

USC Viterbi

School of Engineering

Queues & Bacteria:

a Tale of Modeling and Experiment

Urbashi Mitra

Ming Hsieh Department of Electrical Engineering

Department of Computer Science

Viterbi School of Engineering

University of Southern California

ubli@usc.edu

Thanks to ONR N00014-15-1-2550,
NSF CPS-1446901, NSF CCF-1410009,
NSF CNS-1213128, AFOSR
FA9550-12-1-0215, NSF CCF-1117896

Bacteria and RF analogies?

for their discoveries concerning genetic control of enzyme and virus synthesis

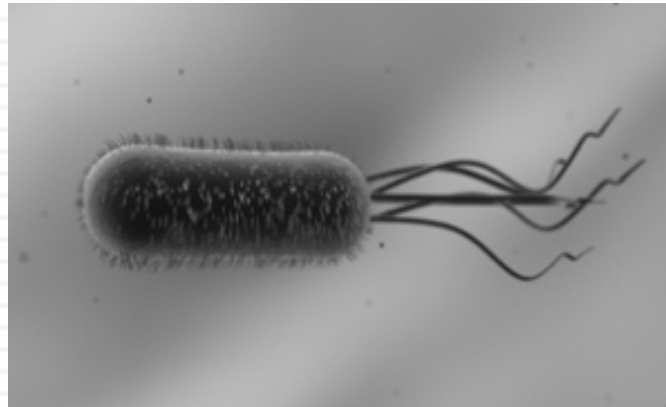
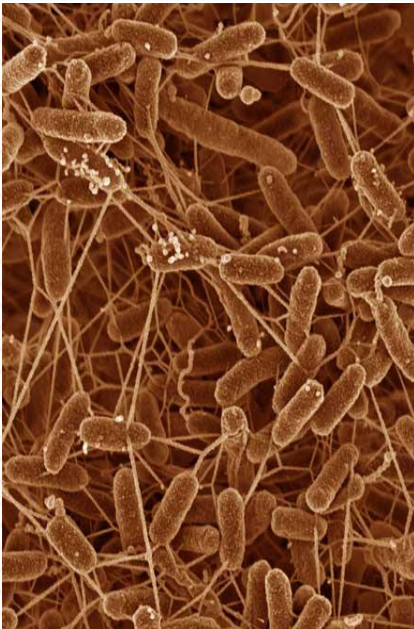
FRANÇOIS JACOB

Genetics of the bacterial cell

Nobel Lecture, December 11, 1965

If I find myself here today, sharing with Andre Lwoff and Jacques Monod this very great honor which is being bestowed upon us, it is undoubtedly because, when I entered research in 1950, I was fortunate enough to arrive at the right place at the right time. At the right place, because there, in the attics of the Pasteur Institute, a new discipline was emerging in an atmosphere of enthusiasm, lucid criticism, nonconformism, and friendship. At the right time, because then biology was bubbling with activity, changing its ways of thinking, discovering in microorganisms a new and simple material, and drawing closer to physics and chemistry. A rare moment, in which ignorance could become a virtue.

Bacterial Communities

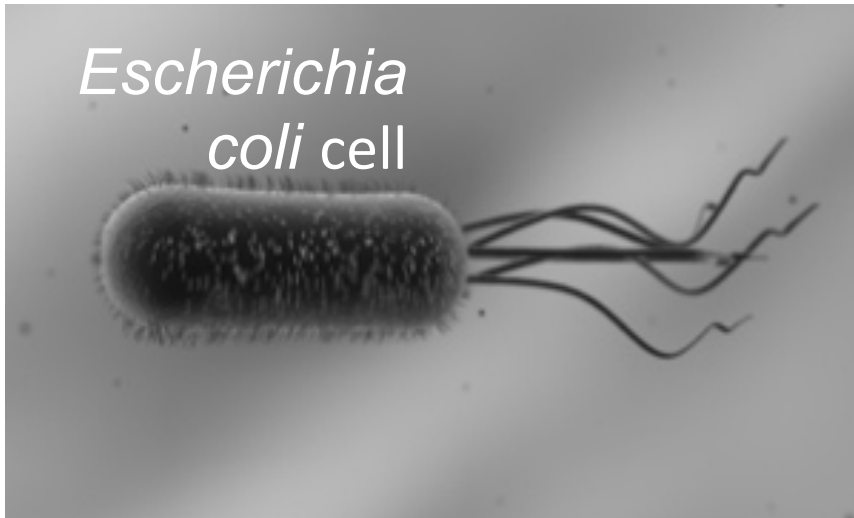


Analyze electron transport in bacterial cables
Develop models for quorum sensing

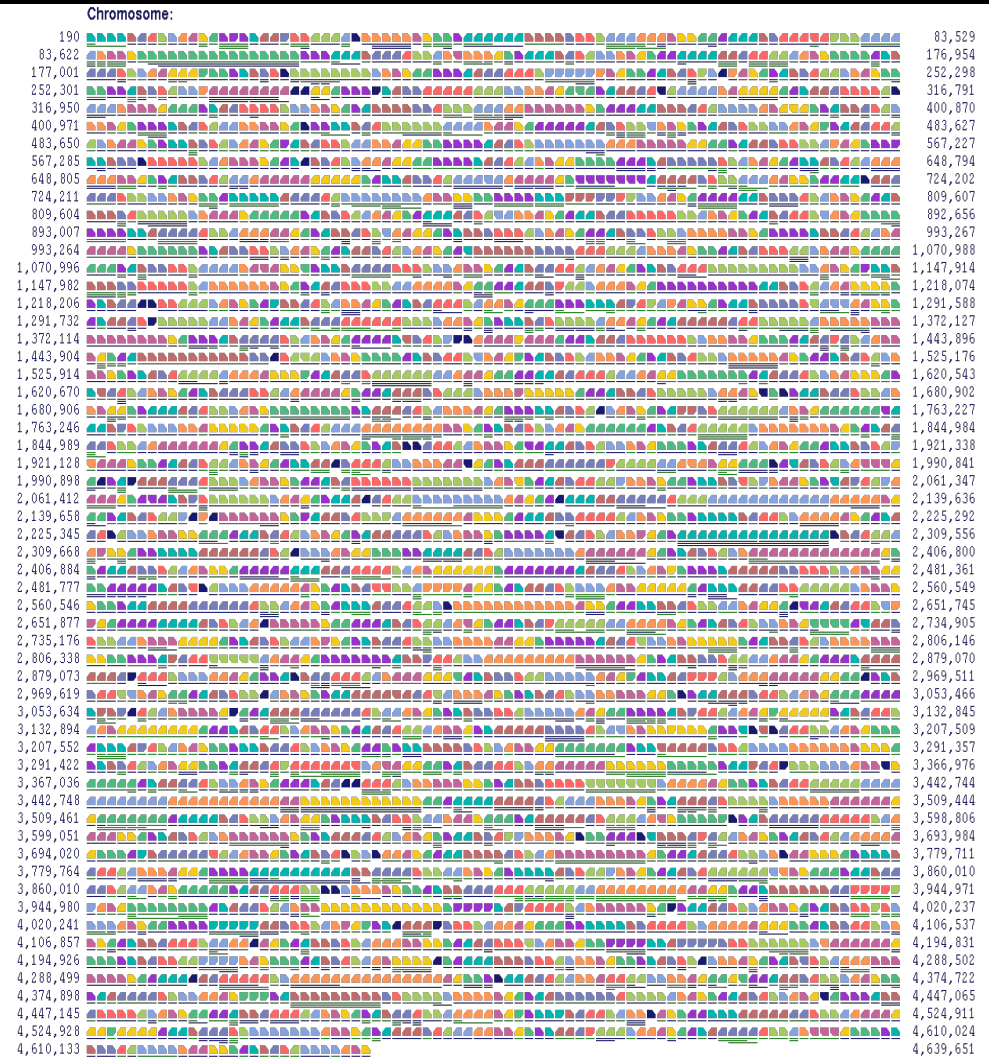
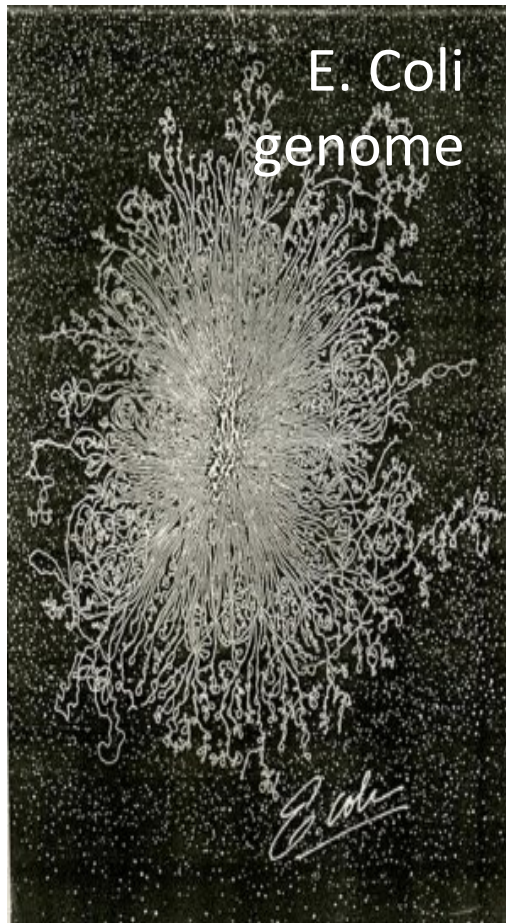
Why bacteria?

- Unicellular organisms
- One of the earliest forms of life (3-4 billion years ago)
- Aggregate biomass larger than all other plants/animals combined
- Relevant for bioremediation, plant growth, human and animal digestion, global elemental cycles including the carbon-cycle, and water treatment

Escherichia coli cell



Not as simple as they seem..



What is communication?

The fundamental problem of communication is that of reproducing at one point either exactly or approximately a message selected at another point.

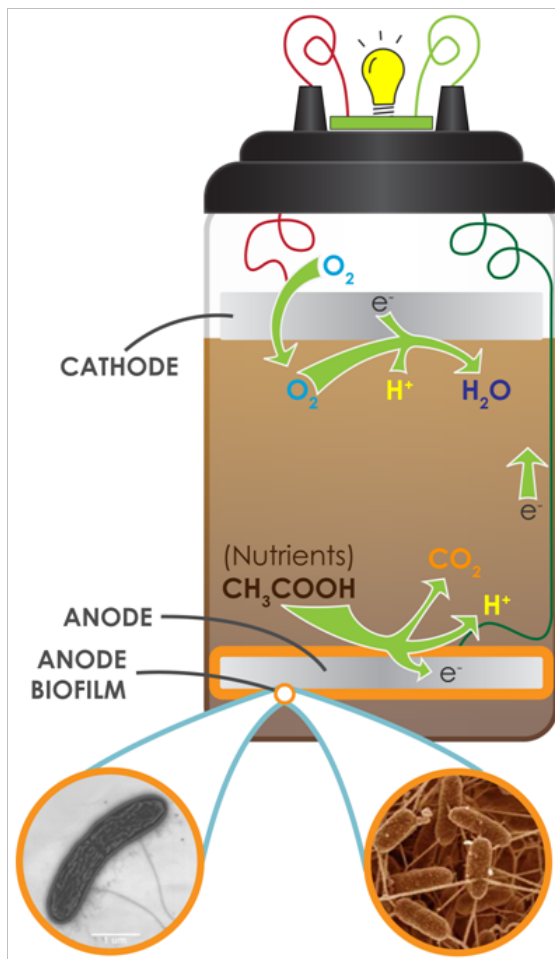
Claude Shannon, A Mathematical Theory of Communication, 1948



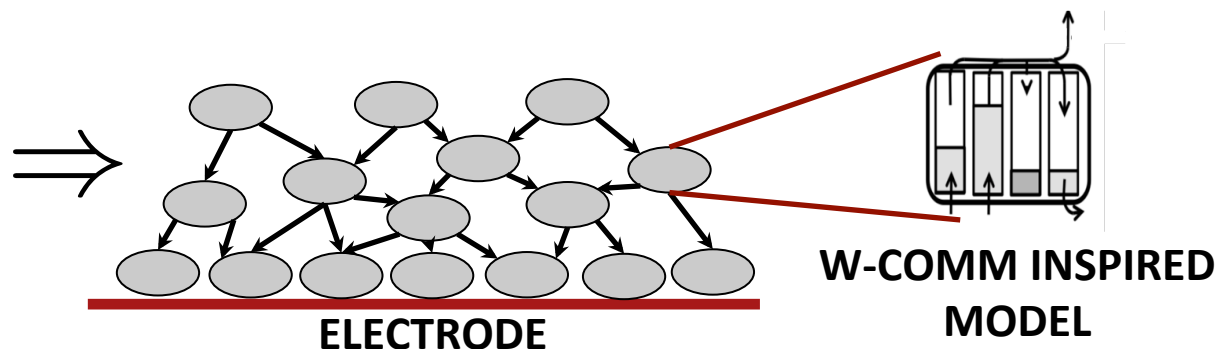
What is capacity for bacteria?

13

MICROBIAL FUEL CELL (MFC)



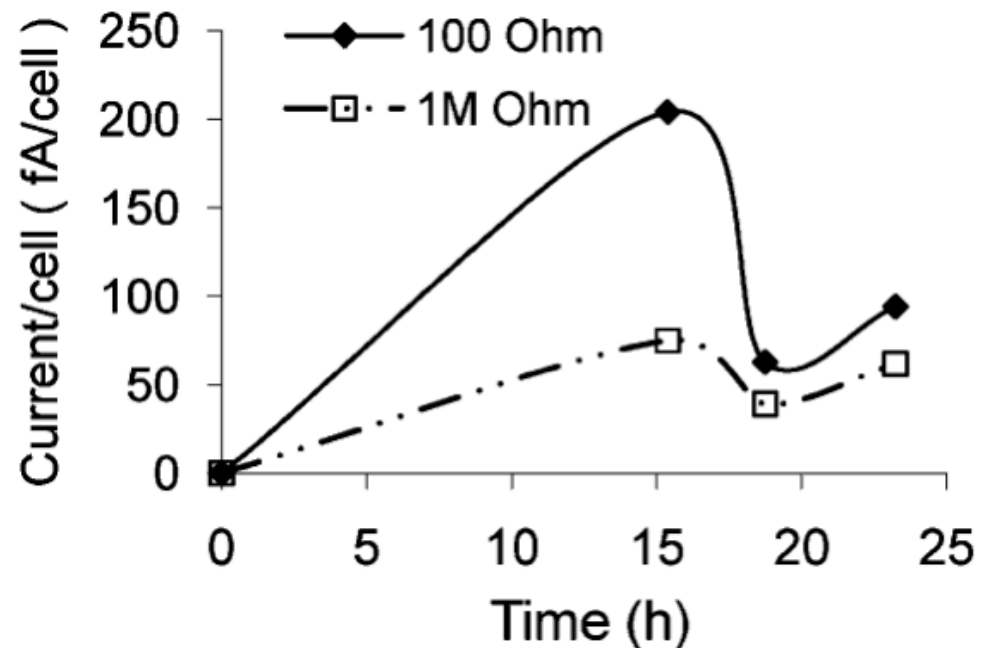
- ❑ Bacteria as “devices” that sense the environment, estimate, react
- ❑ **Idea:** tools from information theory and communications to model & predict bacterial networks:
 - Interactions, dynamics, formation
 - Do bacteria realize *optimal* control strategies?
 - *E.g.*: optimize MFC growth



How to achieve the sweet spot?

14

- ❑ Microbes on a 2D electrode
- ❑ Population grows as a function of time
- ❑ What happens at 15h?
- ❑ How are bacteria interacting?
- ❑ What is electron transport?

