Fighting Infections and Antimicrobial Resistance Through GPU-Accelerated In Silico Models

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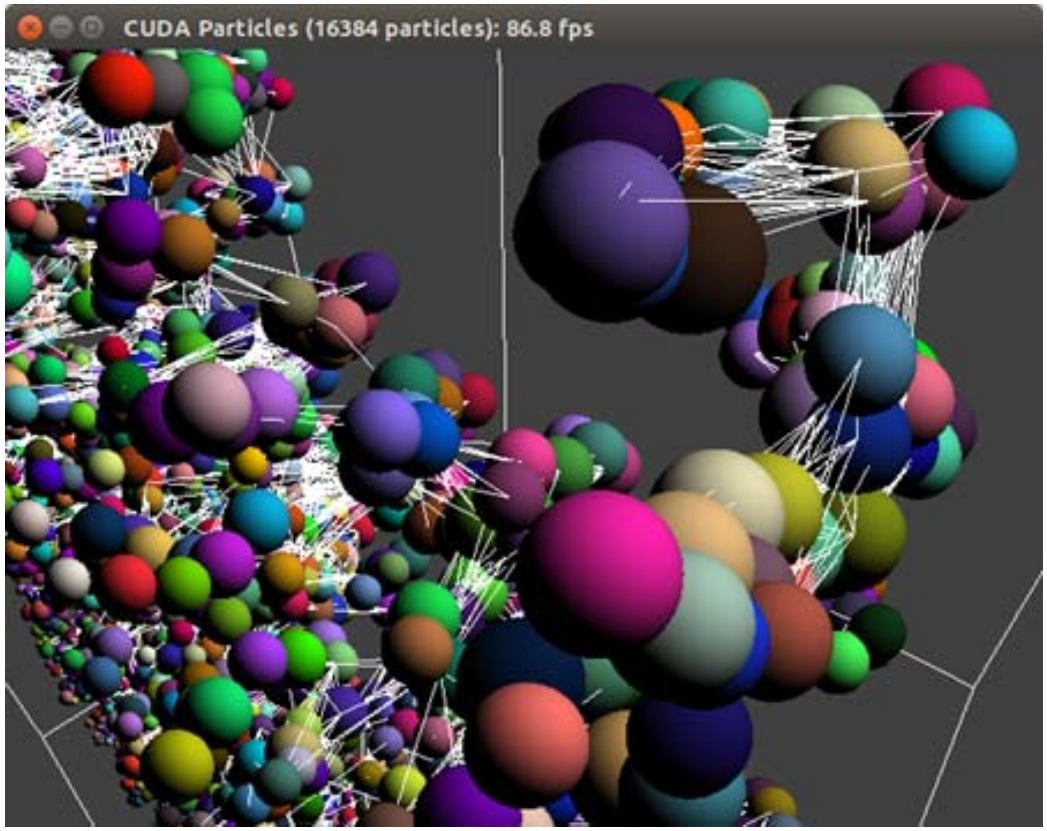
GTC, April 5, 2016



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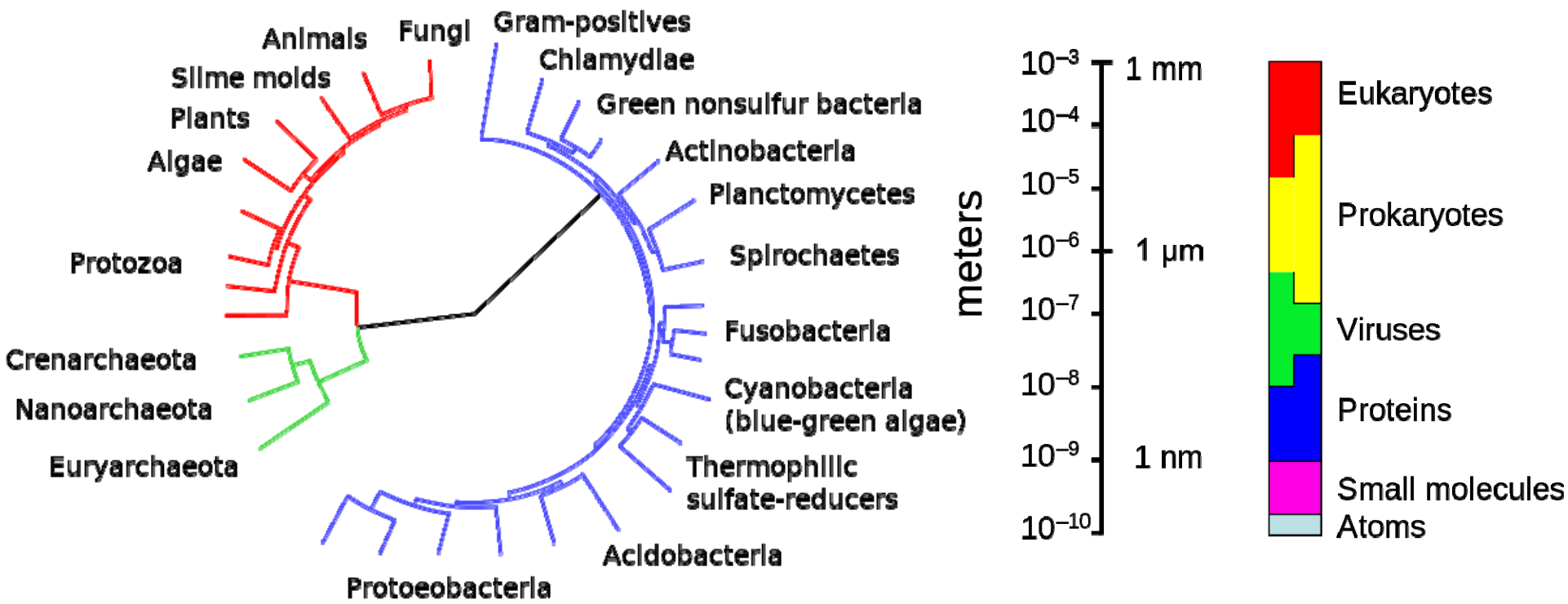
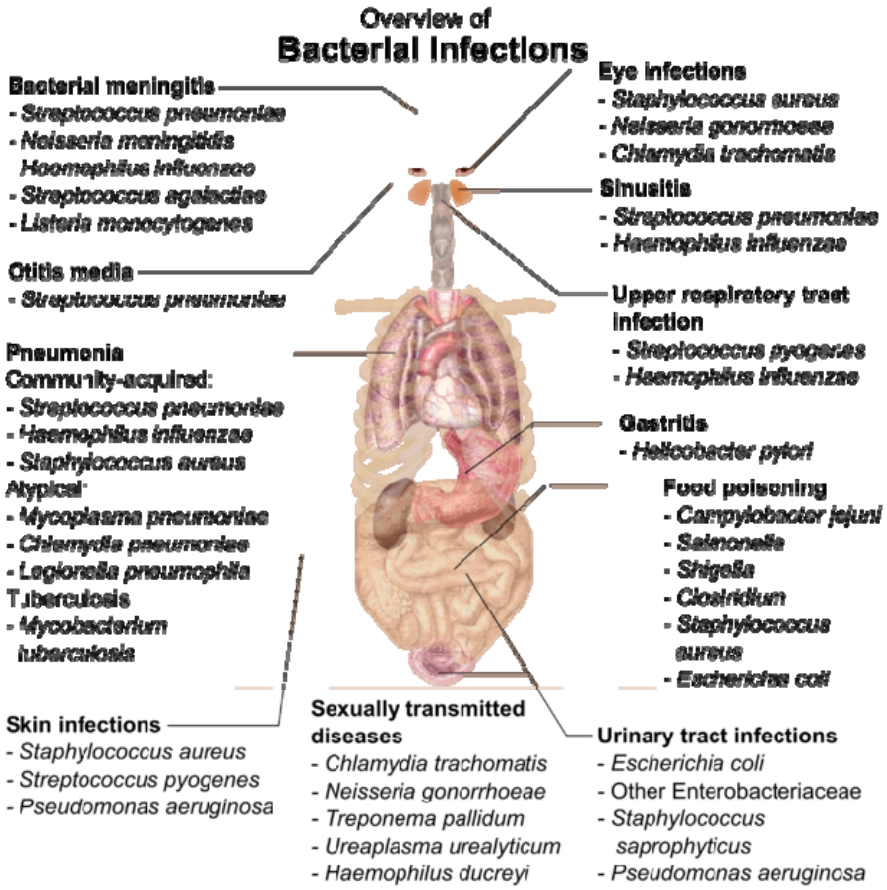
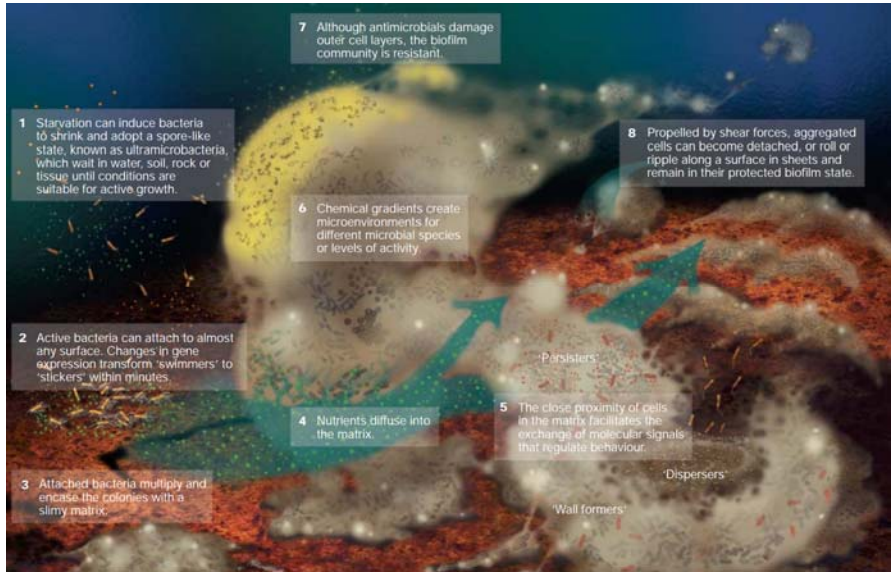
Bacteria are among the earliest forms of life that appeared on Earth billions of years ago. Studied since 1676…



