Understanding virus evolutionary dynamics using single molecule sequencing and droplet microfluidics

PI: Rahul Roy

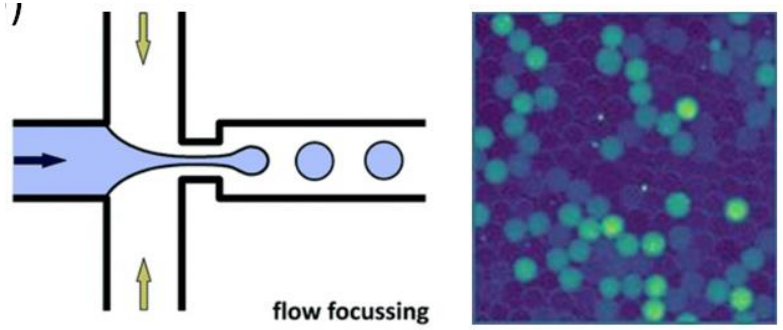
Chemical Engineering

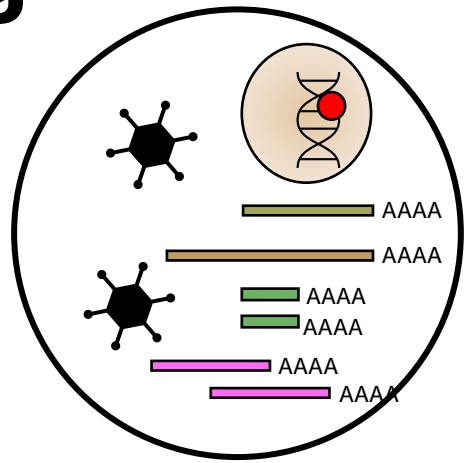
Center for BioSystems Science and Engineering

Viruses

- Infect and grow inside the host. Their growth is affected host cell processes. (see eg. Chhajer et al. 2020 that presented a universal mathematical model for the virus growth in cells)
- Due to low error correction during their copying, they generate a large number of mutants (viral quasispecies).
- Mutants with better ‘fitness’ escape host immune response (rendering vaccines ineffective), reduce drug efficacy and cause new waves of pandemic.
- Understanding virus evolution is difficult since no high throughput methods exist to investigate them.

Droplet Microfluidics and Single Cell Sequencing





Gene expression changes

Viral quasispecies

Combine droplet microfluidics to trap single cells and viruses to understand how viruses infect, grow and evolve in the host cells.

The project leverages developments by the current lab members in both isothermal amplification of single molecules in water-in-oil microdroplets and single RNA sequencing.

Expected outcomes

- Development of a first-of-a-kind method to sequence ‘all’ virus genomes in a single population to understand viral quasispecies diversity
- Understand how viruses evolve in hosts, acquire ‘escape’ mutations and tackle host selection pressures
- Thorough understanding of how host cells cope with a ’moving target’ that continues to evolve by acquiring mutations

References:

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3. Stuart, T., Satija, R. Integrative single-cell analysis. Nat Rev Genet 20, 257–272 (2019). https://doi.org/10.1038/s41576-019-0093-7