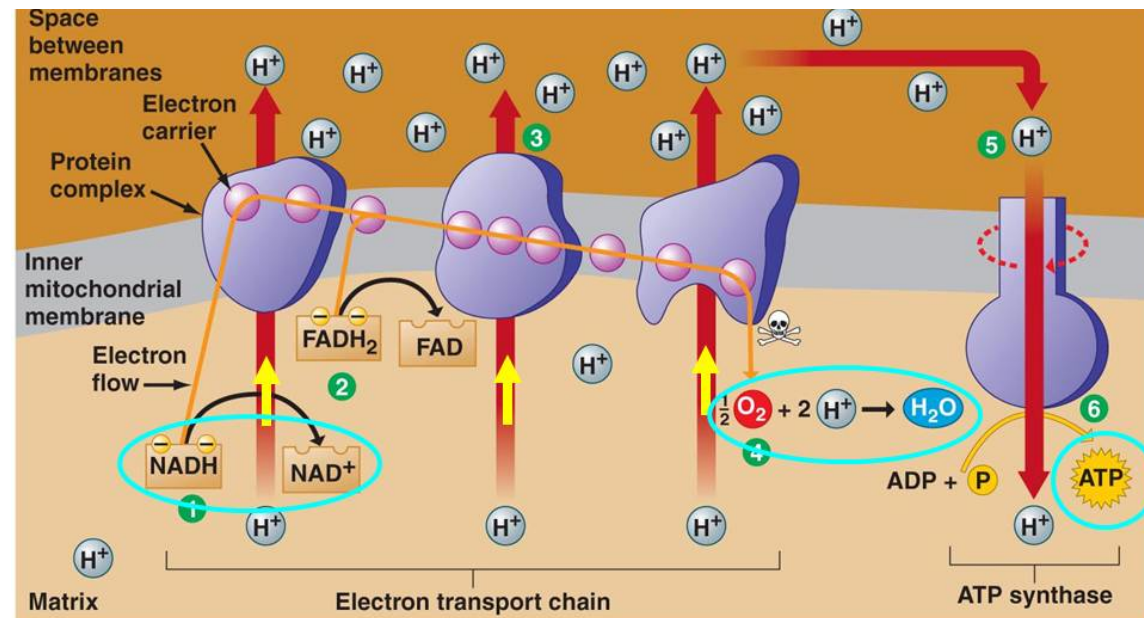


From Ken Nealson group, USC, Earth Sciences

e^- transport chain (ETC)

15

- ❑ Fundamental (and well known) process in cellular respiration



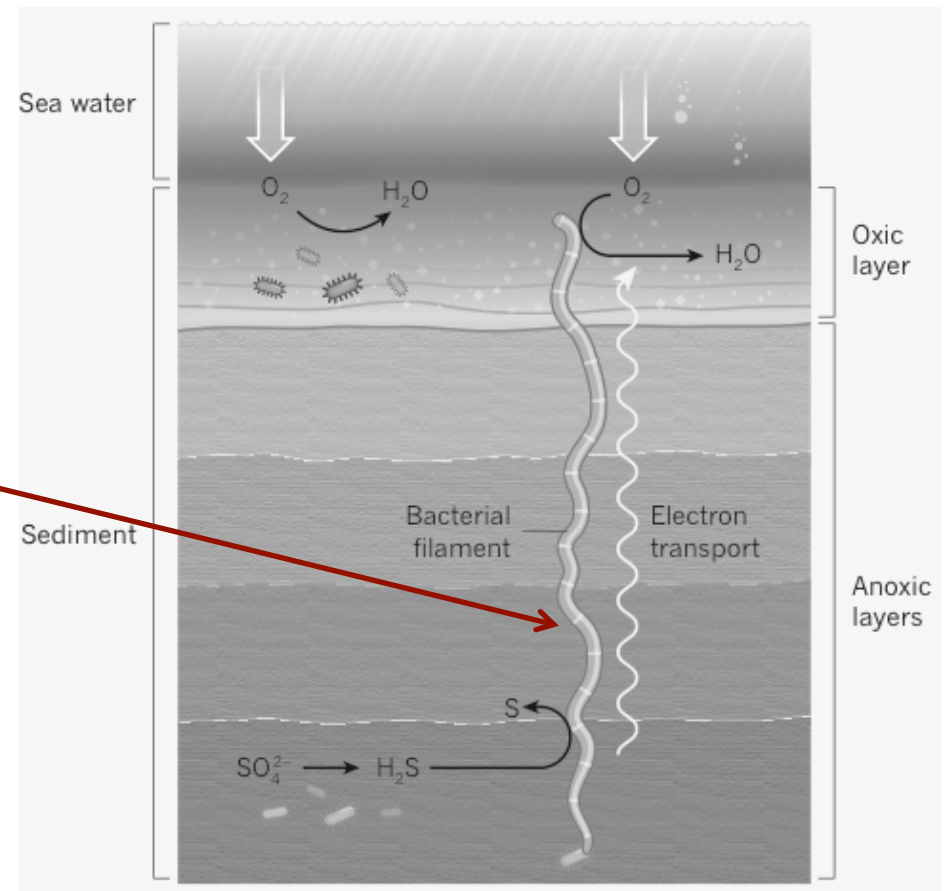
- ❑ e^- flow creates proton gradient to pump synthesis of Adenosine triphosphate (ATP, cell's energy currency)
- ❑ **Cells need a constant electron flow to produce energy (ATP)**

e^- transport

16

- ❑ e^- transport over cm-lengths
 - bacterial nanowires, biofilms, bacterial cables

multi-hop
communication
“network” from
 e^- donor (ED) to
 e^- acceptor (EA)

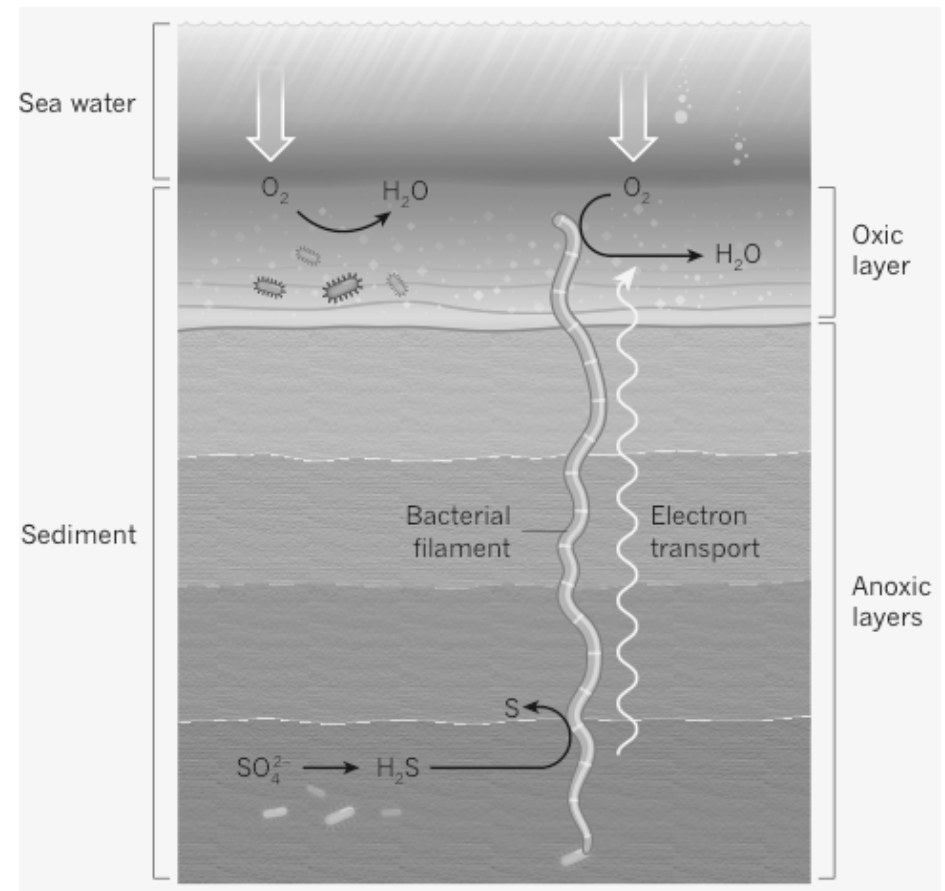


Bacterial cable (1D), Source: [Reguera, Nature'12]

e^- transport

17

- ❑ e^- transport over cm-lengths
 - bacterial nanowires, biofilms, bacterial cables
- ❑ *Use communication strategies to optimize e^- transfer*
- ❑ *Capacity as proxy for maximal e^- transfer*
- ❑ New dimension (& new models) *information-energy coupling*
 - Capacity \neq bottleneck, vs wireless communications
 - Instead, local interactions & energy coupling, cells may die



Bacterial cable (1D), Source: [Reguera, Nature '12]

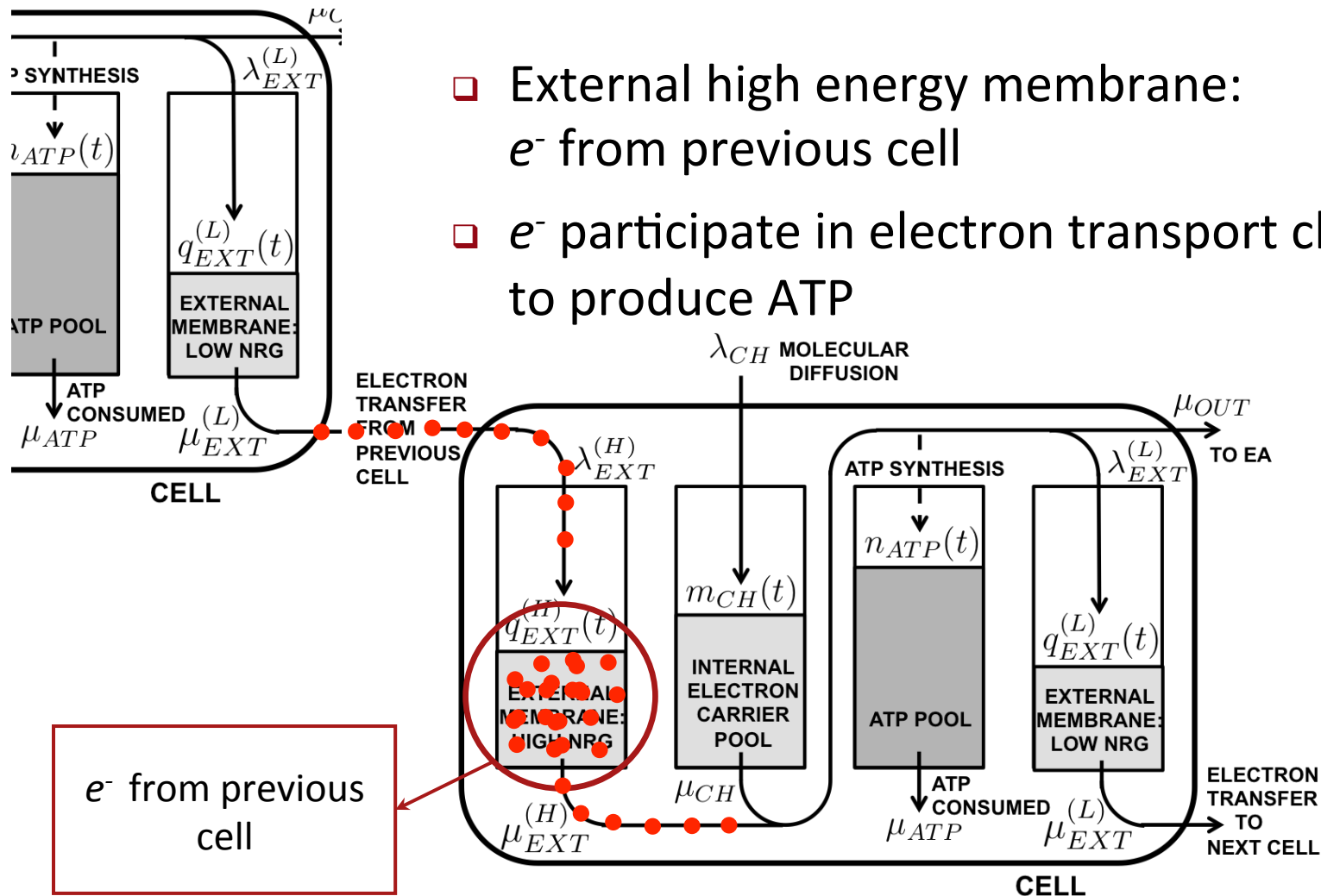
Stochastic queuing model

- ❑ **BEFORE:** modeling via deterministic ODE/PDE
 - *E.g., [Klapper&Dockery,'10], [Picioreanua et al.,'07], [Marcus et al.,'07]*
 - Detailed master equations & chemical reactions → huge complexity

- ❑ **NOW:** abstraction → stochastic queuing model inspired by W-COM
 - Chemical/electron concentrations → *queues*
 - Small-scale, local interactions as nuisances → *stochastic model*
 - *Still high complexity, but tools for complexity reduction from W-COM can be exploited*