Bacteria are of immense importance because of their extreme flexibility, capacity for rapid growth and reproduction.

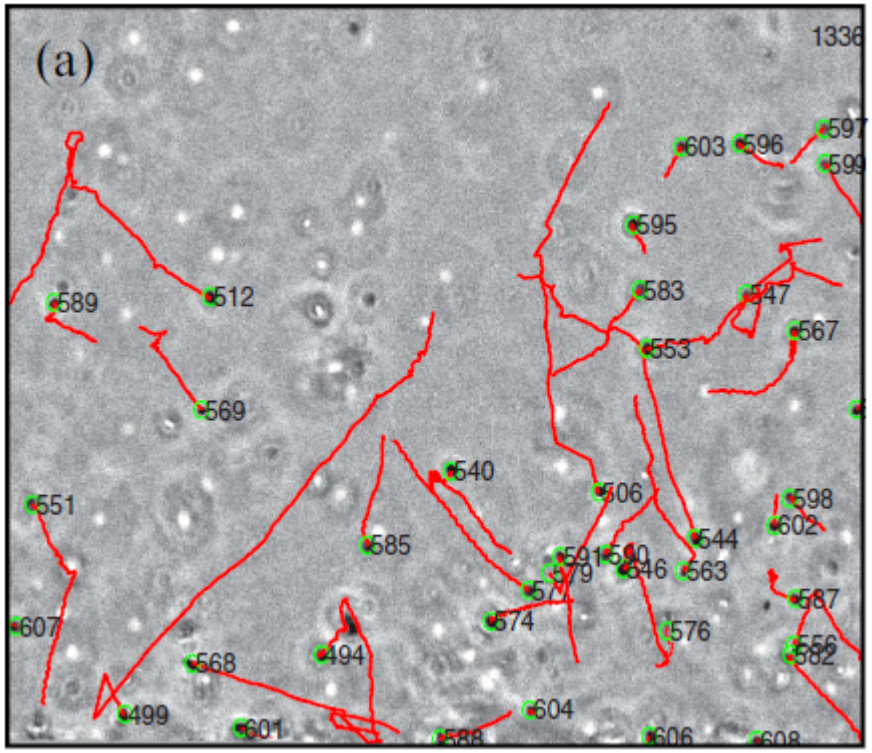
The fight against bacterial infection represents one of the big challenges of modern medicine.





Focus on intercellular communication to understand behavior at population-level

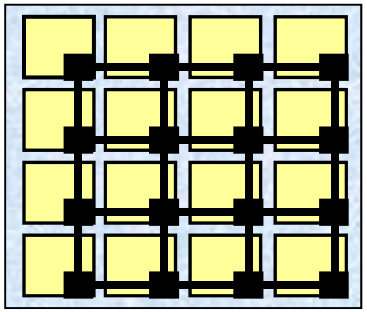
Mathematical characterization of the collective dynamics of such bacterial swarms represents a major challenge



Having a quantitative model of pathogen interactions is crucial for understanding how to fight them.

This presentation focuses on the “network” paradigm and ways to engineer communication

Biological networks
Cellular communication

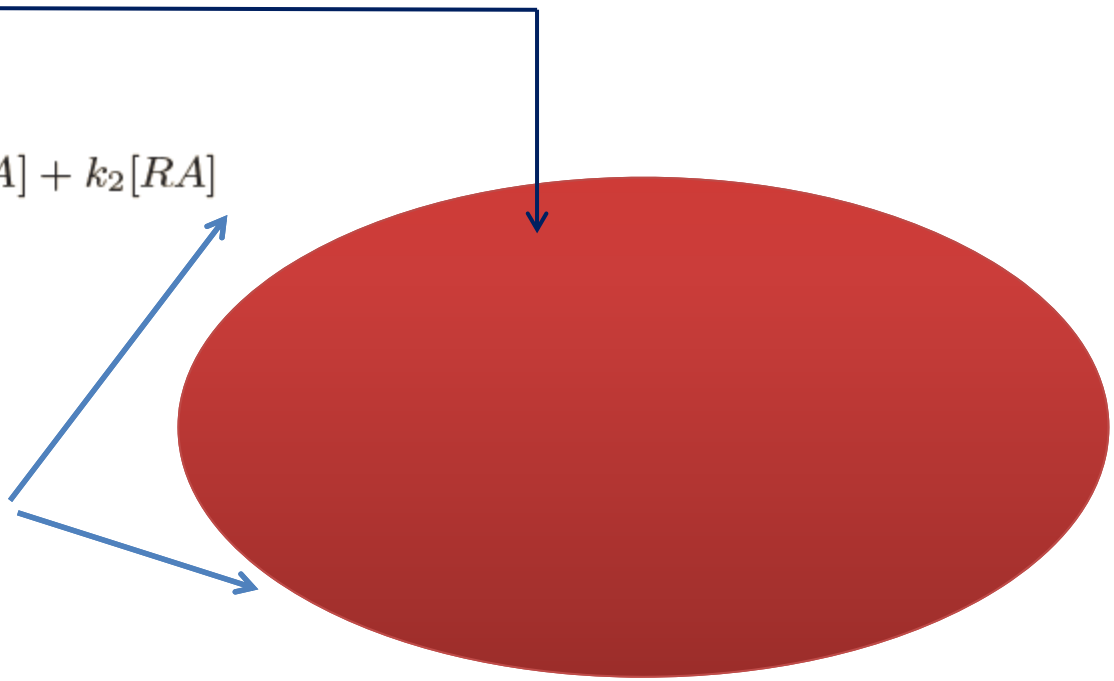


Silicon networks
On-chip communication

Bacteria form a “social network” to coordinate their behavior, build the biofilm and resist treatment.

