Technion+Weizmann, June 2009

Competition between multiple TASEPs for a finite pool of particles

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D.A. Adams, B. Schmittmann and R.K.P. Zia, JSTAT P06009 (2008)
L. Jonathan Cook and R. K. P. Zia, JSTAT P02012 (2009) & tbp

Supported by Materials Theory, Division of Materials Research

Outline

- Brief summary of TASEP
  - Early TASEP's (~40 years ago)
  - Physicists' contributions (since the 90's)
- Effects of finite resources
  - A natural generalization and motivations from biology
  - Consequences for a single TASEP (shock localization)
  - Competition between many TASEP's
  - Some answers and puzzles
- Summary and Outlook

Why study TASEP ?

- *mathematicians*: "Consider… this stochastic process"
- *biochemists*:

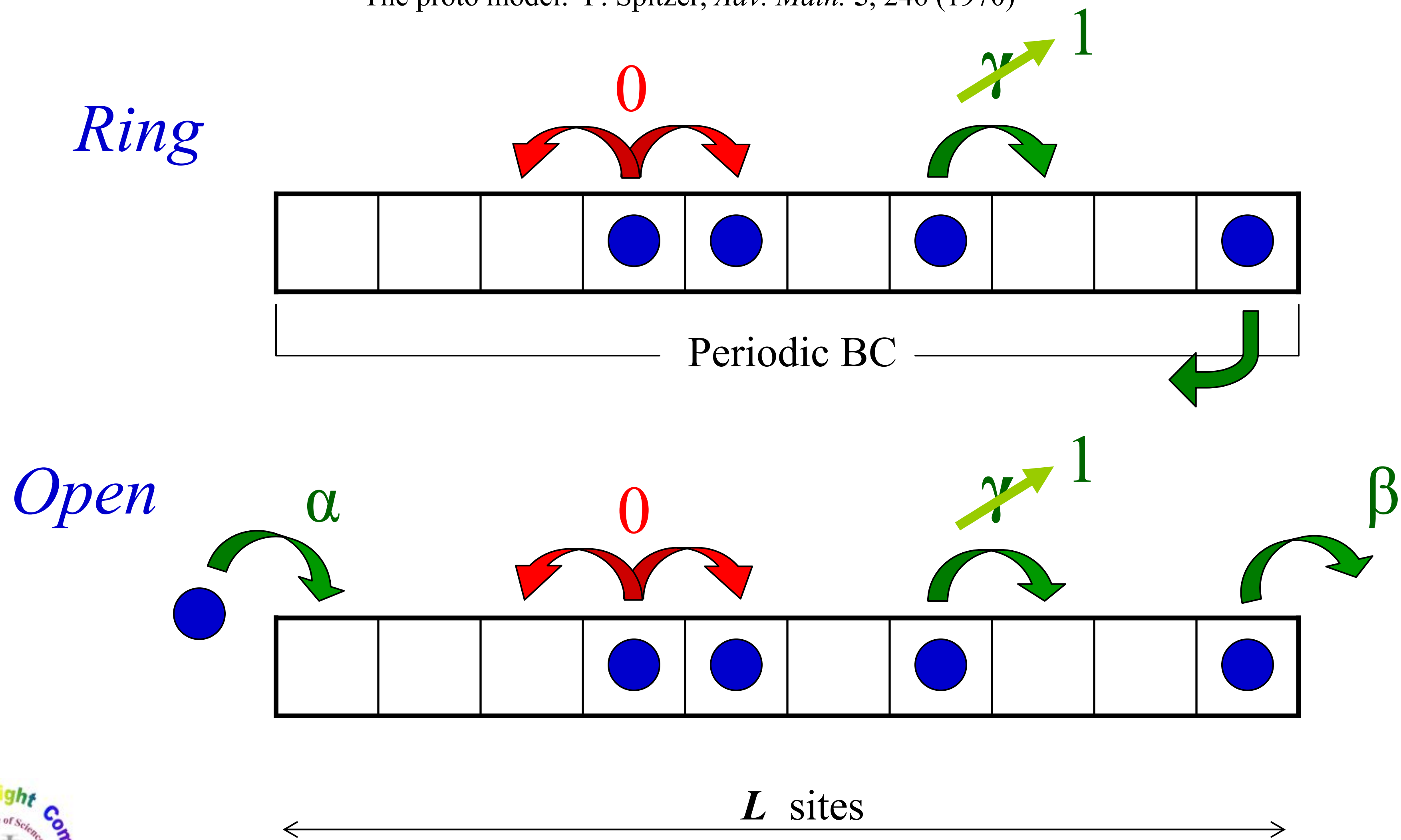
  simple minded model for protein synthesis
- *physicists (like me)*:
  - Non equilibrium statistical mechanics
  - Interacting systems with dynamics that ***violate***

    detailed balance, time reversal
  - Novel states and stationary distributions
  - Many other potential applications

    ⋮

What's TASEP ?