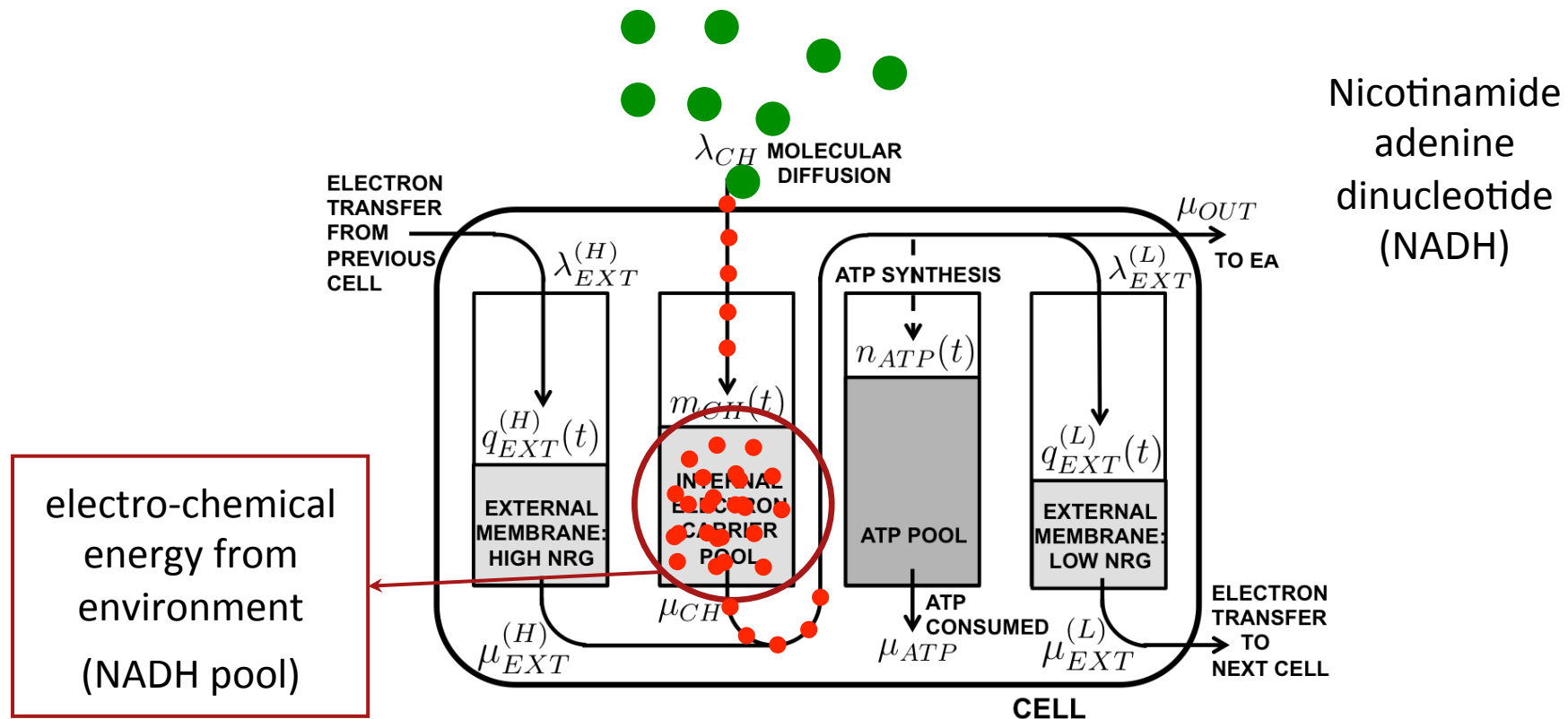
Stochastic queuing model

20



Stochastic queuing model

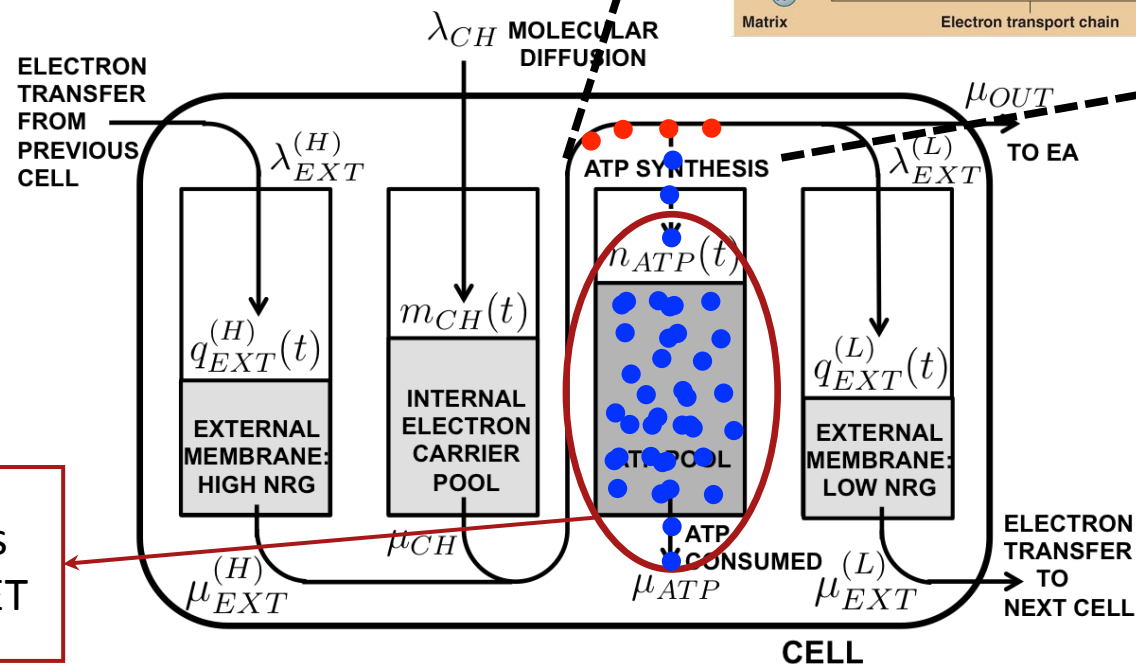
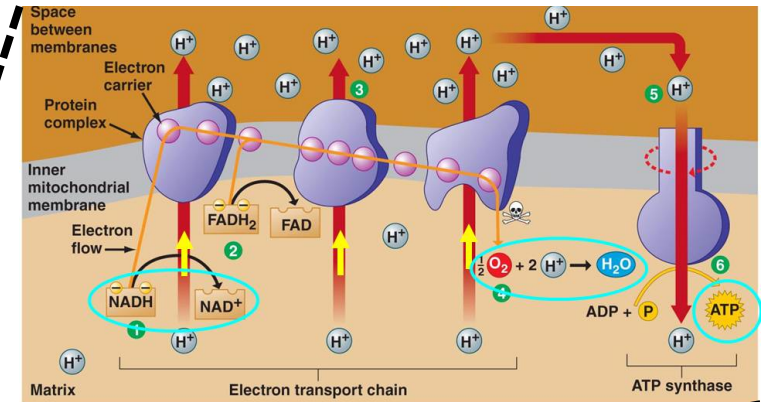
- Internal e^- carrier pool: e^- from external ED
- e^- participate in electron transport chain to produce ATP



Stochastic queuing model

22

- ATP pool: ATP molecules produced via e^- transport
- ATP consumed to sustain cell

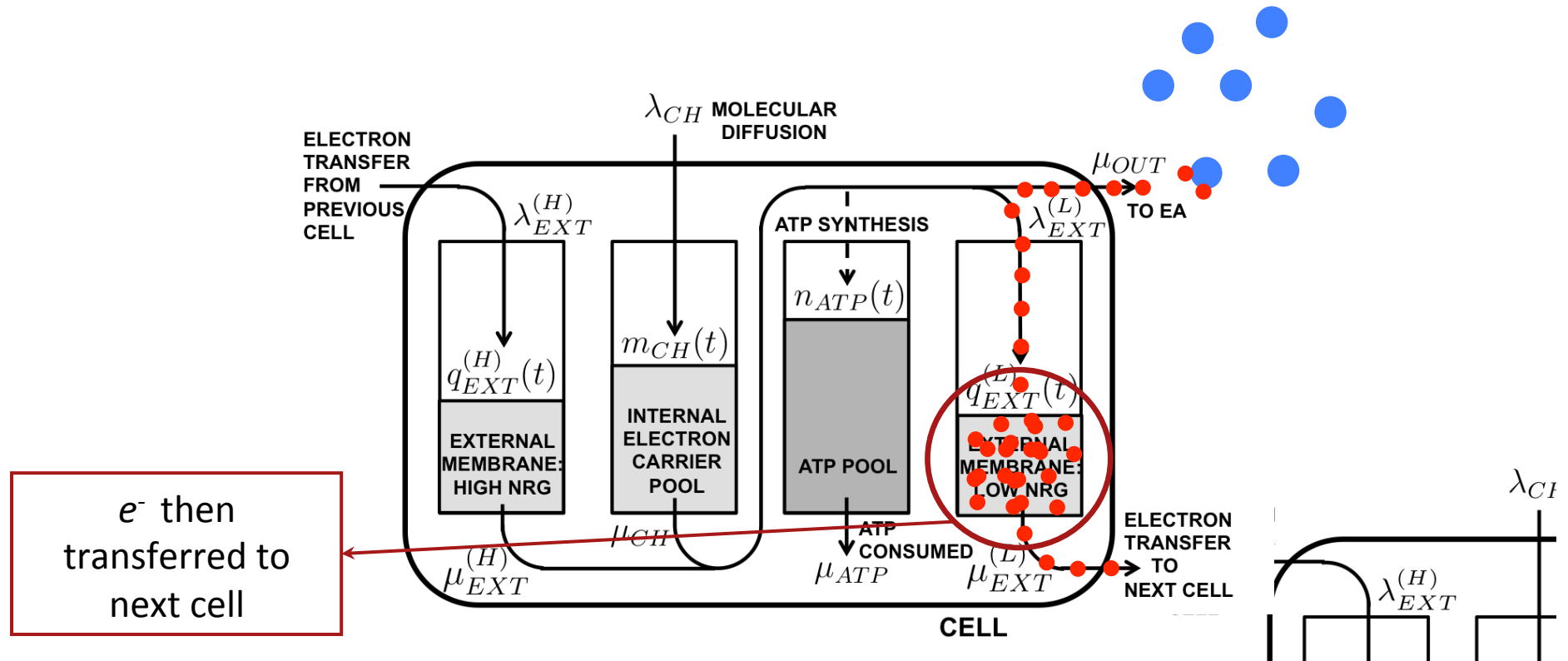


ATP molecules generated via ET

Stochastic queuing model

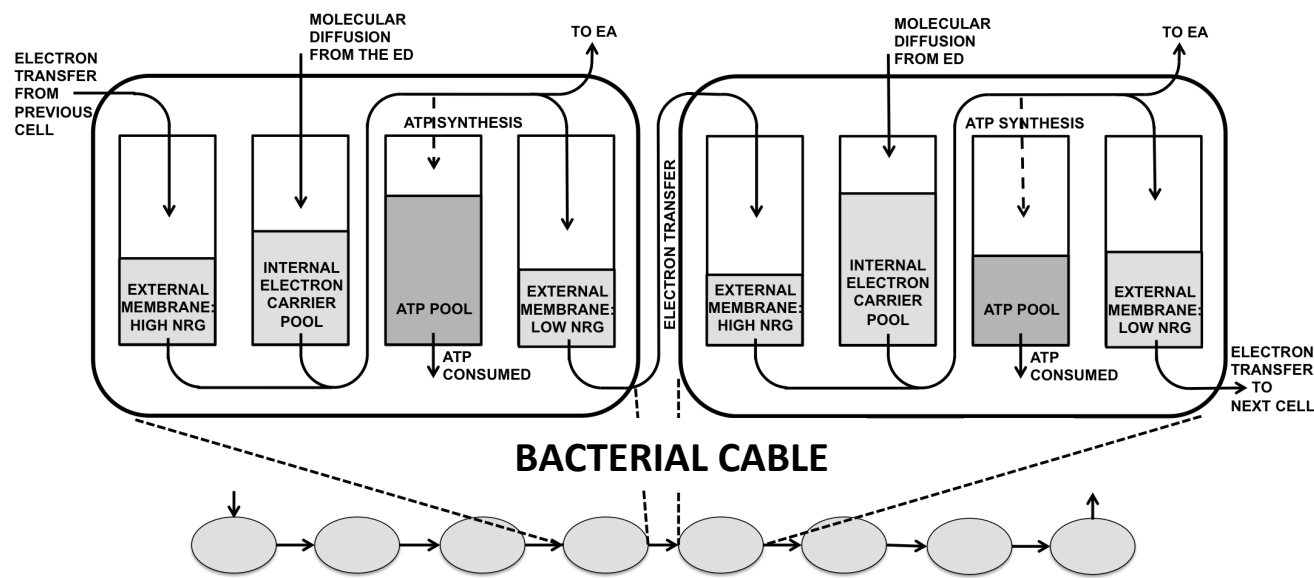
23

- External low energy membrane carries e^- after ETC. 2 paths:
 - Reduction to EA
 - e^- transfer to next cell or electrode



Stochastic queuing model

- ❑ Molecular diffusion & e^- transfer coexist
- ❑ ATP level = energetic state of the cell
 - **Energy dimension**: ATP low \rightarrow cell may die
 - **Information dimension**: ATP level too high \rightarrow clogging



Isolated cell: experimental validation

- ❑ Setup [Ozalp&al., Journal of Biological Chemistry, '10]
 - Suspension of yeast *Saccharomyces cerevisiae* (isolated cells)
 - ED added abruptly to starved cells
 - NADH (electron-carrier pool) and ATP levels measured
- ❑ Use experimental data to fit parameters

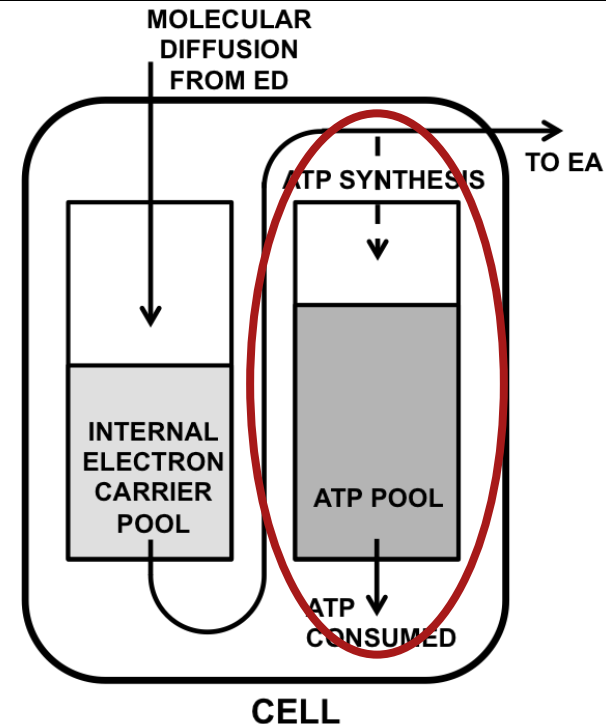
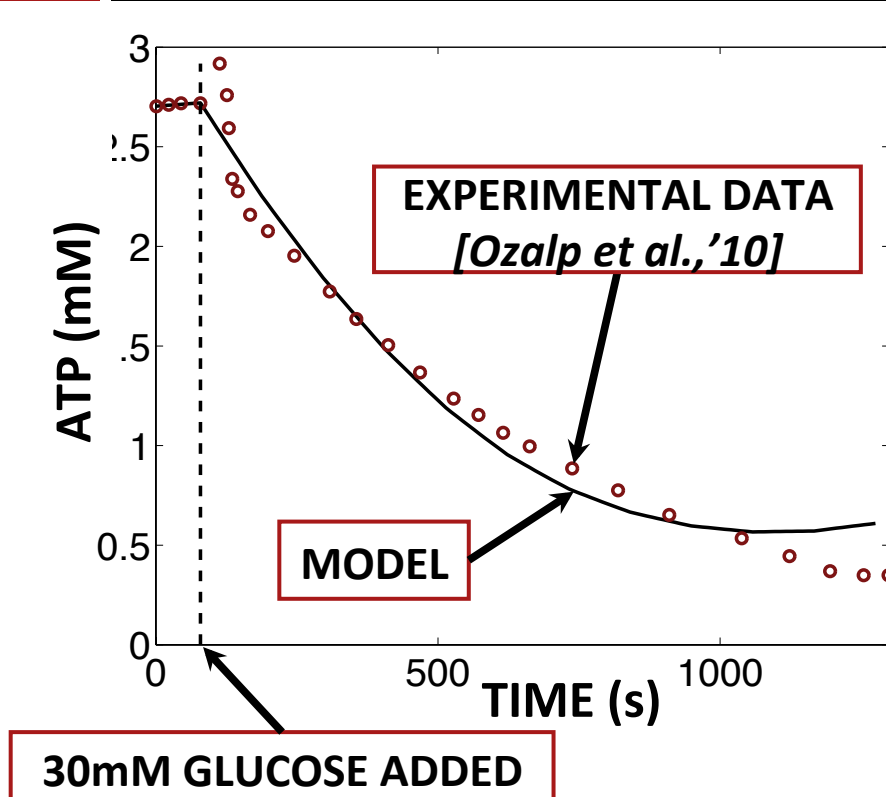
$$(\hat{\mathbf{x}}, \hat{\boldsymbol{\pi}}_0) = \arg \min_{\mathbf{x} \geq 0, \boldsymbol{\pi}_0 \in \mathcal{P}} \frac{1}{2} \sum_{k=0}^N \left\| \mathbf{y}_k - \boldsymbol{\pi}_0^T \prod_{j=1}^k \mathbf{P}_{\Delta}(\mathbf{x}, \mathbf{s}_{E,j-1})^{n_j - n_{j-1}} \mathbf{Z} \right\|_F^2$$

Measured ATP/NADH
(average over population)

State distribution

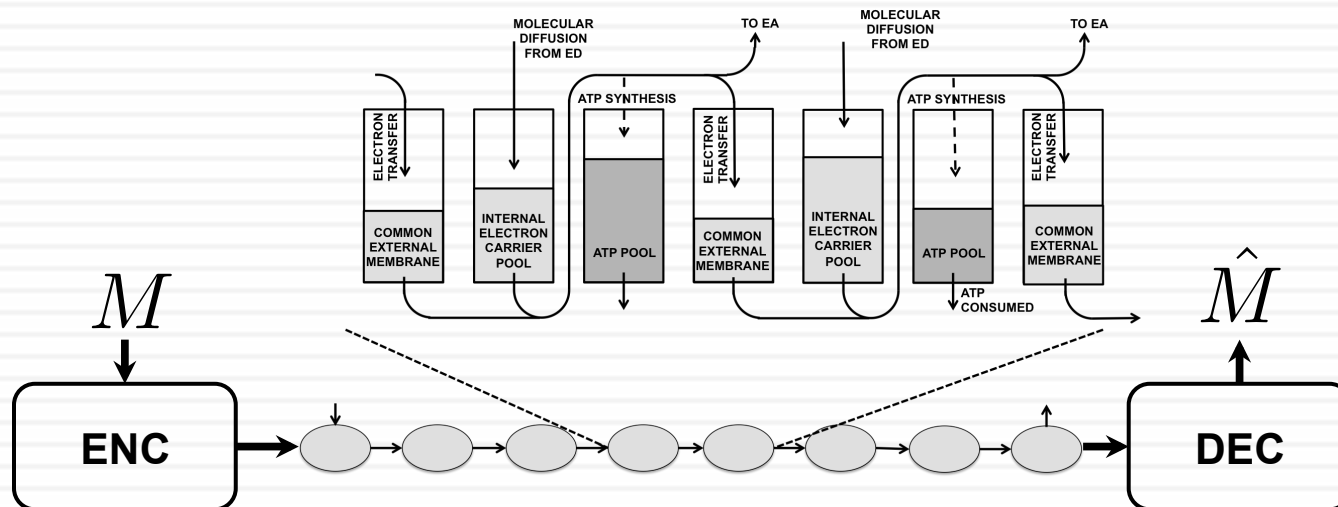
Fixed matrix:
State indicator

Isolated cell: experimental validation



- Good fitting of experimental curve and model
- Stochastic queuing model simpler than detailed “physical” models, but captures salient features

Information theoretic aspects



Multihop Capacity

- Cascade of links
 - Persistently studied
- Via cut-set bounds can show that capacity is that of worst-case link

$$C = \min_j C_j$$

- Achieved by decode-and-forward



- What happens in biological systems?
 - Communication over channels with state!
 - There is coupling between the links

USC
Viterbi

The diagram illustrates the proposed channel state estimation framework. It consists of three main components: an Encoder (ENC), a Channel, and a Decoder (DEC).