A New Frontier – Quorum Sensing. QS is a density-dependent collective behavior that enables communication

$$\frac{d[A]}{dt} = c_A + \frac{k_A[C]}{K_A+[C]} - k_0[A] - k_1[R][A] + k_2[RA]$$

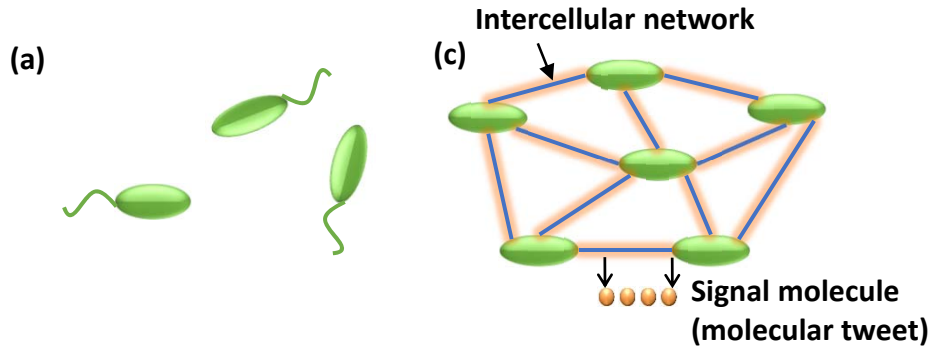


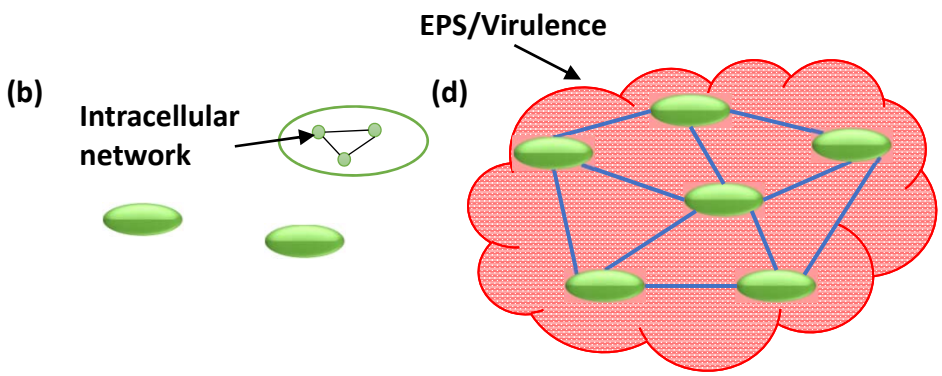
QS upregulates multiple virulence genes

[G. Wei, Marculescu, NanoCom, 2014]

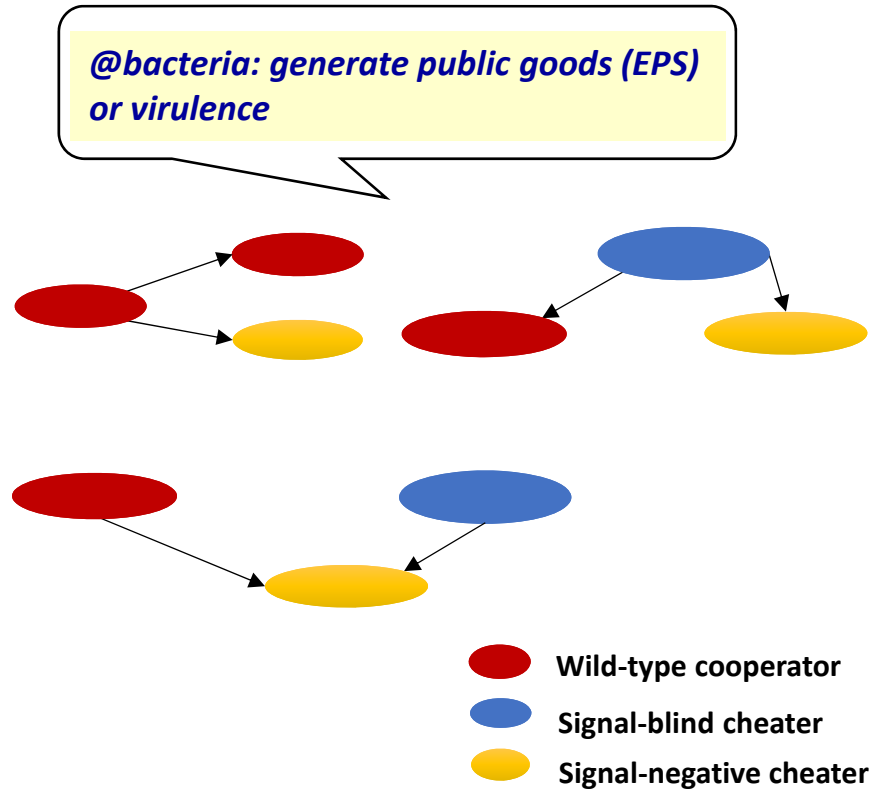
Gram-negative bacteria use largely homologous QS networks, where the AIs are detected and regulated via genetic circuits.

Bacterial biofilm: Use Twitter-like metaphor to explain participants and network formation





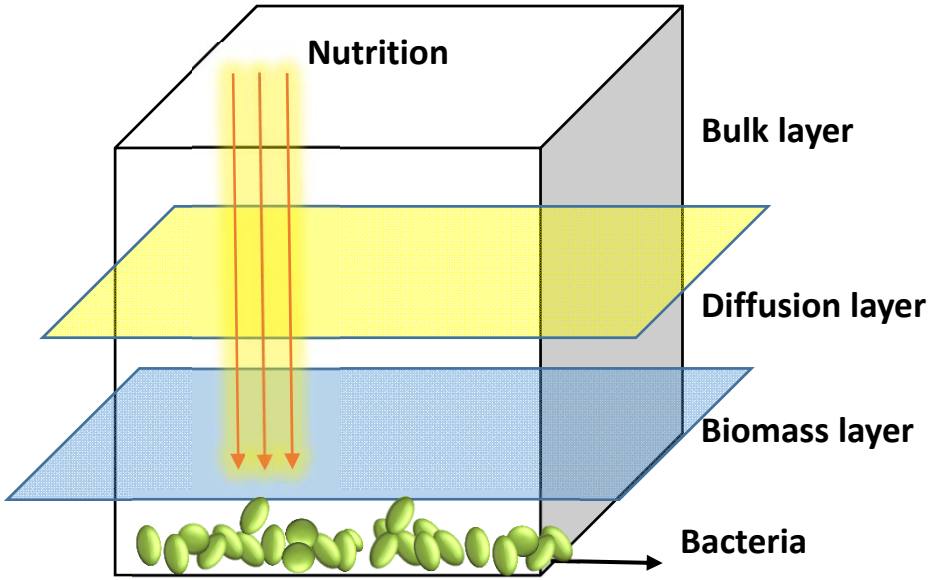
$$\frac{d[EPS]}{dt} = K_{eps}\frac{[C]}{[C]+K_R}$$

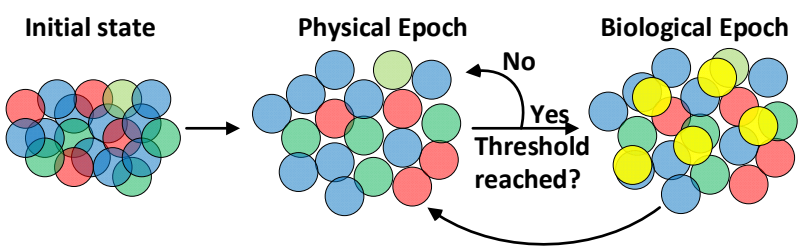


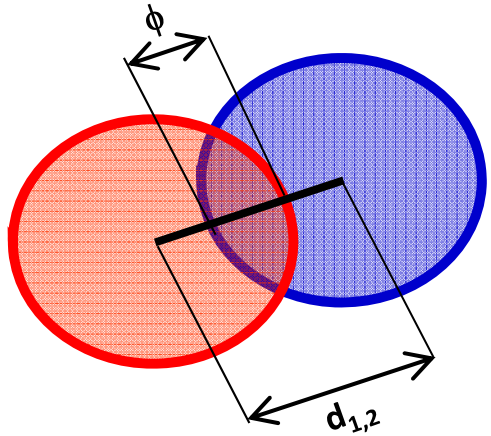
[G. Wei et al., ACM BCB, 2015]