The proto model: F. Spitzer, *Adv. Math.* **5**, 246 (1970)



Biochemists' interest in TASEP

Working independently of, and most likely simultaneously as Spitzer,

J. H. Gibbs, a chemist + A. C. Pipkin, an applied mathematician

studied a model for protein synthesis.

This study formed the PhD thesis of

C. T. MacDonald

at Brown, and published as two papers:

C.T. MacDonald, J.H. Gibbs, and A.C. Pipkin, *Biopolymers* (1968+69)

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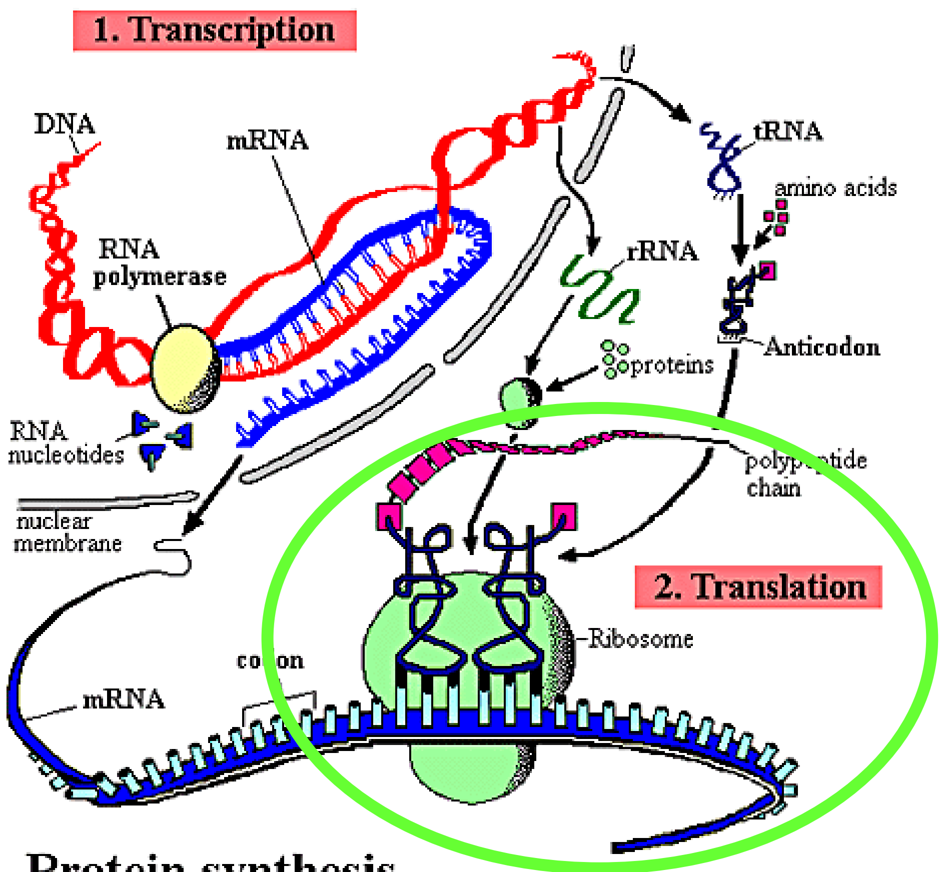
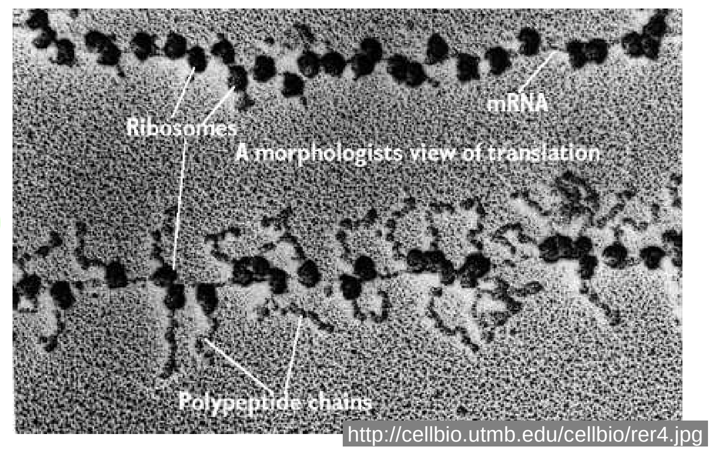
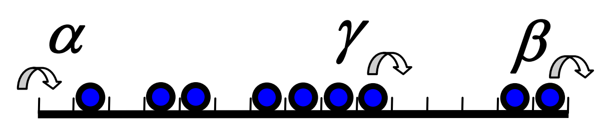