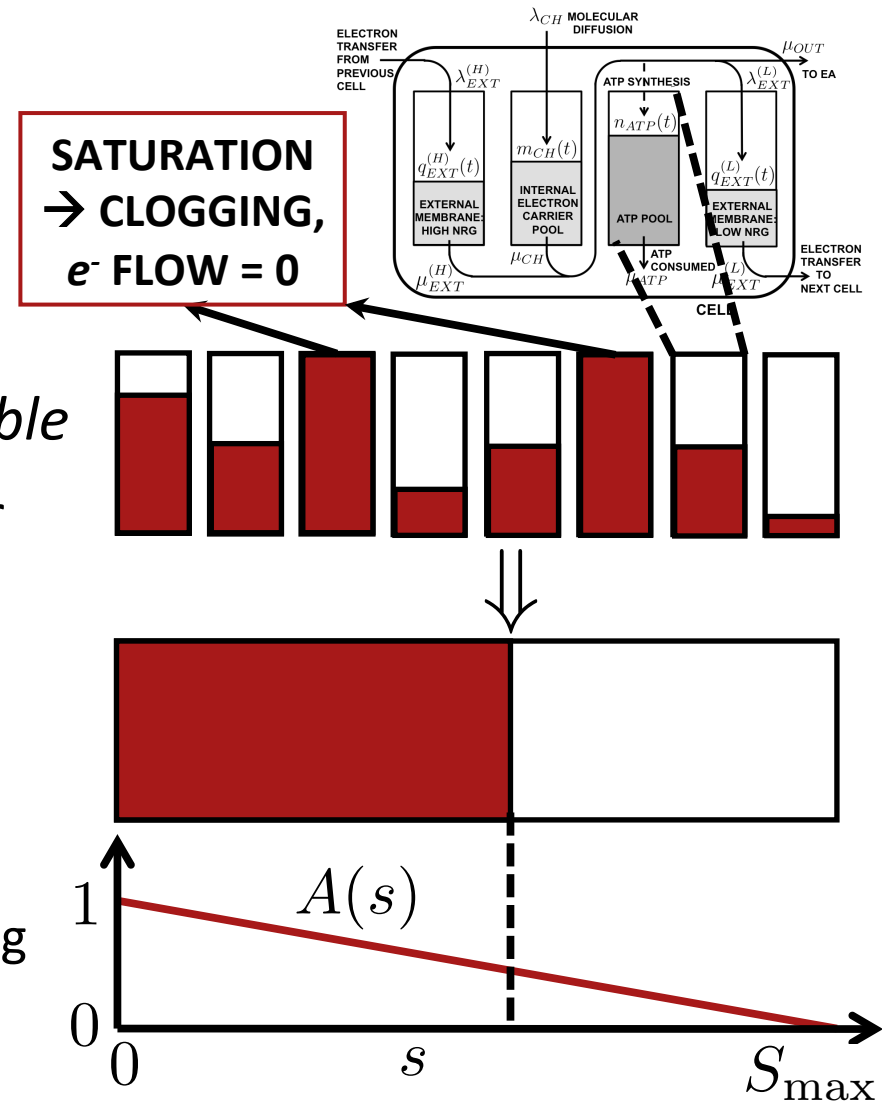
- Encoder (ENC):** Receives an input e^- intensity $\lambda(t) \in [\lambda_{\min}, \lambda_{\max}]$ and a message M . It outputs a signal to the Channel.
- Channel:** Represented by a sequence of states $S(t)$ and a physical channel model. The states $S(t)$ are shown as a sequence of boxes, each containing a bar chart representing the distribution of e^- intensity. The physical channel model is shown as a sequence of nodes connected by arrows.
- Decoder (DEC):** Receives the output signal $Y(t)$ from the Channel and provides Channel State Information (CSI) back to the Encoder. The output of the Decoder is the estimated message \hat{M} .

- ❑ **Challenge:** signal is coupled with energetic state of cells (channel state)
- ❑ ATP level = energetic state of the cell
 - **Energy dimension:** ATP low → cell may die
 - **Information dimension:** ATP high → *clogging, e^- transfer stopped*

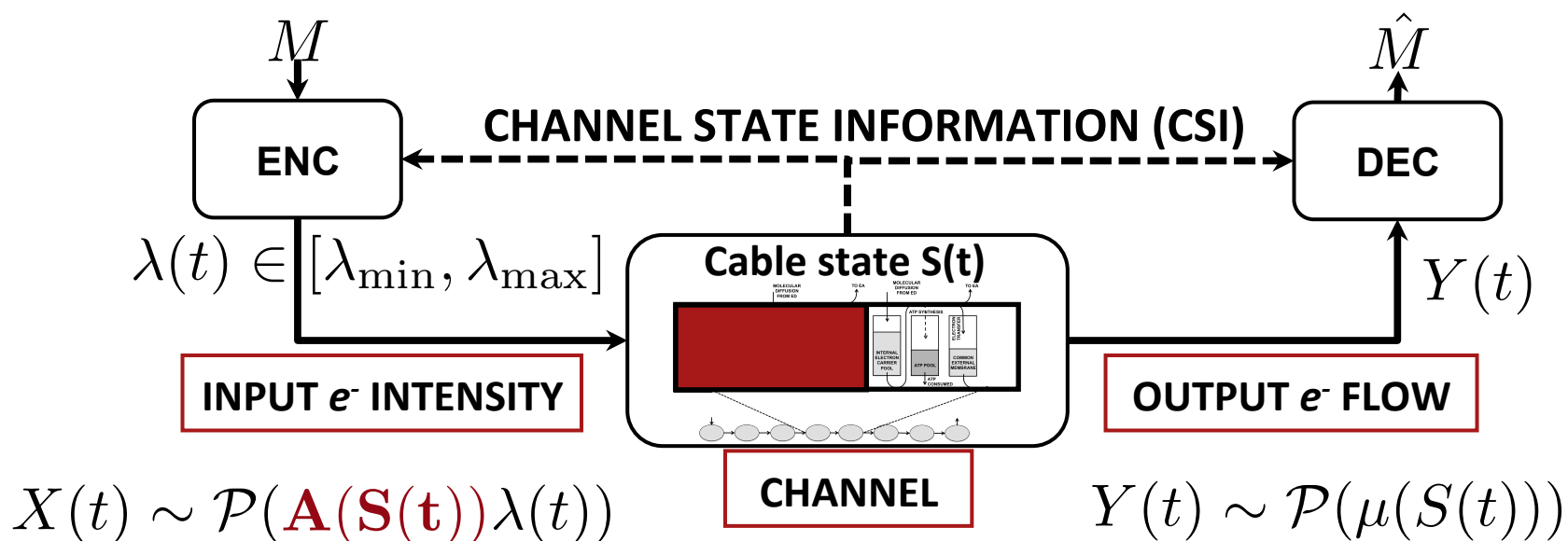
Simplified cable model

32

- ❑ $S(t)$ = Interconnection of *all* cells' states
- ❑ **Simplified model:** $S(t) = \# e^-$ in the cable
 - **Local** interactions averaged out over spatial dimension
 - **Global** effects captured by **clogging state** $A(s)$
 - $S(t)$ small \rightarrow cells "starved"
 - $S(t)$ large \rightarrow ATP saturation, clogging
 - $A(s)$ = ratio of e^- accepted



Communication over Poisson channels with states

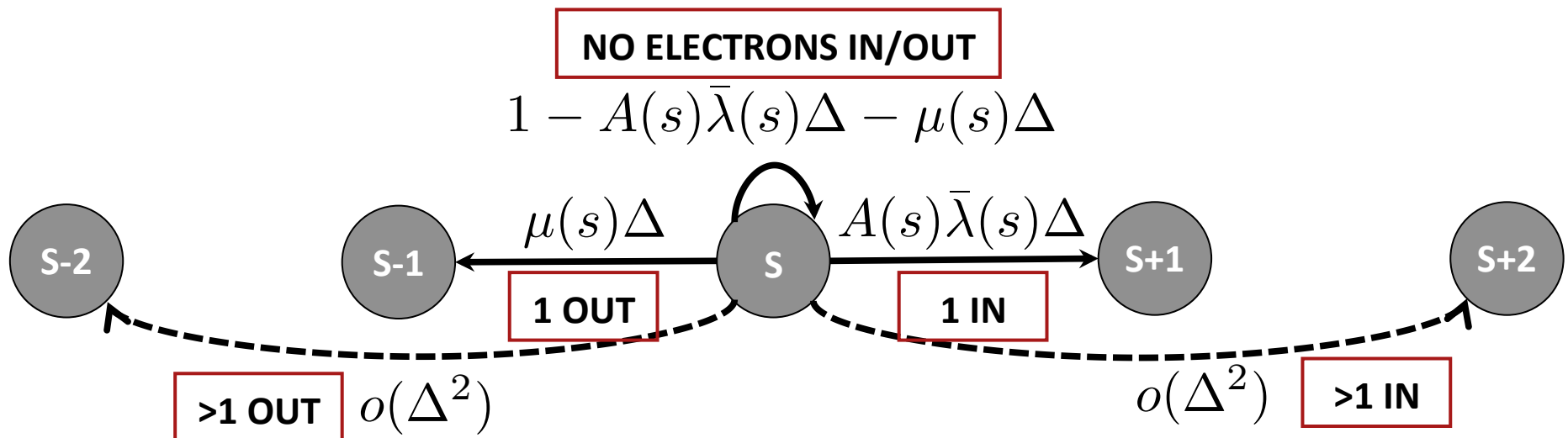


Prior Work

- **Uncontrolled case, no CSI:** *[Goldsmith&Varaiya'96] iid coding*
- **Uncontrolled case, partial CSIT, CSIR:** *[Yuksel&Tatikonda'07]*
- **I.i.d. state controlled by actions, CSIT:** *[Weissman'10], [Choudhuri&Mitra,'12]*
- **Controlled case, no CSI:** *[Pfister et al.'01] i.i.d. coding; with FB:*
[Tatikonda&Mitter] POMDP
- **Controlled case, full CSI & FB:** *[Chen&Berger'05] optimality of Markov coding, optimization via DP*
- *In our case, Markov state controlled by signal, full CSI case*
- **Finite-state continuous-time Markov Poisson channel**
 - **Static** Poisson channels *[Wyner'88]*
 - *We extend to finite-state Markov channels (**dynamic**)*
 - Discrete-time: *upper & lower bounds [Lapidoth&Moser'09]*

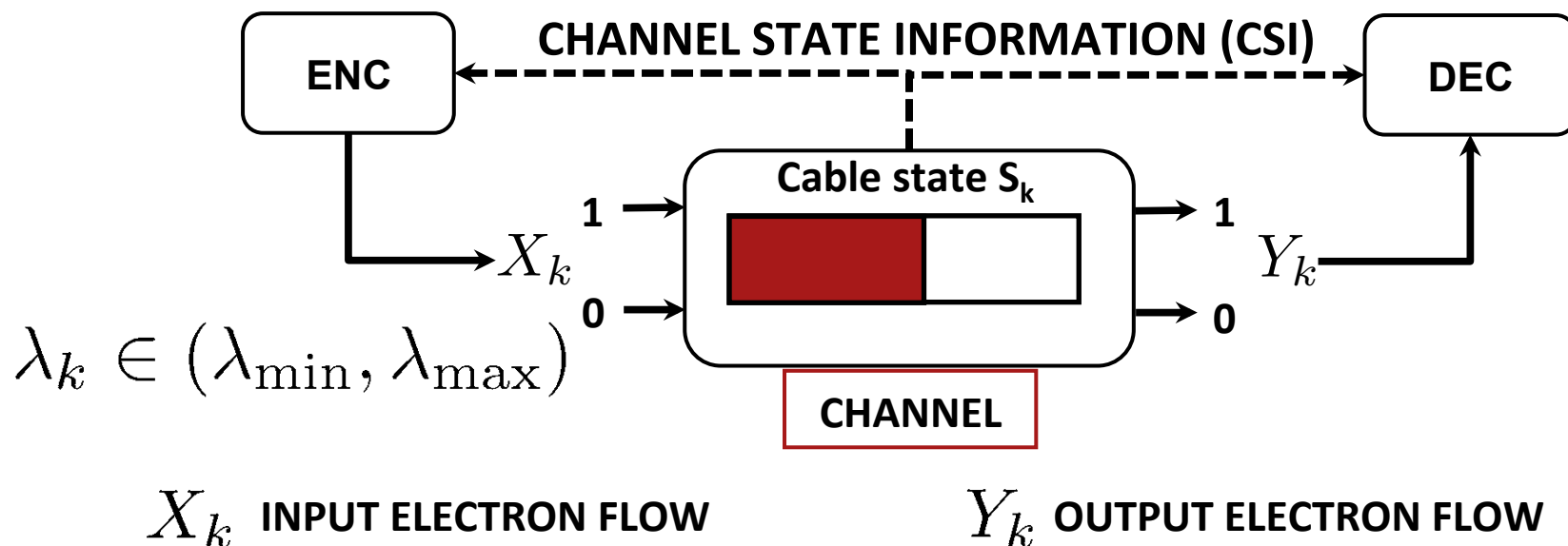
Discrete time model: approximation

- **Assumption:** “small” slot duration Δ [Wyner'88]



- Other events: probability $o(\Delta^2) \rightarrow$ **neglected**
- Only consider adjacent states

Discrete time model: approximation



- ❑ **Assumption:** “small” slot duration [Wyner’88]
- ❑ Channel with state (ENC controls intensity only)
- ❑ State “controlled” by input process; state-dependent output
 - Finite-state Markov [Chen&Berger’05]

Capacity of finite-state Markov channel

- Stationary Markov coding optimal [*Chen&Berger'05*]
- Capacity as **dynamic program**
 - *Action/control: rate selection*
 - *Reward: $I_f^{(\Delta)}(s)$ mutual information conditioned on past state, control function*
- **THEOREM:** capacity achieved by feedback independent inputs
 - [*Chen&Berger'05*] assumes feedback

Asymptotic capacity of Poisson Markov channels

$$C^* = \max_{\bar{\lambda}} \max_{f \in \mathcal{F}(\bar{\lambda})} \sum_{s=0}^{S_{\max}} \pi_{\bar{\lambda}}(s) I_f(s)$$