The structure and dynamics of the inter-cellular communication network is heavily influenced by its environment

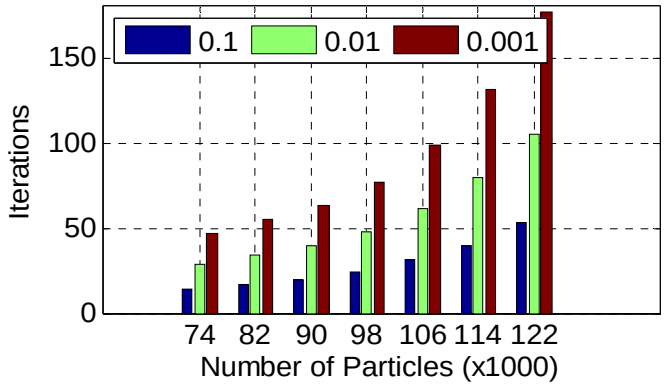
Bacterial population dynamics is a complex problem. Direct wet-lab experimentation is costly and often impractical.





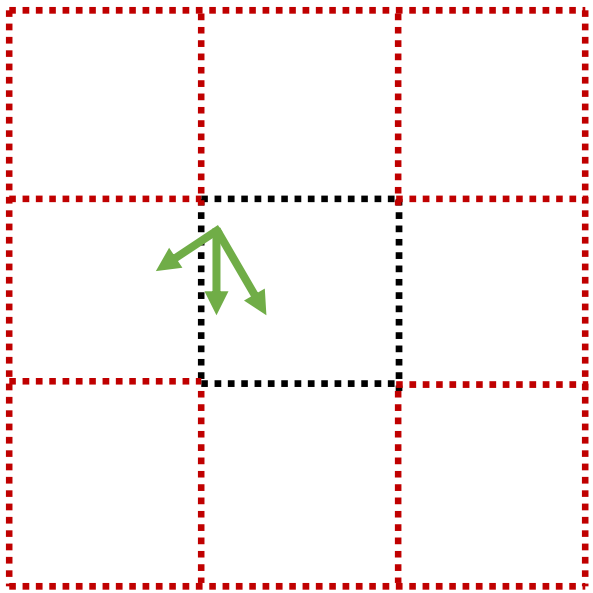


High-Accuracy = More iterations



Experimenting with efficient GPU kernels using NVIDIA Thrust allows to achieve 100x acceleration with GTX980 GPUs.

Parallelize all agents on the GPU. Execute many of these physical interactions concurrently

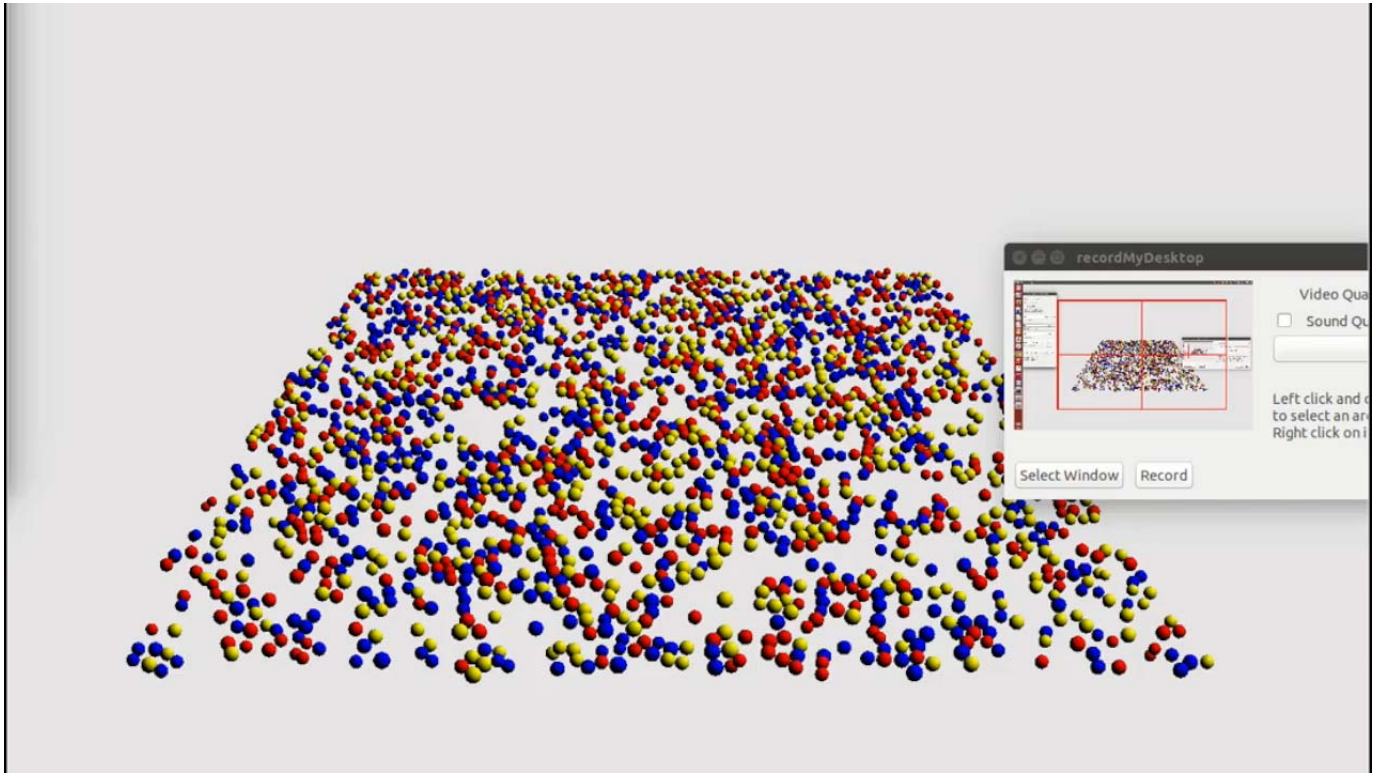


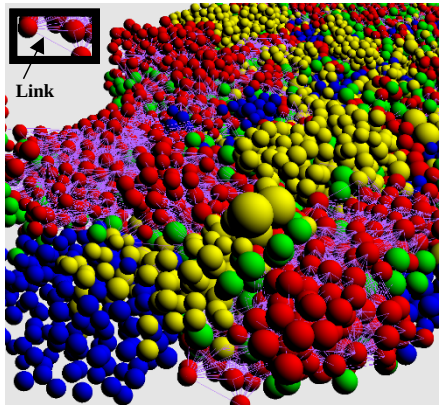
- Arrange the data by physical location
  - thrust::sort_by_key
- For each agent
  - Examine adjacent grid space
    - Utilize __shared__ cuda memory
  - Determine movement vectors between agent and all other cells
  - Move agent with movement vector
- Repeat until system approaches steady state
  - thrust::transform_reduce to get total movement in the system