Protein synthesis

A ribosome…

- starts at one end (initiation)
- goes to the other, “knitting” the aa-chain (elongation)
- releases aa-chain at the end and falls off mRNA (termination)





initiation elongation termination

Some Answers for TASEP

- What is stationary distribution: $\boldsymbol{P}^*(n_i)$?
  - What is full dynamics $\boldsymbol{P}(n_i, t)$?
- For the *Ring*, $\boldsymbol{P}^* \propto \mathbf{1}$
  - but with non-trivial dynamics
- For the *Open case*, $\boldsymbol{P}^*$ non-trivial *(B. Derrida et al. 1992)*
  - with even more interesting dynamics

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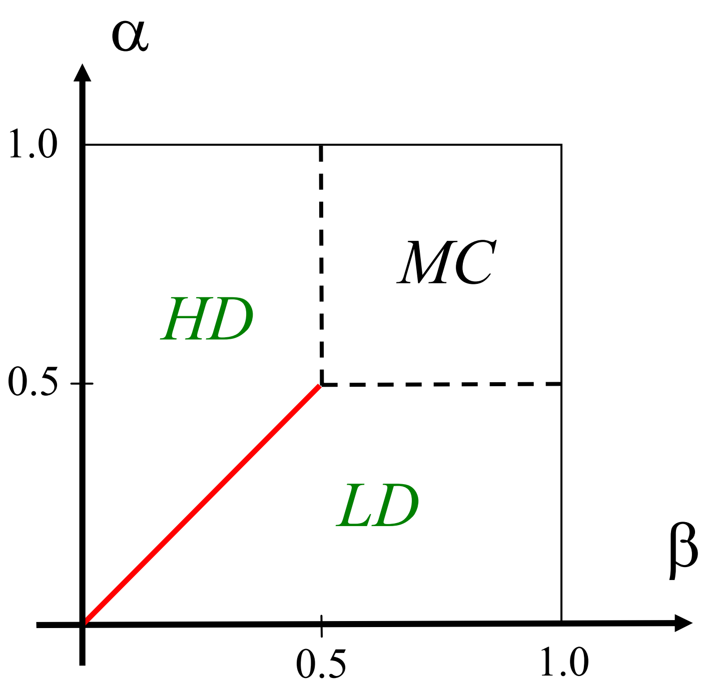
The Open TASEP

3 phases: *M*ax *C*urrent, *H*igh/*L*ow *D*ensity

Steady state, “ordinary” TASEP



MC: average density $\equiv \rho^* = 0.5$

HD/LD: $\rho^* = 1-\beta > 0.5$ / $\rho^* = \alpha < 0.5$

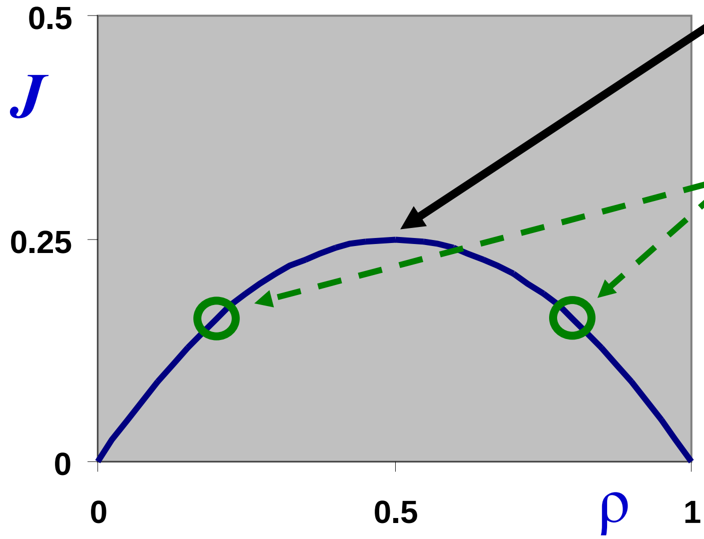
- - - - continuous (“second order”) transition

—— discontinuous transition; coexistence of *HD/LD* regions; sharp interface; shock “phase” *SP*

underlying particle-hole symmetry: $\alpha \Leftrightarrow \beta$ & $\rho^* \Leftrightarrow \rho^*_h = 1-\rho^*$