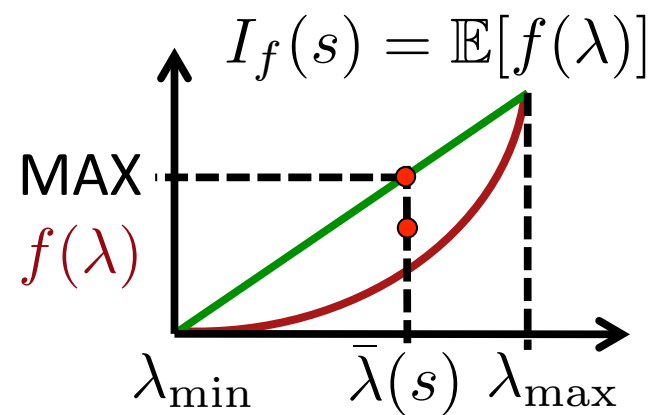
□ **Information-Energy coupling:**

▪ **Energy dimension:**

- Determined by $\bar{\lambda}(s)$

▪ **Information dimension:**

- **PROP:** Stationary distribution $\pi_f(s)$ depends only on $\bar{\lambda}(s) = \mathbb{E}[\lambda|s]$
- **Impact:** Optimize over ENC functions f with same $\bar{\lambda}(s)$



▪ **THEOREM:** Binary signal optimal $\lambda_k \in \{\lambda_{\min}, \lambda_{\max}\}$

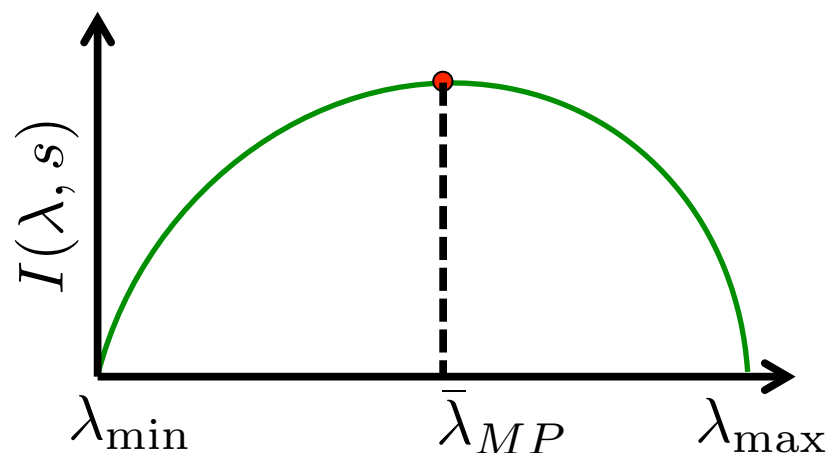
- **Impact:** easier to operate with a binary signal

Myopic scheme

43

- Myopic scheme: maximizes $I_f(s)$ in each slot
 - Can compute average rate in closed form
 - Independent of state s , no CSIT required (however, CSIR still required)

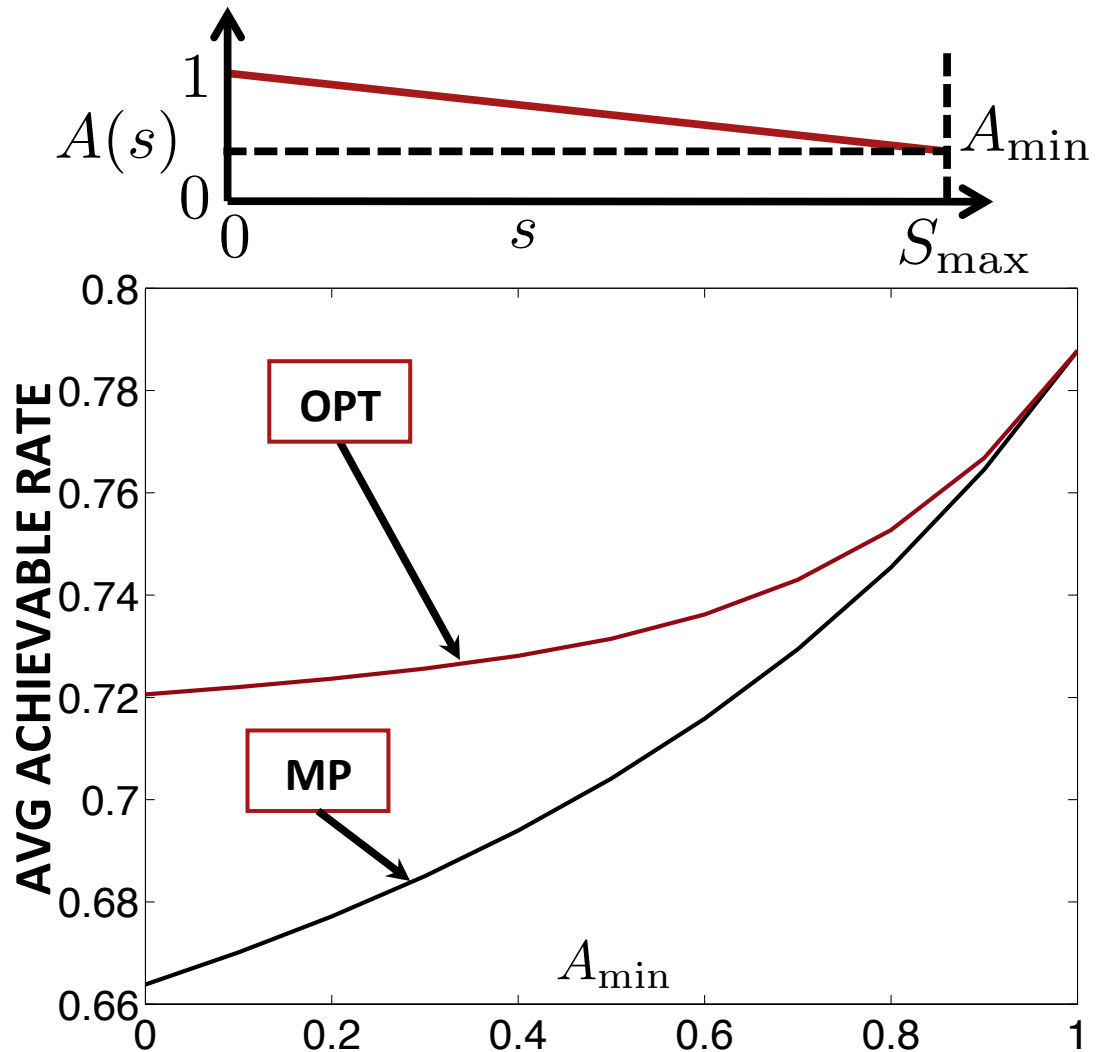
- **THEOREM:** $\bar{\lambda}^*(s) \leq \bar{\lambda}_{MP}$ (otherwise, fast recharges & low rate)
 - **Proof:** properties of n -step value function



MP & OPT

46

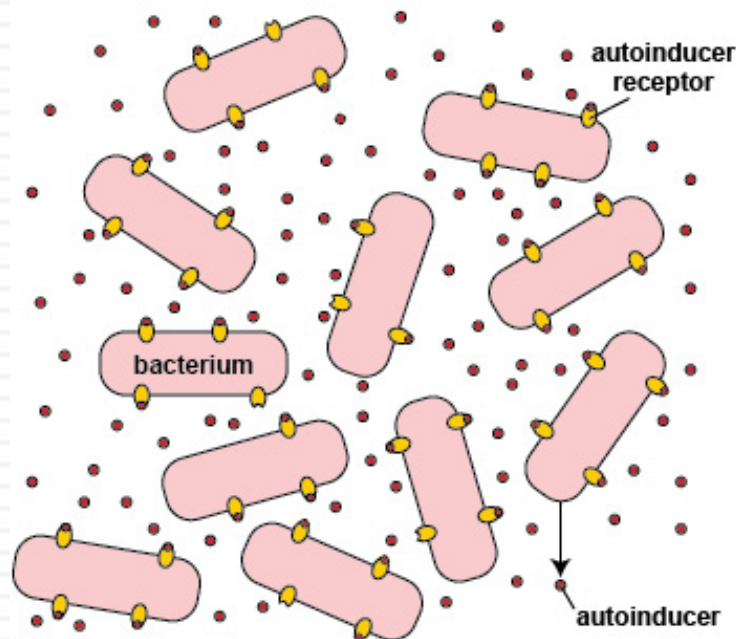
- ❑ Myopic scheme: greedy one step
- ❑ OPT 10% better than MP
 - MP: Greedy information transfer maximization achieves poor performance
- ❑ Information transfer maximization vs “wellness” maximization



Question

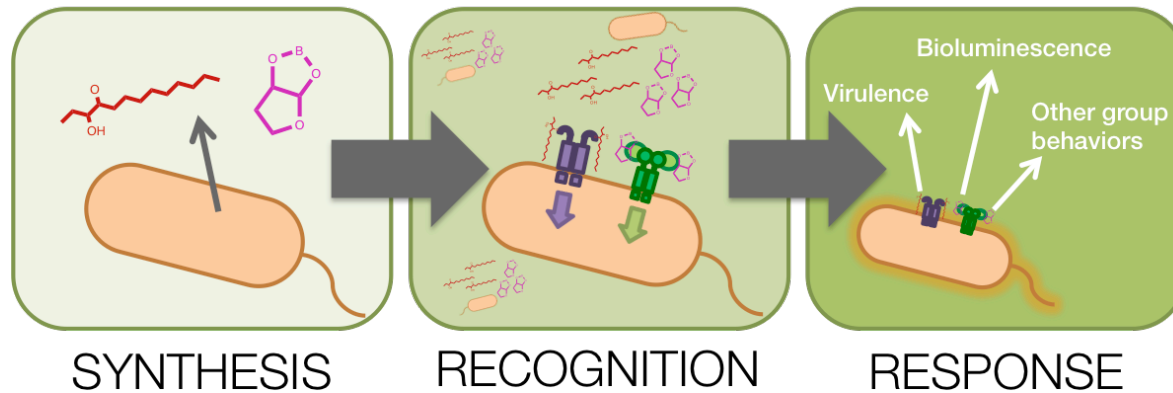
- ❑ **Q:** Can we apply these queueing theoretic approaches to OTHER bacterial networks?
- ❑ **A:** YES!
 - Quorum sensing...

Queuing models for Quorum Sensing

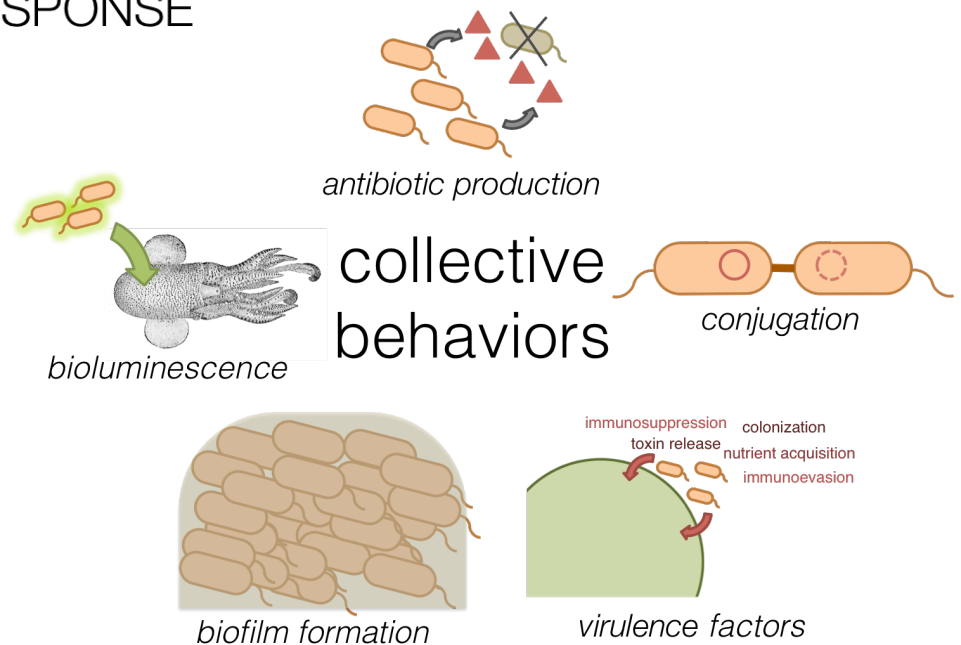


Quorum Sensing 101

52



- Gene expression regulation in response to fluctuations in cell-population density
- Bacteria produce autoinducers that increase in concentration as a function of cell density
- regulates many diseases



<http://sites.tufts.edu/quorumsensing/quorumsensing101/>

Quorum Sensing

USC
Viterbi

53

JOURNAL OF BACTERIOLOGY, October 1970, p. 313-322
Copyright © 1970 American Society for Microbiology

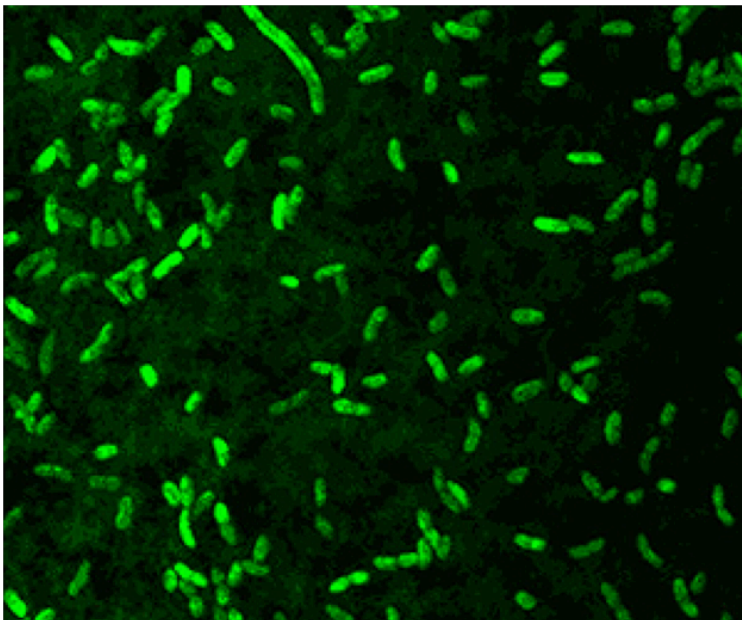
Vol. 104, No. 1
Printed in U.S.A.

Cellular Control of the Synthesis and Activity of the Bacterial Luminescent System¹

KENNETH H. NEALSON, TERRY PLATT, AND J. WOODLAND HASTINGS

*Biological Laboratories, Harvard University, Cambridge, Massachusetts, 02138 and
Marine Biological Laboratory, Woods Hole, Massachusetts 02534*

Received for publication 30 April 1970







luminescent bacteria growing in shake flasks, the enzyme luciferase has been shown to be synthesized in a relatively short burst during the period of exponential growth. The luciferase gene appears to be completely inactive in a freshly inoculated culture; the pulse of preferential luciferase synthesis which occurs later is a consequence of its activation at the level of deoxyribonucleic acid transcription and is attributed to an effect of a "conditioning" of the medium by the growing of the bacteria. Although cells grown in a minimal medium also exhibit a similar burst of synthesis of the luminescent system, the amount of synthesis is quantitatively less, relative to cell mass. Under such conditions, added arginine results in a striking stimulation of bioluminescence. This is attributed to a stimulation of existing patterns of gene expression and not to induction or derepression per se.