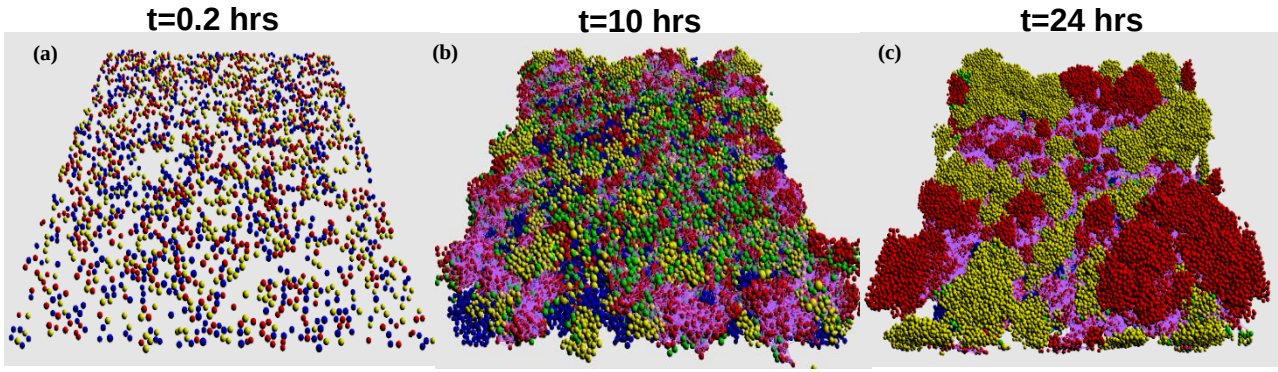
GPUs allow us to maintain high accuracy during the physical interactions within reasonable time constraints (hours vs days)

S4 – 1/3WT, 1/3SB, 1/3SN: Bacteria communication enables social intelligence (“molecular tweeting”)

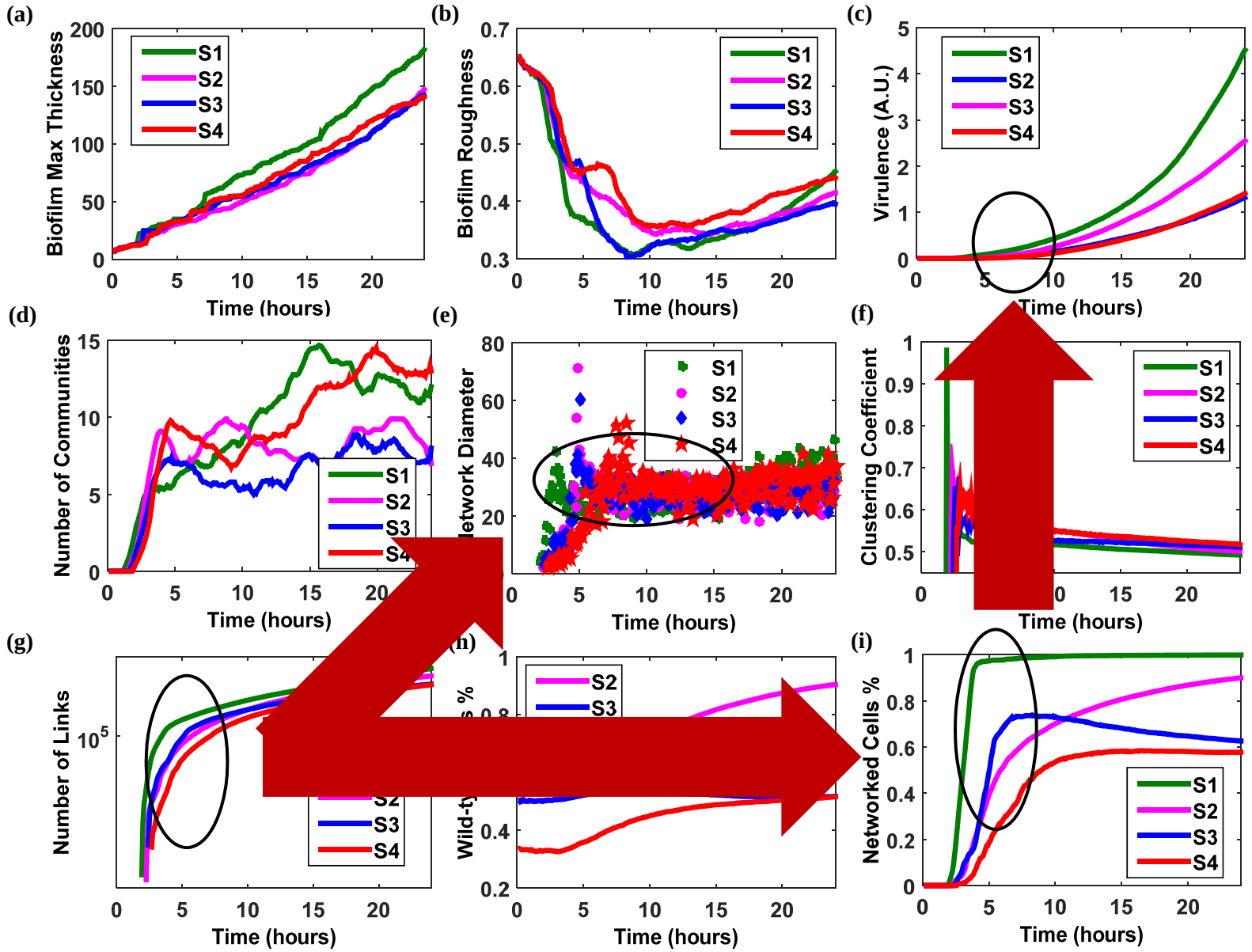
(300x300x500μm^3)
Red: WT
Blue: SB
Yellow: SN
Green: EPS



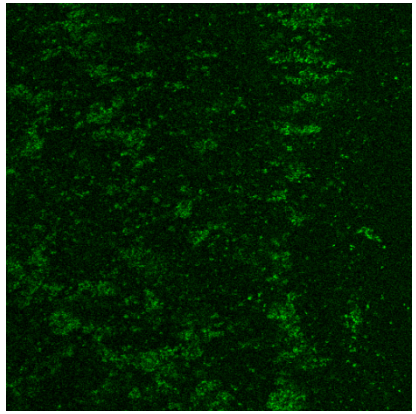




Dynamics of network evolution



Effect of QSIs



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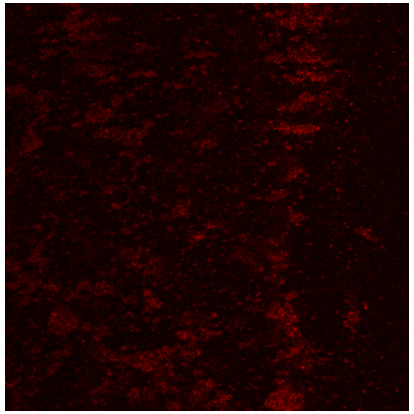

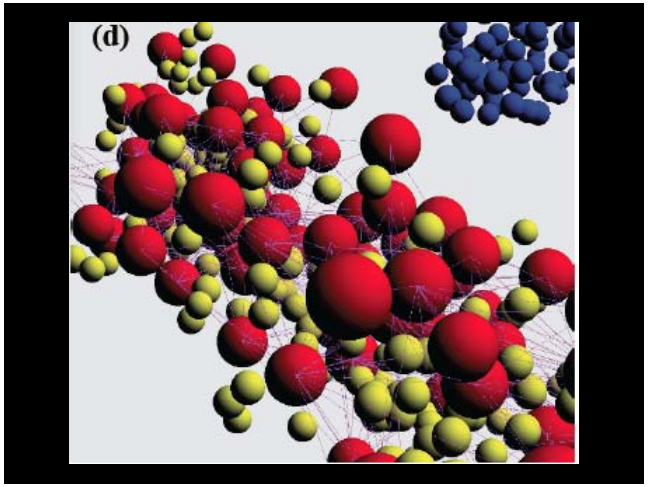

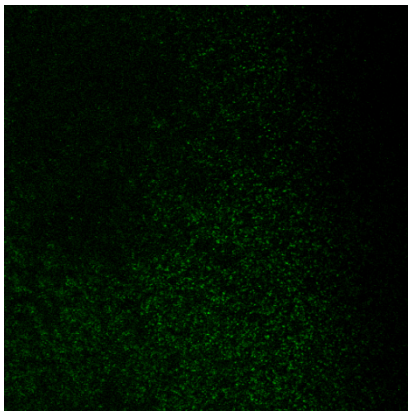

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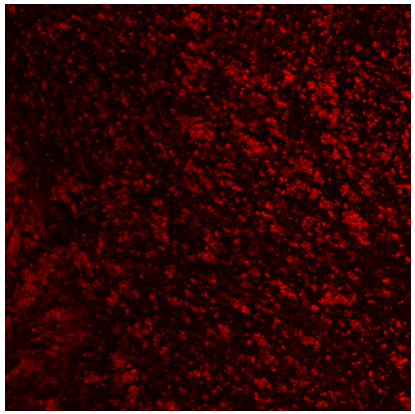