The Open TASEP

3 phases: *M*ax *C*urrent, *H*igh/*L*ow *D*ensity



MC: average density $\equiv \rho^* = 0.5$

HD/LD: $\rho^* = 1-\beta > 0.5$ / $\rho^* = \alpha < 0.5$

In all cases, simple relationship between current, ***J***, and ρ exists:

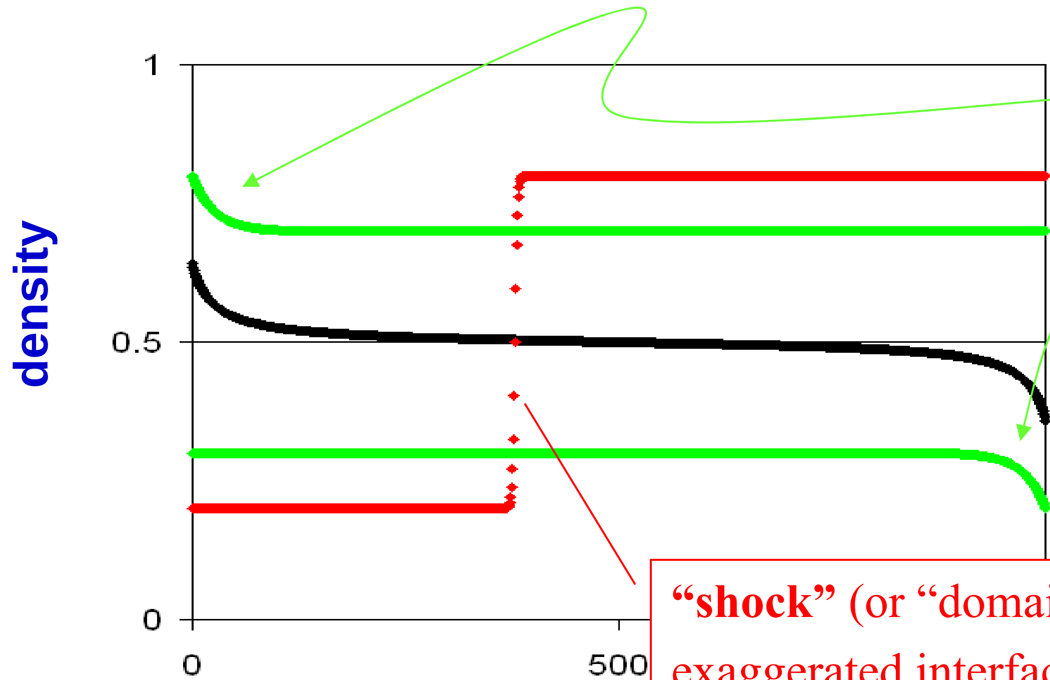
$$\boldsymbol{J}^* = \rho^* \rho^*_h = \rho^*(1-\rho^*)$$

where $\rho^*_h \equiv$ *hole* density $= 1 - \rho^*$

(exact, though MF-like)

The Open TASEP

Typical profiles: *MC*, *HD*/*LD*, and *SP*



exaggerated tails, typically O(1)

"tangent"

"shock" (or "domain wall") :
exaggerated interface width, typically O(1);
wanders randomly ⇔ linear *average* profile

Much, much more is known exactly. See, e.g., review by G. Schütz (2000).

TASEP for protein synthesis

- TASEP is, literally, "simple" and misses many ingredients (essential or otherwise) of protein synthesis:
- Essential ones studied so far:
  - extended objects: ribosomes are large; ℓ-exclusion
  - inhomogeneous hopping rates: codes related to tRNA and so, to relative concentrations of aa-tRNA; $\{\gamma_i\}$
- Here, another possibly essential one…

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Effects of finite resources

The supply of ribosomes in a cell is finite!

All mRNA's compete for this resource.