Vibrio Fischeri luminescing

Towards a model of QS

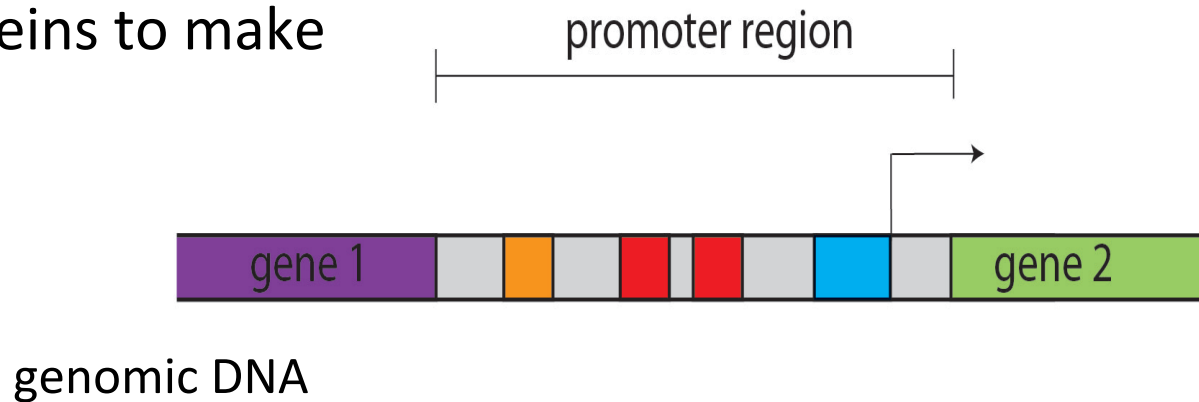
“Ingredients” of QS

1. Microbial community (*e.g.*, *Pseudomonas Aeruginosa*)
2.  Autoinducers $A(t)$ only global parameter, others by cell, i
 - Emitted by each cell in the environment
3.  Receptors $R_i(t)$
 - They bind to autoinducers within each cell to form *complexes*
4.  Complexes $C_i(t)$
 - 1 autoinducer bound to 1 receptor
5.  Synthases $S_i(t)$
 - “machines” that produce autoinducers
6. DNA binding sites
 - Complexes bind to them to produce *synthases, receptors & virulence factors*

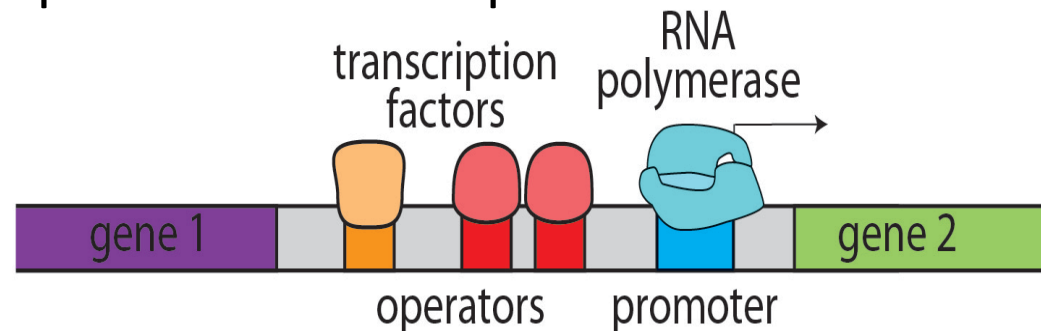
Gene Expression

61

- The promoter region between genes determines which proteins to make



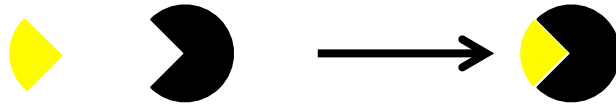
- Decision of whether or not to transcribe a gene depends on binding to operators and the promoter




From James Boedicker, USC

Underlying processes

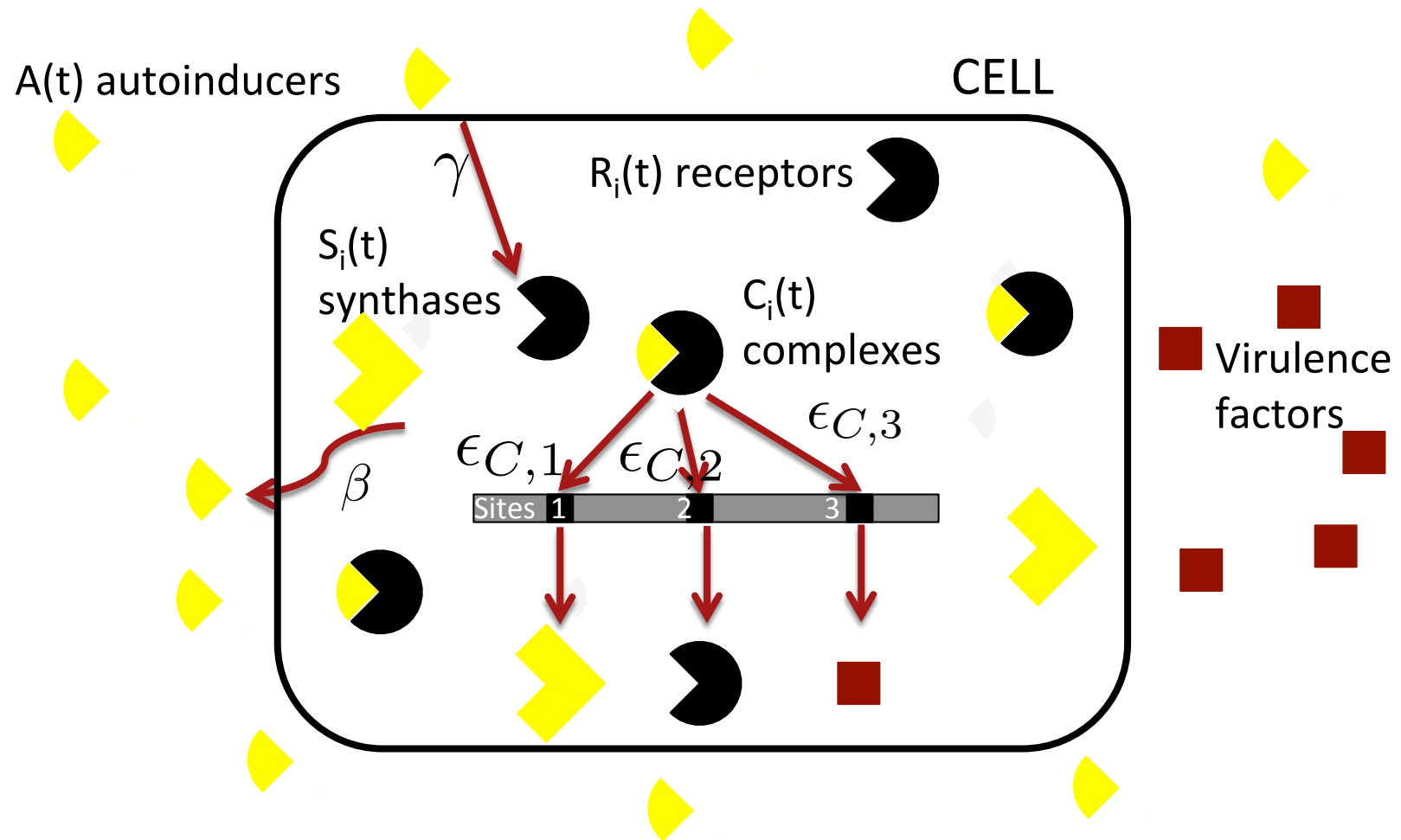
- Autoinducers bind to receptors to create complexes



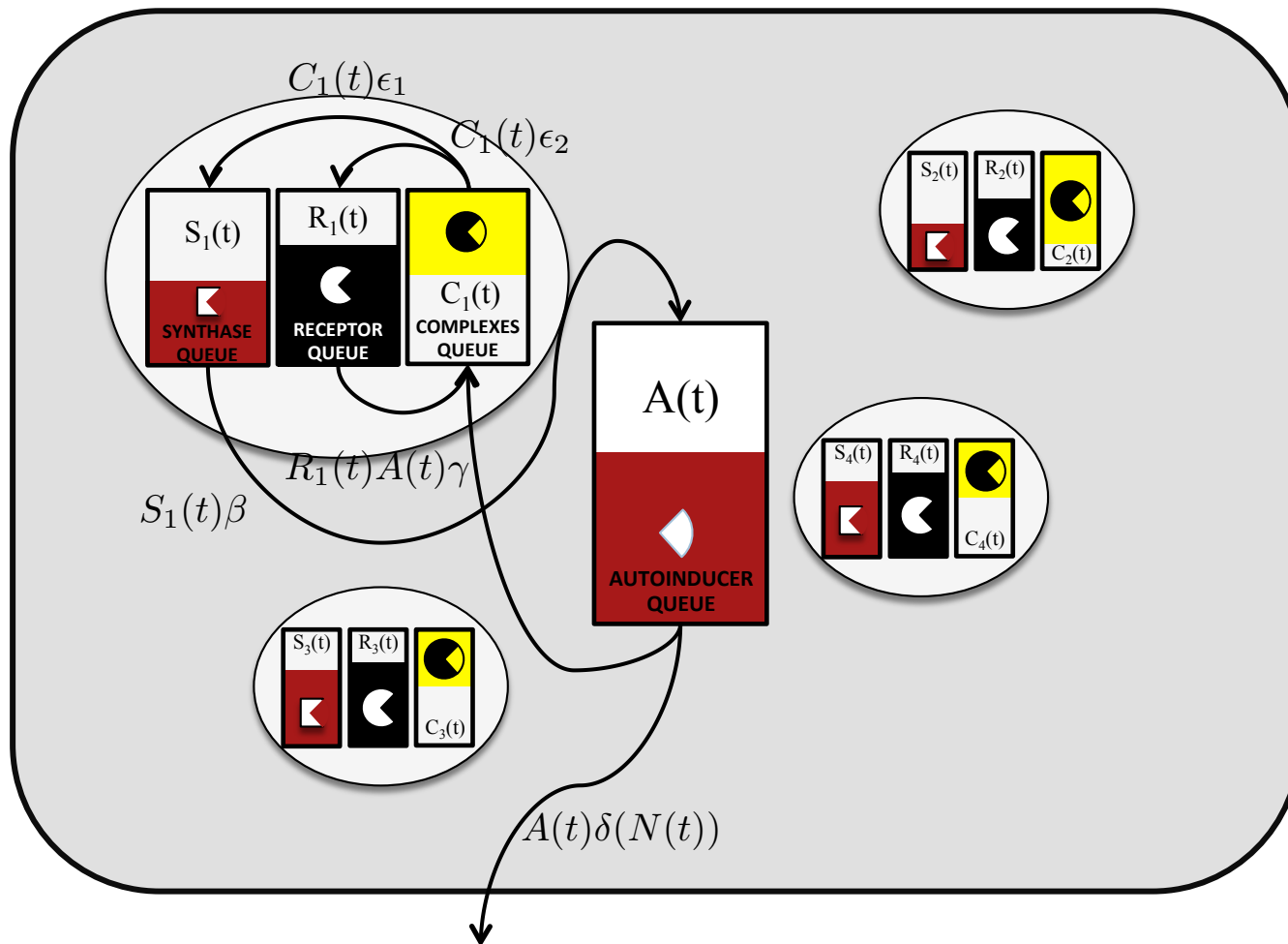
- Number of autoinducers/receptors decrease by 1
- Complexes can bind to one of three sites to create
 - Synthases (create autoinducers)
 - Receptors
 - Virulence factors (BAD)  cause disease, don't affect QS
 - Each have unique binding rates
- Complexes, synthases, receptors can degrade
- Cells do not die, but can duplicate



Abstraction of QS



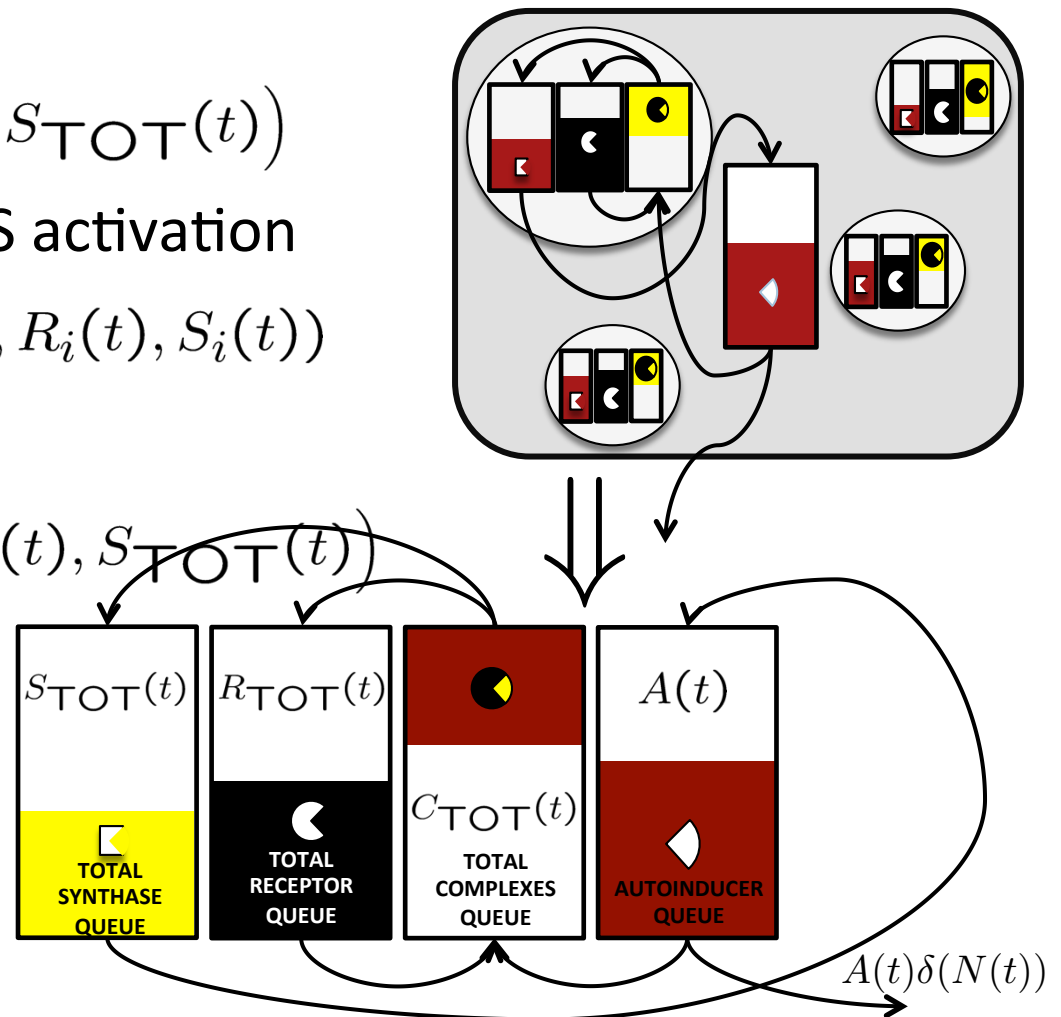
Queuing model of QS



Compact state space representation

THEOREM:

- $(N(t), C_{\text{TOT}}(t), R_{\text{TOT}}(t), S_{\text{TOT}}(t))$
is a sufficient statistic for QS activation
- Don't need to track $(C_i(t), R_i(t), S_i(t))$ for each cell,
track $(C_{\text{TOT}}(t), R_{\text{TOT}}(t), S_{\text{TOT}}(t))$ at the population level
 - Lower complexity!