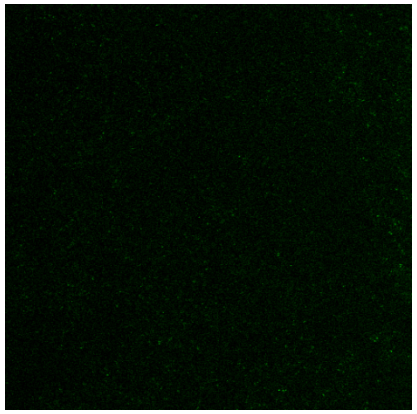

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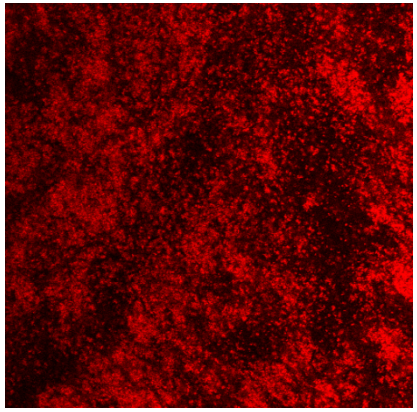
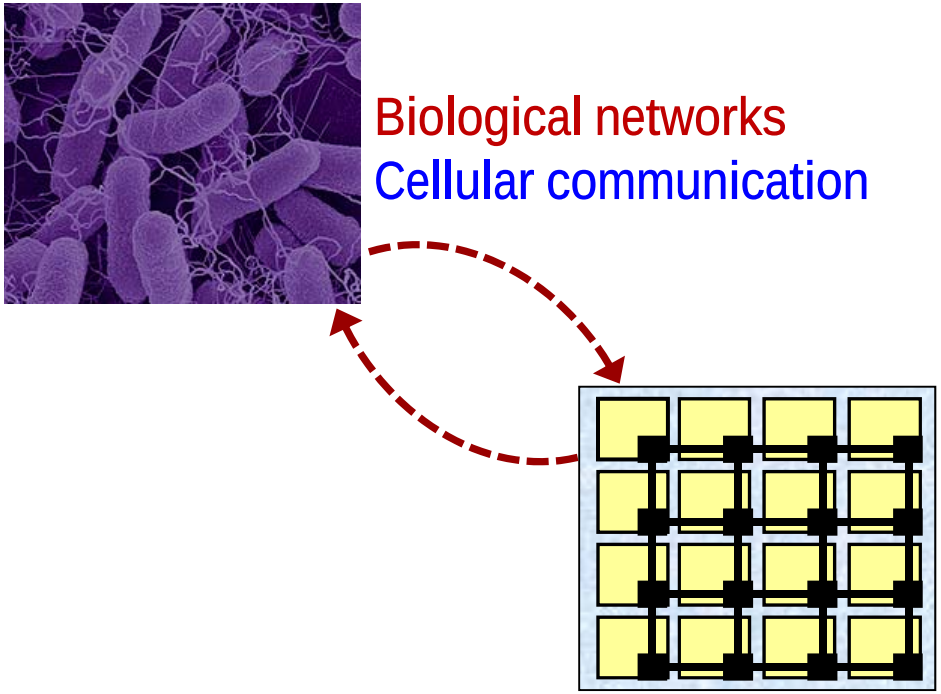


This presentation focuses on the “network” paradigm and ways to engineer communication

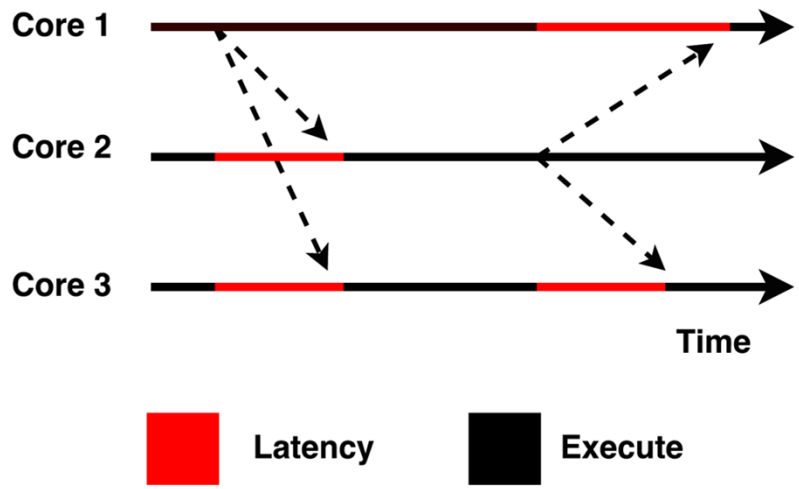


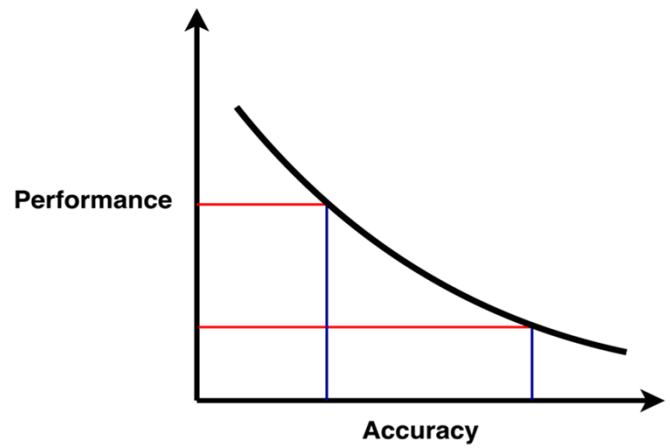
Biological networks
Cellular communication

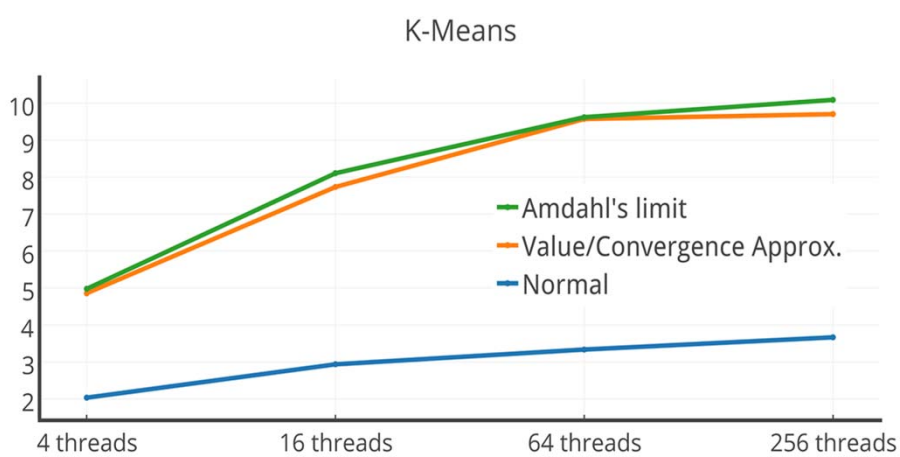
Silicon networks
On-chip communication

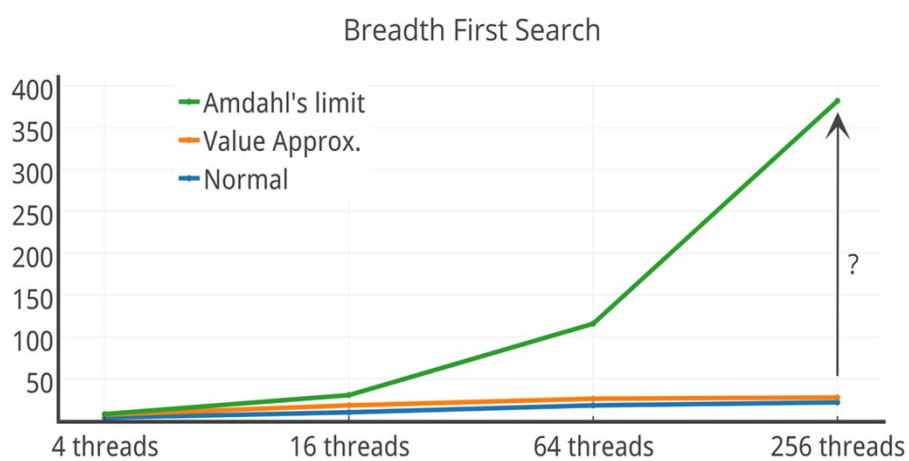
Bacteria form a “social network” to coordinate their behavior, build the biofilm and resist treatment.

