerns, questions, or would simply like to know more, contact Stanley.lo@mail.utoronto.ca with the email title: “Surface Simulation Troubleshooting”