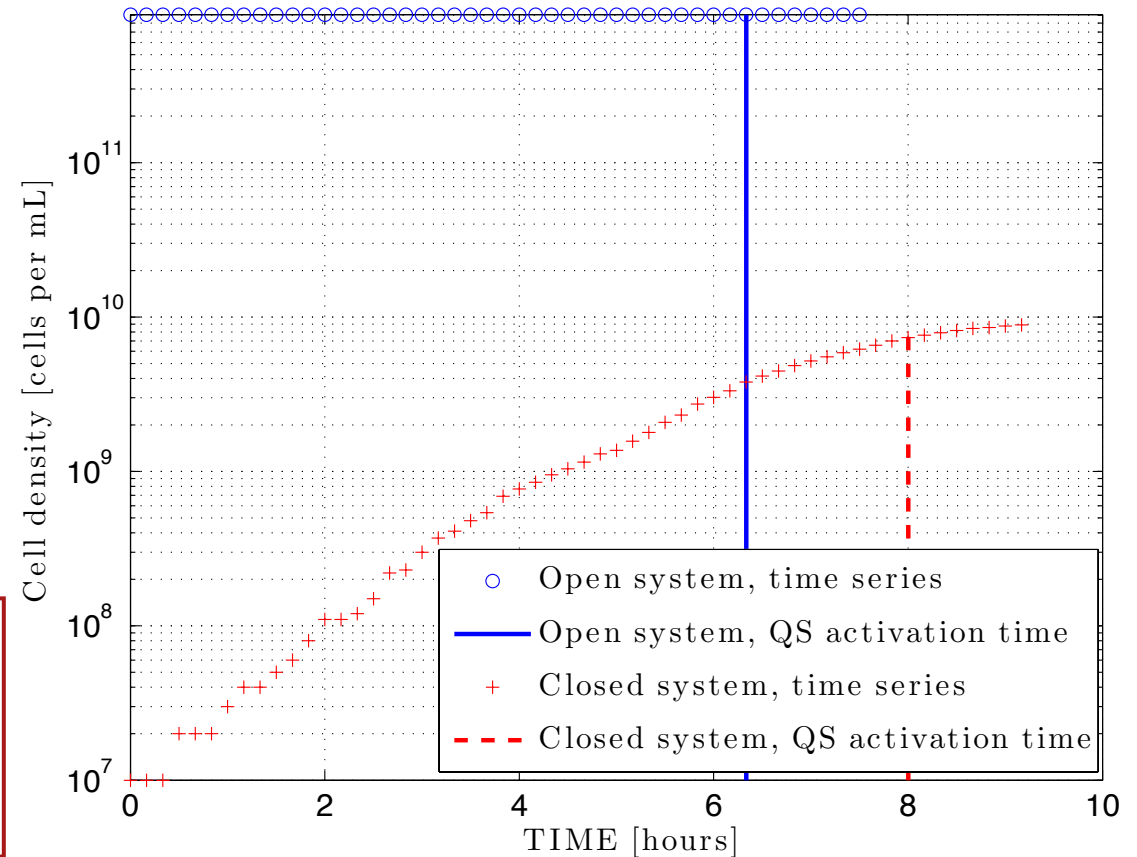
Simulations

□ Simulation tools based on queuing model

- Cell density is higher in open system
 - Larger concentration of autoinducers
 - Faster activation time

OPEN SYSTEM: cells grow in open space (no boundaries → leakage of autoinducers)

CLOSED SYSTEM: cells grow in finite box (boundaries → no leakage)



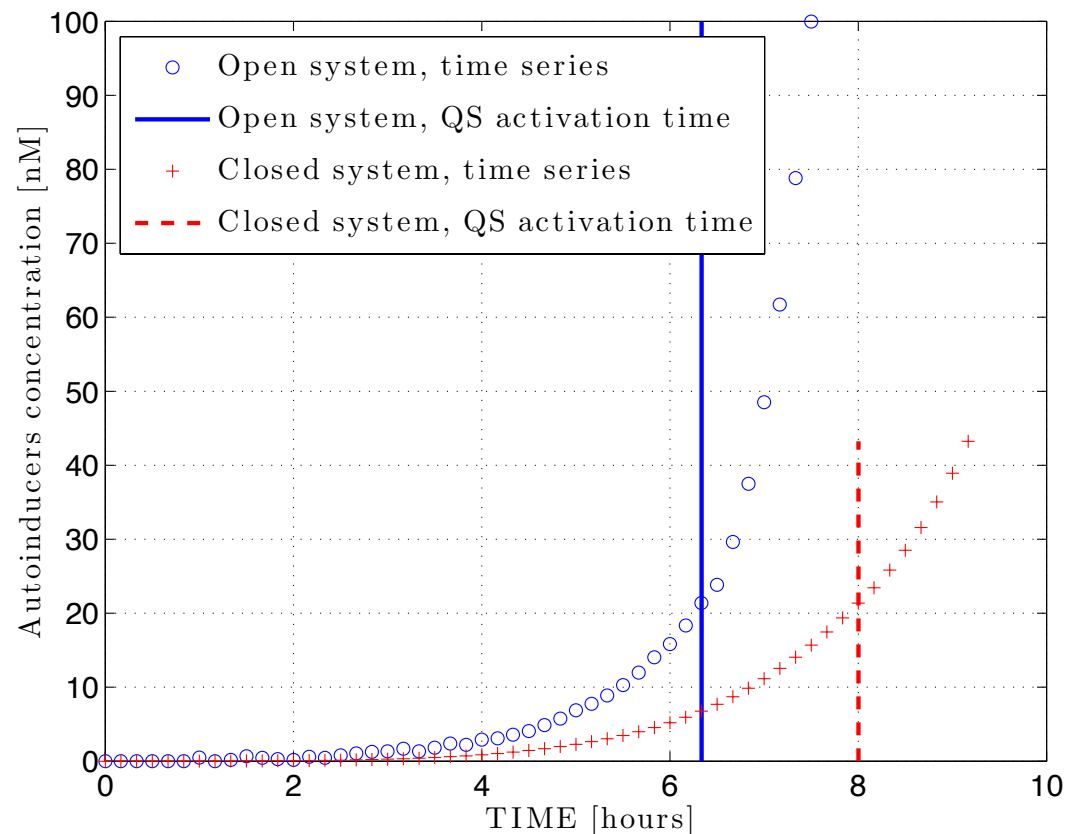
Simulations

❑ Simulation tools based on queuing model

- Model allows realistic performance evaluation in short time
- Use of complexity reduction tools from wireless comm

OPEN SYSTEM: cells grow in open space (no boundaries → leakage of autoinducers)

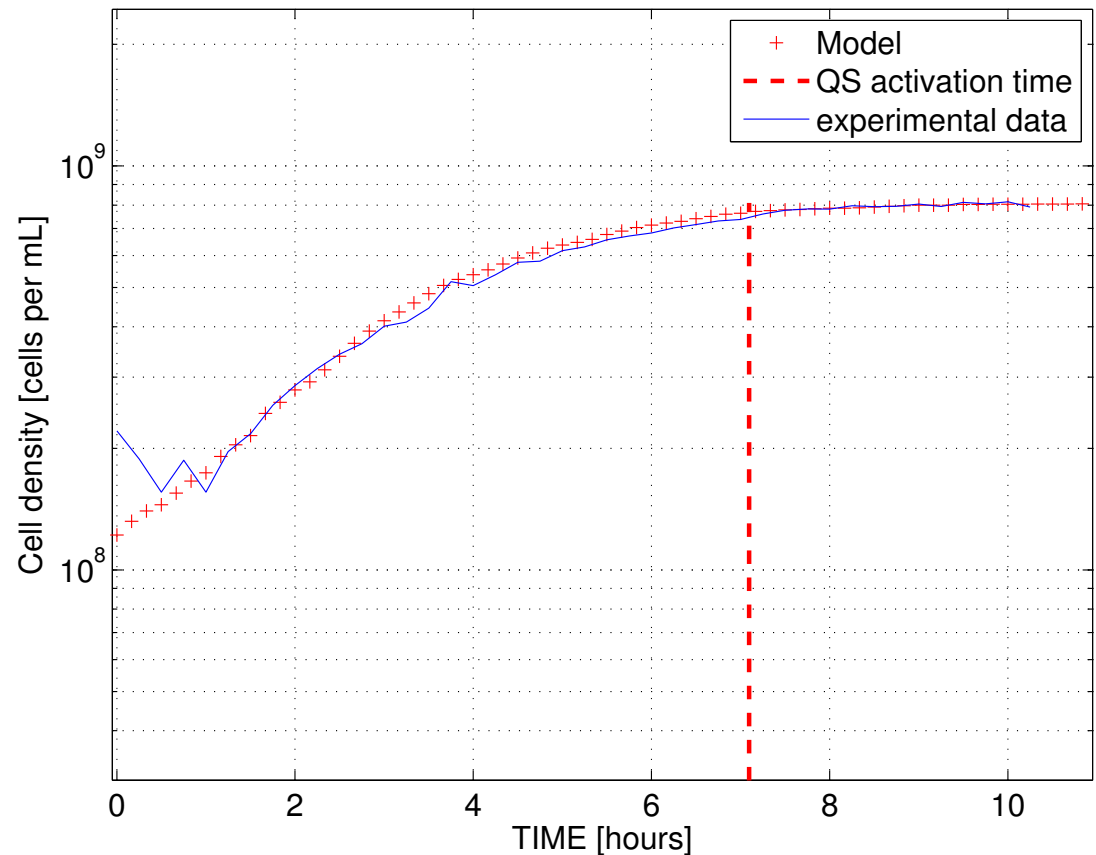
CLOSED SYSTEM: cells grow in finite box (boundaries → no leakage)



Experimental results

68

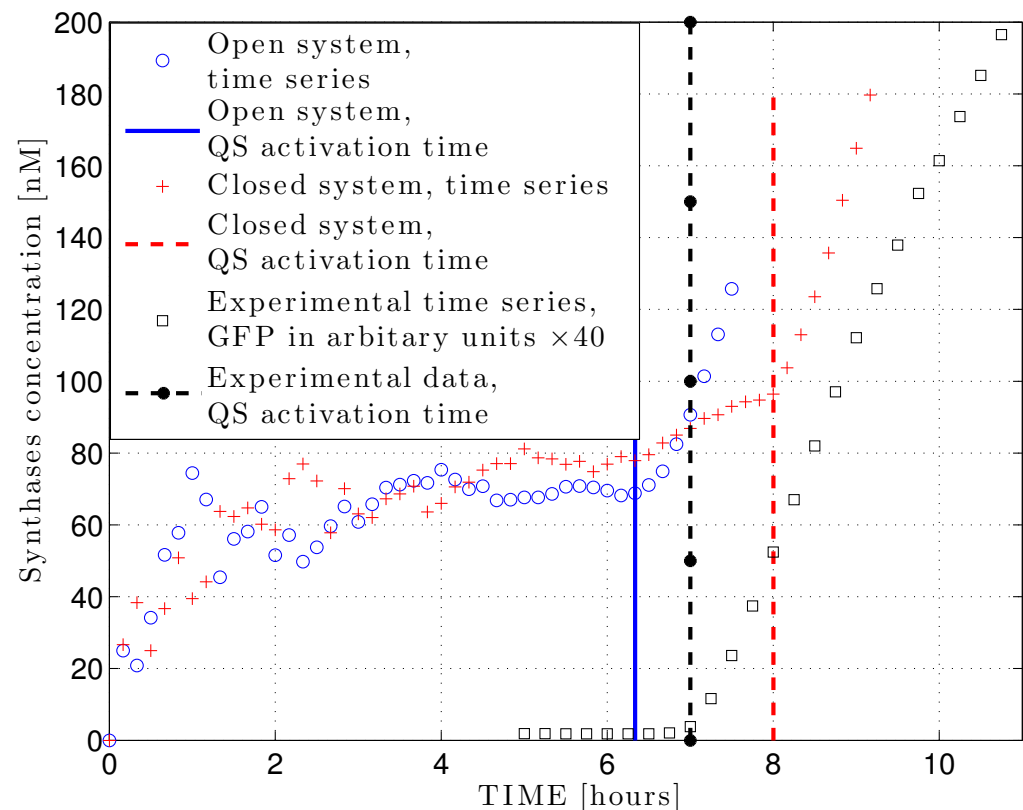
- Closed system
- *Escherichia coli* cells grown in LB media at 37C
- Green Fluorescence protein (GFP) monitored (~ gene expression activity)



Experimental results

69

- Closed system
- *Escherichia coli* cells grown in LB media at 37C
- Green Fluorescence protein (GFP) monitored (~ gene expression activity)
- Model & experiments:
 - Similar qualitatively
 - But GFP=0 before QS activation (low basal expression rate) → further investigation needed



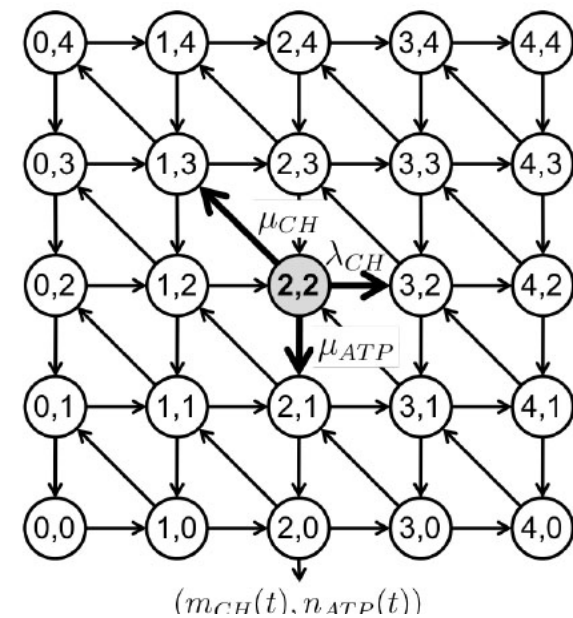
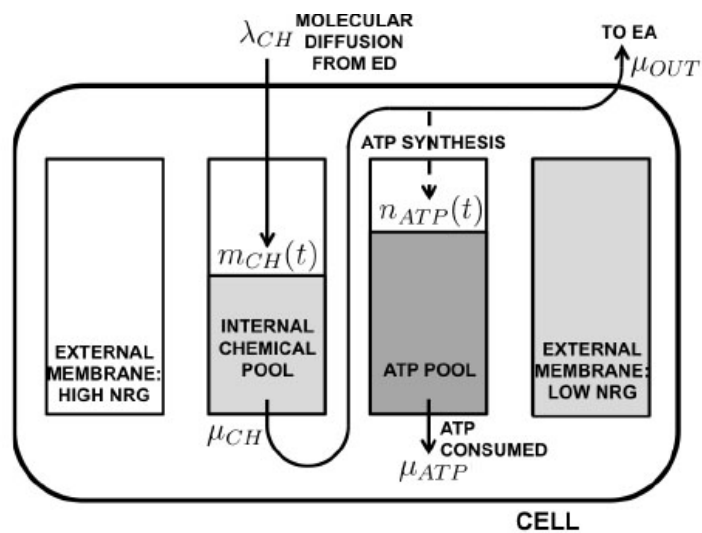
USC
Viterbi