Parallel programs enforce correctness through communication (i.e., synch primitives and cache coherence)





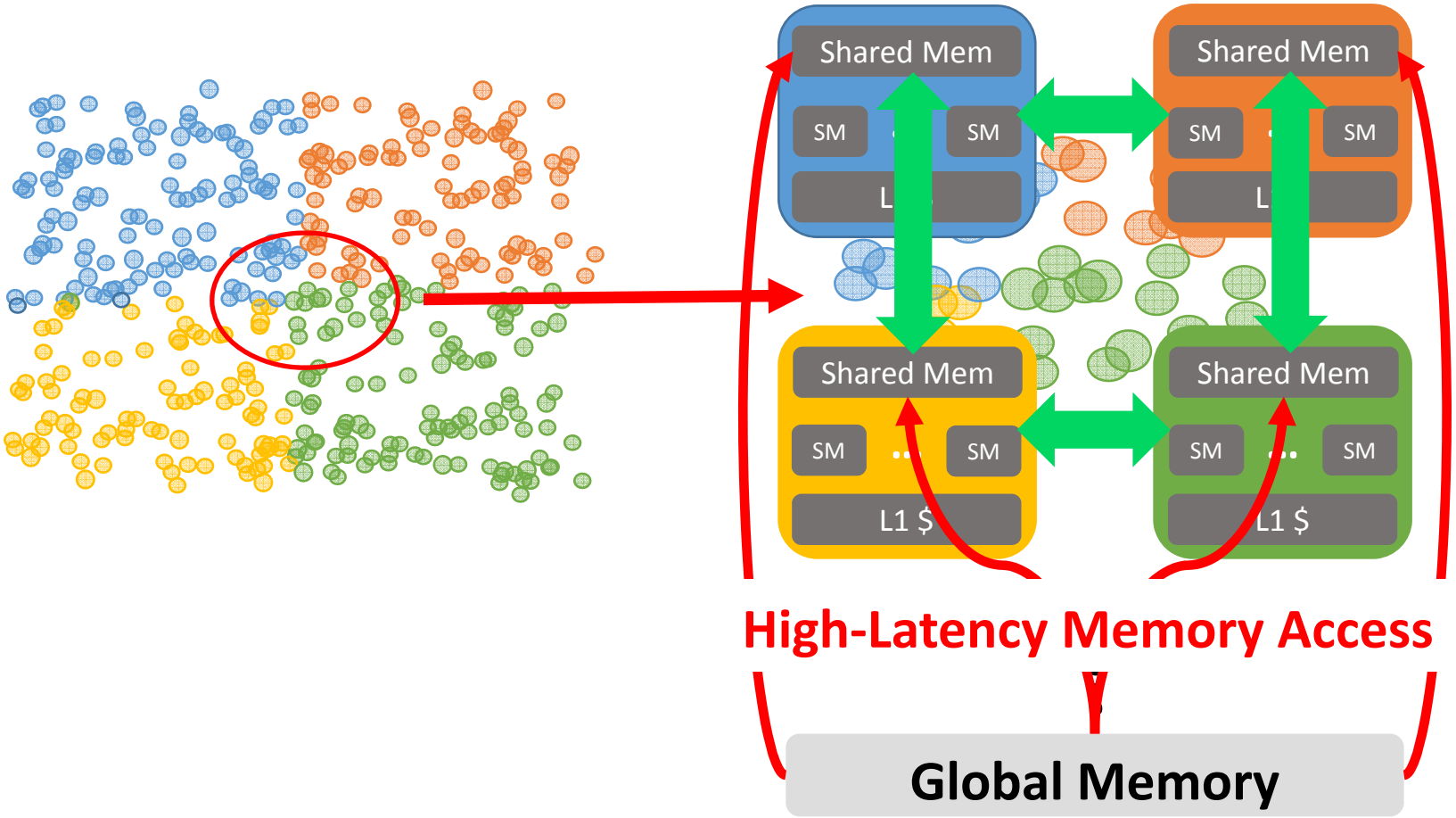




[V. Balaji et al., WAX 2016]

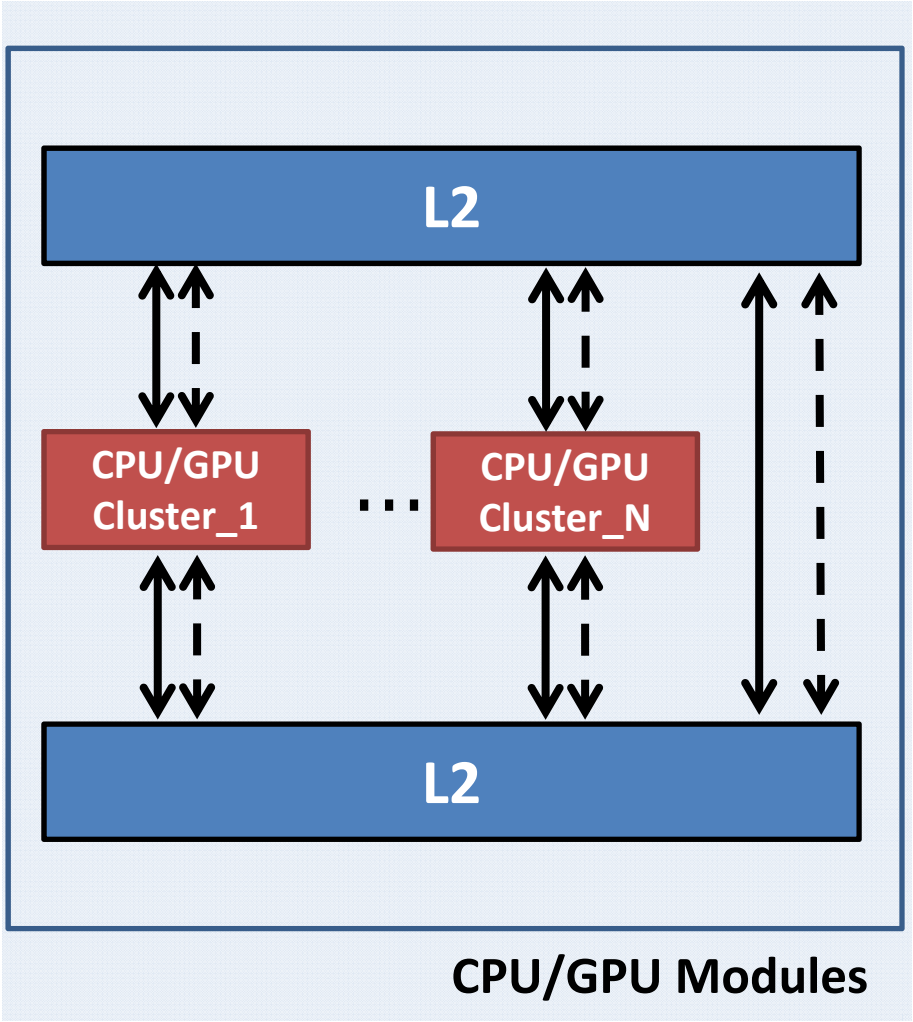
Physical interactions are computationally-intensive and require new approaches to heterogeneous parallel computing.