The diagram illustrates the Las and Pqs quorum sensing systems in *Pseudomonas aeruginosa*. The Las system involves LasR, LasI, and LasII. LasI produces LasR, which binds to LasR to form a complex that activates the LasR promoter. LasR also binds to LasR, which activates the LasR promoter. LasR also binds to LasR, which activates the LasR promoter. The Pqs system involves PqsR, PqsA, PqsB, PqsC, PqsD, PqsE, PqsF, PqsG, PqsH, PqsI, PqsJ, PqsK, PqsL, PqsM, PqsN, PqsO, PqsP, PqsQ, PqsR, PqsS, PqsT, PqsU, PqsV, PqsW, PqsX, PqsY, PqsZ, PqsAA, PqsAB, PqsAC, PqsAD, PqsAE, PqsAF, PqsAG, PqsAH, PqsAI, PqsAJ, PqsAK, PqsAL, PqsAM, PqsAN, PqsAO, PqsAP, PqsAQ, PqsAR, PqsAS, PqsAT, PqsAU, PqsAV, PqsAW, PqsAX, PqsAY, PqsAZ, PqsBA, PqsBB, PqsBC, PqsBD, PqsBE, PqsBF, PqsBG, PqsBH, PqsBI, PqsBJ, PqsBK, PqsBL, PqsBM, PqsBN, PqsBO, PqsBP, PqsBQ, PqsBR, PqsBS, PqsBT, PqsBU, PqsBV, PqsBW, PqsBX, PqsBY, PqsBZ, PqsCA, PqsCB, PqsCC, PqsCD, PqsCE, PqsCF, PqsCG, PqsCH, PqsCI, PqsCJ, PqsCK, PqsCL, PqsCM, PqsCN, PqsCO, PqsCP, PqsCQ, PqsCR, PqsCS, PqsCT, PqsCU, PqsCV, PqsCW, PqsCX, PqsCY, PqsCZ, PqsDA, PqsDB, PqsDC, PqsDD, PqsDE, PqsDF, PqsDG, PqsDH, PqsDI, PqsDJ, PqsDK, PqsDL, PqsDM, PqsDN, PqsDO, PqsDP, PqsDQ, PqsDR, PqsDS, PqsDT, PqsDU, PqsDV, PqsDW, PqsDX, PqsDY, PqsDZ, PqsEA, PqsEB, PqsEC, PqsED, PqsEE, PqsEF, PqsEG, PqsEH, PqsEI, PqsEJ, PqsEK, PqsEL, PqsEM, PqsEN, PqsEO, PqsEP, PqsEQ, PqsER, PqsES, PqsET, PqsEU, PqsEV, PqsEW, PqsEX, PqsEY, PqsEZ, PqsFA, PqsFB, PqsFC, PqsFD, PqsFE, PqsFF, PqsFG, PqsFH, PqsFI, PqsFJ, PqsFK, PqsFL, PqsFM, PqsFN, PqsFO, PqsFP, PqsFQ, PqsFR, PqsFS, PqsFT, PqsFU, PqsFV, PqsFW, PqsFX, PqsFY, PqsFZ, PqsGA, PqsGB, PqsGC, PqsGD, PqsGE, PqsGF, PqsGG, PqsGH, PqsGI, PqsGJ, PqsGK, PqsGL, PqsGM, PqsGN, PqsGO, PqsGP, PqsGQ, PqsGR, PqsGS, PqsGT, PqsGU, PqsGV, PqsGW, PqsGX, PqsGY, PqsGZ, PqsHA, PqsHB, PqsHC, PqsHD, PqsHE, PqsHF, PqsHG, PqsHH, PqsHI, PqsHJ, PqsHK, PqsHL, PqsHM, PqsHN, PqsHO, PqsHP, PqsHQ, PqsHR, PqsHS, PqsHT, PqsHU, PqsHV, PqsHW, PqsHX, PqsHY, PqsHZ, PqsIA, PqsIB, PqsIC, PqsID, PqsIE, PqsIF, PqsIG, PqsIH, PqsII, PqsIJ, PqsIK, PqsIL, PqsIM, PqsIN, PqsIO, PqsIP, PqsIQ, PqsIR, PqsIS, PqsIT, PqsIU, PqsIV, PqsIW, PqsIX, PqsIY, PqsIZ, PqsJA, PqsJB, PqsJC, PqsJD, PqsJE, PqsJF, PqsJG, PqsJH, PqsJI, PqsJJ, PqsJK, PqsJL, PqsJM, PqsJN, PqsJO, PqsJP, PqsJQ, PqsJR, PqsJS, PqsJT, PqsJU, PqsJV, PqsJW, PqsJX, PqsJY, PqsJZ, PqsKA, PqsKB, PqsKC, PqsKD, PqsKE, PqsKF, PqsKG, PqsKH, PqsKI, PqsKJ, PqsKK, PqsKL, PqsKM, PqsKN, PqsKO, PqsKP, PqsKQ, PqsKR, PqsKS, PqsKT, PqsKU, PqsKV, PqsKW, PqsKX, PqsKY, PqsKZ, PqsLA, PqsLB, PqsLC, PqsLD, PqsLE, PqsLF, PqsLG, PqsLH, PqsLI, PqsLJ, PqsLK, PqsLL, PqsLM, PqsLN, PqsLO, PqsLP, PqsLQ, PqsLR, PqsLS, PqsLT, PqsLU, PqsLV, PqsLW, PqsLX, PqsLY, PqsLZ, PqsMA, PqsMB, PqsMC, PqsMD, PqsME, PqsMF, PqsMG, PqsMH, PqsMI, PqsMJ, PqsMK, PqsML, PqsMM, PqsMN, PqsMO, PqsMP, PqsMQ, PqsMR, PqsMS, PqsMT, PqsMU, PqsMV, PqsMW, PqsMX, PqsMY, PqsMZ, PqsNA, PqsNB, PqsNC, PqsND, PqsNE, PqsNF, PqsNG, PqsNH, PqsNI, PqsNJ, PqsNK, PqsNL, PqsNM, PqsNO, PqsNP, PqsNQ, PqsNR, PqsNS, PqsNT, PqsNU, PqsNV, PqsNW, PqsNX, PqsNY, PqsNZ, PqsOA, PqsOB, PqsOC, PqsOD, PqsOE, PqsOF, PqsOG, PqsOH, PqsOI, PqsOJ, PqsOK, PqsOL, PqsOM, PqsON, PqsOO, PqsOP, PqsOQ, PqsOR, PqsOS, PqsOT, PqsOU, PqsOV, PqsOW, PqsOX, PqsOY, PqsOZ, PqsPA, PqsPB, PqsPC, PqsPD, PqsPE, PqsPF, PqsPG, PqsPH, PqsPI, PqsPJ, PqsPK, PqsPL, PqsPM, PqsPN, PqsPO, PqsPP, PqsPQ, PqsPR, PqsPS, PqsPT, PqsPU, PqsPV, PqsPW, PqsPX, PqsPY, PqsPZ, PqsQA, PqsQB, PqsQC, PqsQD, PqsQE, PqsQF, PqsQG, PqsQH, PqsQI, PqsQJ, PqsQK, PqsQL, PqsQM, PqsQN, PqsQO, PqsQP, PqsQQ, PqsQR, PqsQS, PqsQT, PqsQU, PqsQV, PqsQW, PqsQX, PqsQY, PqsQZ, PqsRA, PqsRB, PqsRC, PqsRD, PqsRE, PqsRF, PqsRG, PqsRH, PqsRI, PqsRJ, PqsRK, PqsRL, PqsRM, PqsRN, PqsRO, PqsRP, PqsRQ, PqsRR, PqsRS, PqsRT, PqsRU, PqsRV, PqsRW, PqsRX, PqsRY, PqsRZ, PqsSA, PqsSB, PqsSC, PqsSD, PqsSE, PqsSF, PqsSG, PqsSH, PqsSI, PqsSJ, PqsSK, PqsSL, PqsSM, PqsSN, PqsSO, PqsSP, PqsSQ, PqsSR, PqsSS, PqsST, PqsSU, PqsSV, PqsSW, PqsSX, PqsSY, PqsSZ, PqsTA, PqsTB, PqsTC, PqsTD, PqsTE, PqsTF, PqsTG, PqsTH, PqsTI, PqsTJ, PqsTK, PqsTL, PqsTM, PqsTN, PqsTO, PqsTP, PqsTQ, PqsTR, PqsTS, PqsTT, PqsTU, PqsTV, PqsTW, PqsTX, PqsTY, PqsTZ, PqsUA, PqsUB, PqsUC, PqsUD, PqsUE, PqsUF, PqsUG, PqsUH, PqsUI, PqsUJ, PqsUK, PqsUL, PqsUM, PqsUN, PqsUO, PqsUP, PqsUQ, PqsUR, PqsUS, PqsUT, PqsUU, PqsUV, PqsUW, PqsUX, PqsUY, PqsUZ, PqsVA, PqsVB, PqsVC, PqsVD, PqsVE, PqsVF, PqsVG, PqsVH, PqsVI, PqsVJ, PqsVK, PqsVL, PqsVM, PqsVN, PqsVO, PqsVP, PqsVQ, PqsVR, PqsVS, PqsVT, PqsVU, PqsVV, PqsVW, PqsVX, PqsVY, PqsVZ, PqsWA, PqsWB, PqsWC, PqsWD, PqsWE, PqsWF, PqsWG, PqsWH, PqsWI, PqsWJ, PqsWK, PqsWL, PqsWM, PqsWN, PqsWO, PqsWP, PqsWQ, PqsWR, PqsWS, PqsWT, PqsWU, PqsWV, PqsWW, PqsWX, PqsWY, PqsWZ, PqsXA, PqsXB, PqsXC, PqsXD, PqsXE, PqsXF, PqsXG, PqsXH, PqsXI, PqsXJ, PqsXK, PqsXL, PqsXM, PqsXN, PqsXO, PqsXP, PqsXQ, PqsXR, PqsXS, PqsXT, PqsXU, PqsXV, PqsXW, PqsXX, PqsXY, PqsXZ, PqsYA, PqsYB, PqsYC, PqsYD, PqsYE, PqsYF, PqsYG, PqsYH, PqsYI, PqsYJ, PqsYK, PqsYL, PqsYM, PqsYN, PqsYO, PqsYP, PqsYQ, PqsYR, PqsYS, PqsYT, PqsYU, PqsYV, PqsYW, PqsYX, PqsYY, PqsYZ, PqsZA, PqsZB, PqsZC, PqsZD, PqsZE, PqsZF, PqsZG, PqsZH, PqsZI, PqsZJ, PqsZK, PqsZL, PqsZM, PqsZN, PqsZO, PqsZP, PqsZQ, PqsZR, PqsZS, PqsZT, PqsZU, PqsZV, PqsZW, PqsZX, PqsZY, PqsZZ.

P. aeruginosa and their respective regulons

Bacterial Models

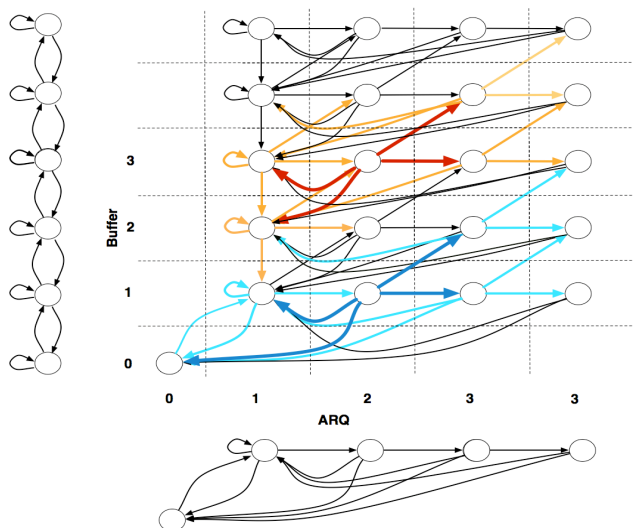
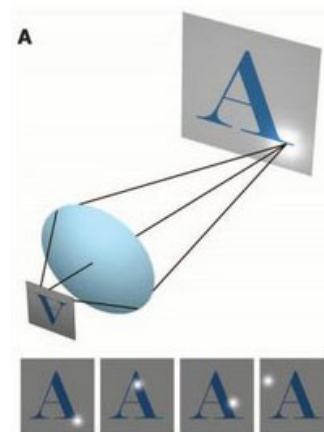
72



Large Scale Networks

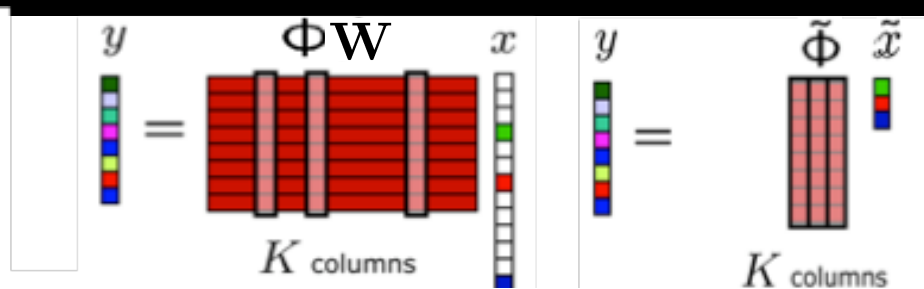
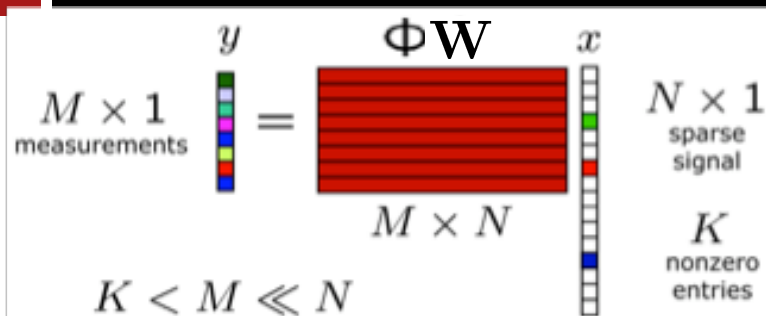
$$\begin{array}{c} y \\ M \times 1 \\ \text{measurements} \end{array} = \begin{array}{c} \Phi \\ M \times N \end{array} \begin{array}{c} x \\ N \times 1 \\ \text{sparse signal} \\ K \text{ nonzero entries} \end{array}$$

$K < M \ll N$



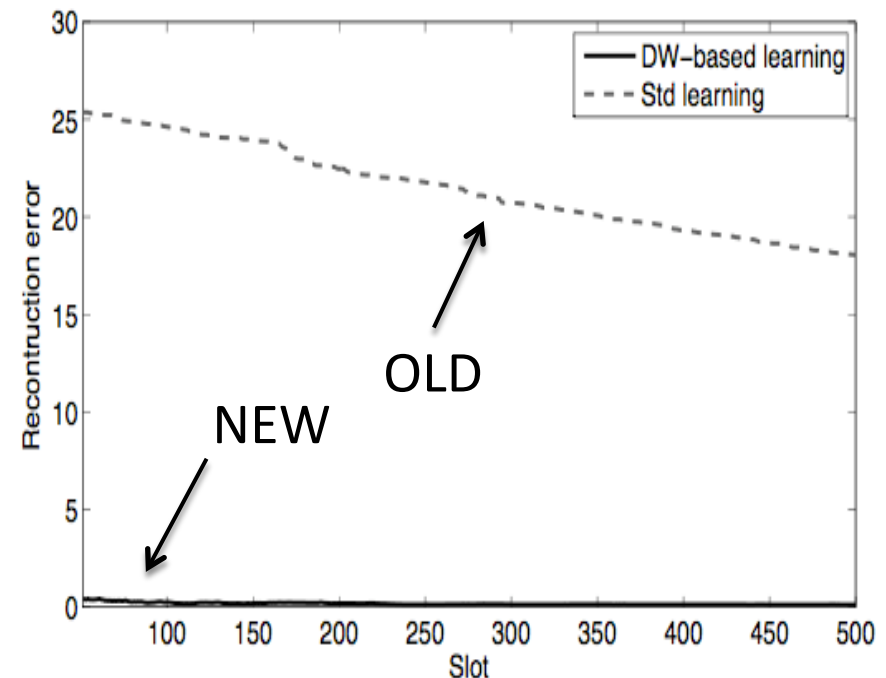
- Can use CS on graphs
- Can learn cost functions (e.g. throughput, SINR, BER, etc.)
- Can learn with **two orders** **magnitude fewer samples**

Use your favorite CS method



Diffusion Wavelet based CS learning

- Using Least Squares Residual Compressed sensing handles instability
 - Vaswani, IEEE Trans on SP 8/2010



Summary

- ❑ Stochastic queuing theoretic model
 - Captures salient features, amenable to complexity reduction using W-COM tools (vs detailed physical models)
- ❑ IT aspects, coupling between
 - *Coupling between wellness & information transfer*
 - *Impact:* state estimation to adapt signal and optimize this trade-off
- ❑ Quorum sensing modeling
 - Need to consider multiple signaling mechanisms
 - Experimental data analysis
 - Optimization to mitigate virulence factors

Thanks to...



Nicolo
Michelusi



Sahand
Pirbadian



Mohammed
El-Naggar



James
Boedicker

PUBLICATIONS

N. Michelusi, S. Pirbadian, M.Y. El-Naggar, U. Mitra, "A Stochastic Model for Electron Transfer in Bacterial Cables", *IEEE JSAC– Series on Molecular, Biological, and Multi-Scale Communications* 32 (12), , pp.2402-2416, Dec. 2014

N. Michelusi, U. Mitra, "Capacity of electron-based communication over bacterial cables: the full-CSI case", *IEEE Transactions on Molecular, Biological, and Multi-Scale Communications*, 1(1), pp. 62-75, March 2015.

N. Michelusi, J. Boedicker, M. El-Naggar, U. Mitra, "Queuing models for abstracting interactions in Bacterial communities," *IEEE JSAC Issue on Emerging Technologies*, to appear.

IEEE TRANSACTIONS ON MOLECULAR, BIOLOGICAL, AND MULTI-SCALE COMMUNICATIONS



Editor-in-Chief

Urbashi Mitra University of Southern California,
USA



Associate Editor-in-Chief

Andrew W. Eckford
York University, Canada

<http://www.comsoc.org/tmbmc>

*principles, design, and analysis of signaling and
information systems beyond conventional electromagnetism,
small-scale and multi-scale applications.
molecular, quantum, chemical and biological techniques*