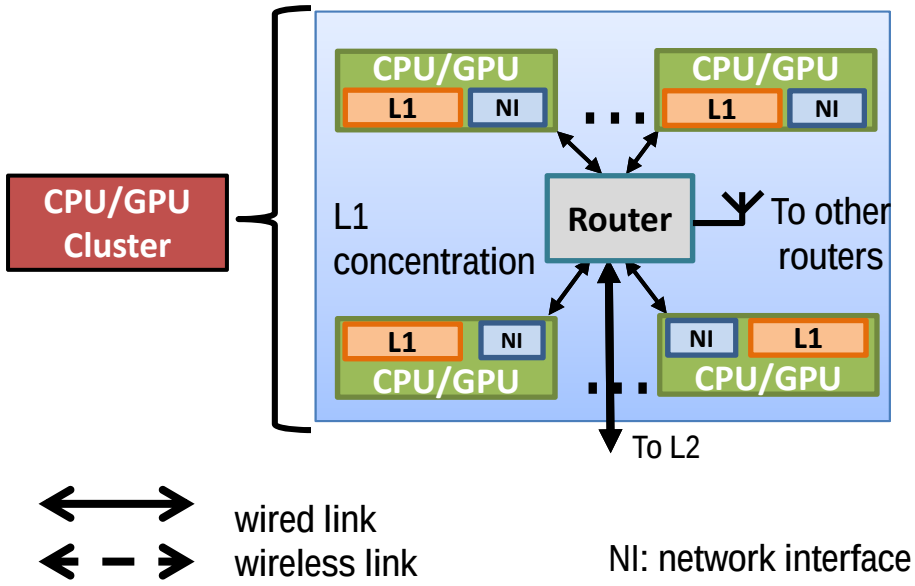
Novel distributed CPU-GPU architecture can take advantage of the data-locality between GPU cores

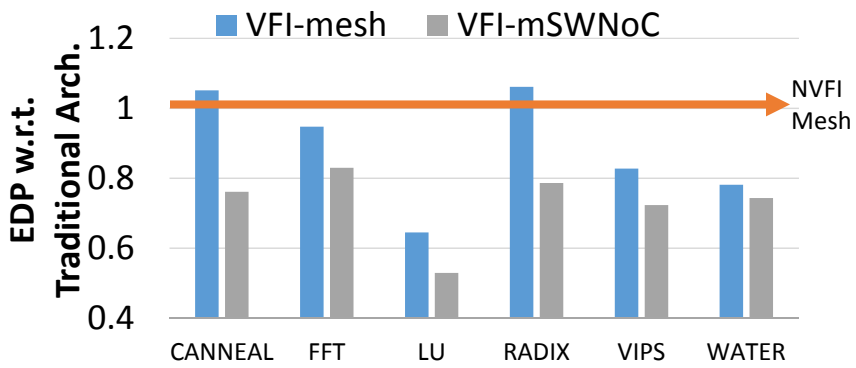


Reduce global access by using low-cost data accesses from adjacent GPUs on an integrated distributed system

How about future architectures? Can we design an on-chip *Computational Microscope*?







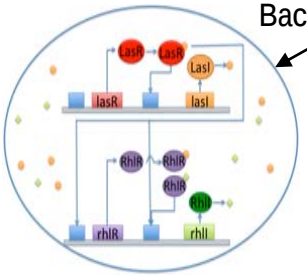
Efficient Wireless NoC Architectures

[R. Kim et al., IEEE TC 2015]

There is a lot more to explore…

Biofilm

Intra-cellular Dynamics

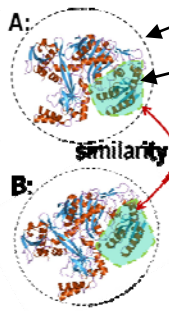


Bacterium (single cell)

Need ~ 10 ODEs per bacterium to characterize intra-cell processes

Microbiome

Molecular Interactions



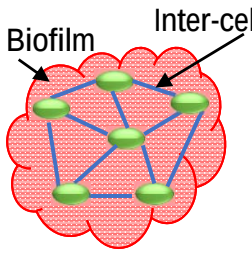
Molecule

Protein

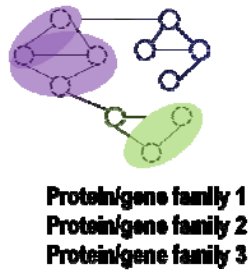
Pairwise molec. comparison ~10^4-10^6 integer updates per pair

A: ...MTVKEQSDIVHGIMSQC...

B: ...MTSKEQS - -VHDIMSQC...



Groups of cells (10^3) ~ 10^4 interaction eqns. (chemical & physical processes)

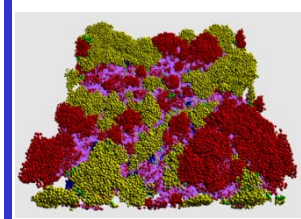


Global molec. interaction

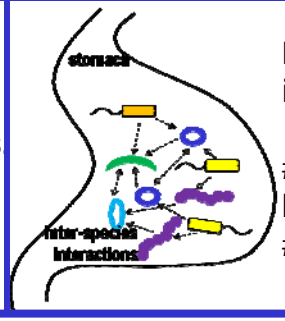
Sequences: ~10^6-10^{10}

Graph edge trav--ersals: ~10^{10}-10^{15}

Population of cells **(10^6-10^9)**



Need ~ 10^7-10^{10} eqns for biofilm dynamics (chemical & physical processes)

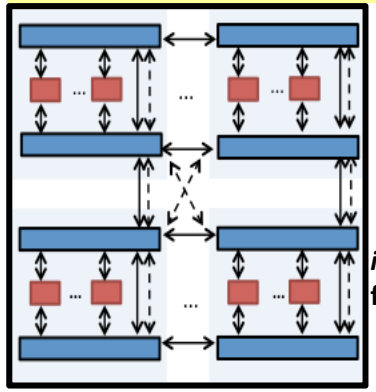


Population-scale interaction

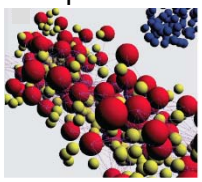
species per micro-biome: ~10^2-10^4

individual cells: ~10^{10}-10^{13}

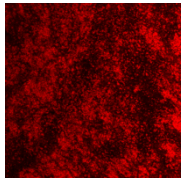
SoC-based Computational Microscope

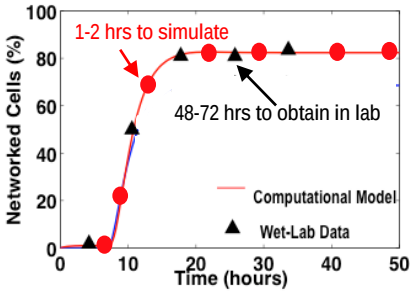


comp. models

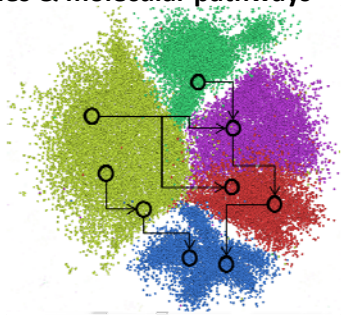


wet lab





in silico **prediction of gene/protein families & molecular pathways**



Summary

- **GPU-based simulation is crucial for obtaining faster than real-time results. Only about 1-2 hrs are needed to simulate a scenario that may take 48-72 hours in the lab**
- **Network metrics correlate well with biofilm metrics and can explain population level behaviors of biological significance. Solid basis for studying socio-microbiology…**
- **Inter-cellular communication is crucial for understanding biological systems (which are or should become of interest to computer engineers…)**

Contributors (in no particular order…)

G. Wei (CMU), I. Cazan (CMU), L. Chieh (CMU), K. Bhardwaj (CMU), C. Walsh (CMU), W. Ehrett (CMU), G. Carvajal (CMU), B. Lucia (CMU), L. Hiller (CMU), M. Sitti (CMU), P. Pande (WSU), A. Kalyanaraman (WSU), R. Kim (WSU).

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