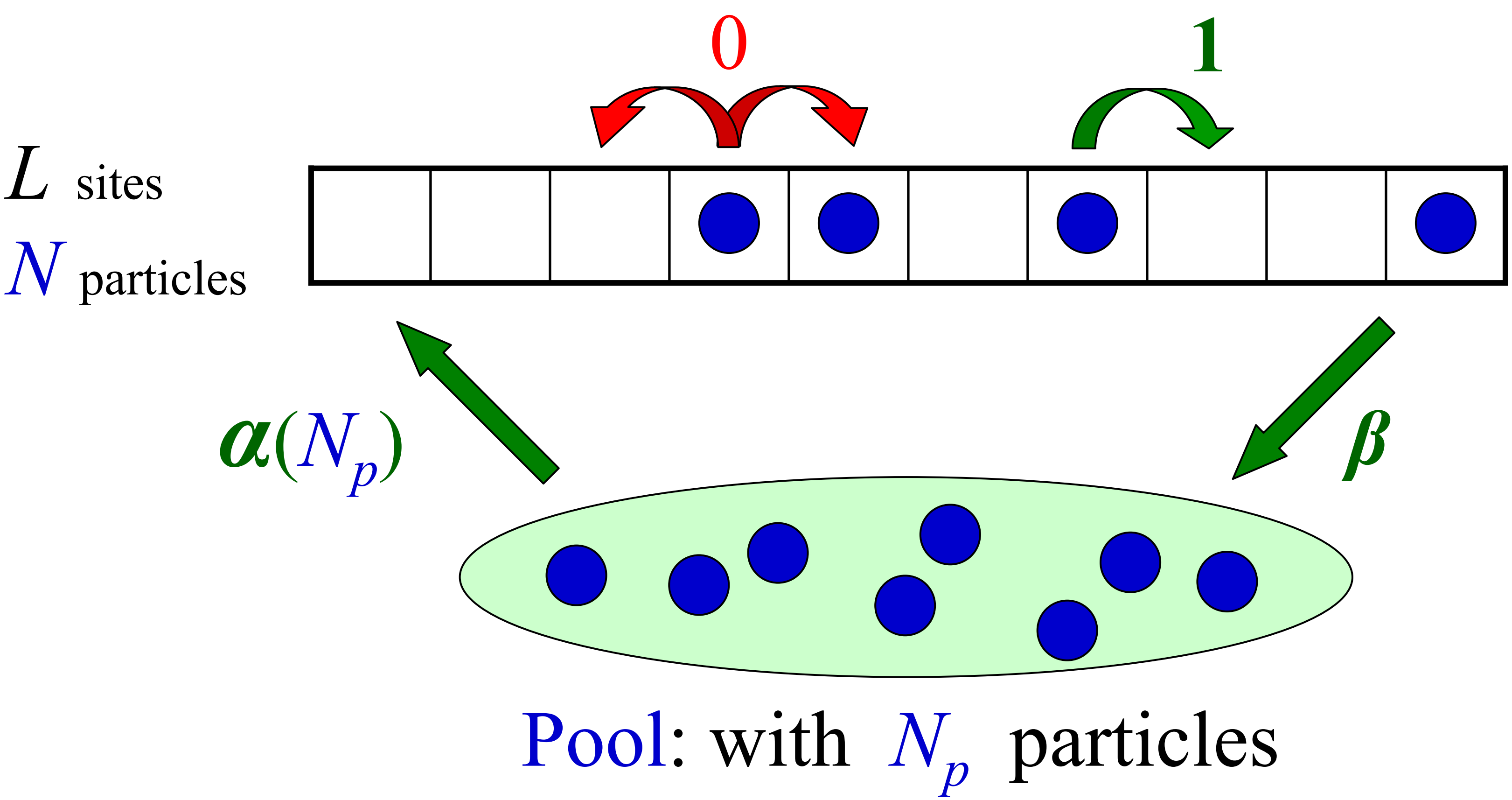
- Who "wins" and who "loses"?
- Should study many TASEP's competing for a pool of particles.

But, to begin with,

How does this affect a ***single*** TASEP?

Constrained TASEP

Adams, Schmittmann, Zia, *JSTAT* P06009 (2008)



"Recycling" of ribosomes, but…diffusion within cell ignored.

Constrained TASEP

ASZ, *JSTAT* P06009 (2008)

$$N_{tot} = N + N_p$$

is a ***fixed*** number of particles in the system

(ribosomes in the cell)

We chose $\alpha(N_p) = \alpha \, \boldsymbol{tanh}(N_p / N_\times)$

…numbers in TASEP feeds back to "on-rate", via $N_{tot} - N$

Some crossover scale, chosen as $\rho^* L$

so that we can "see" an effect easily.

An intrinsic "on (initiation) rate", if the supply were unlimited.

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Constrained TASEP

ASZ, *JSTAT* P06009 (2008)

- Can be thought of as TASEP on a ***ring*** with a special site (say, $i = 0$: "pool", "garage"), where…
- …there is no exclusion (n_0 arbitrary), but the jump rate to the next site ($i = 1$) depends on n_0 (which is $\equiv N_p$).

Constrained TASEP

ASZ, *JSTAT* P06009 (2008)

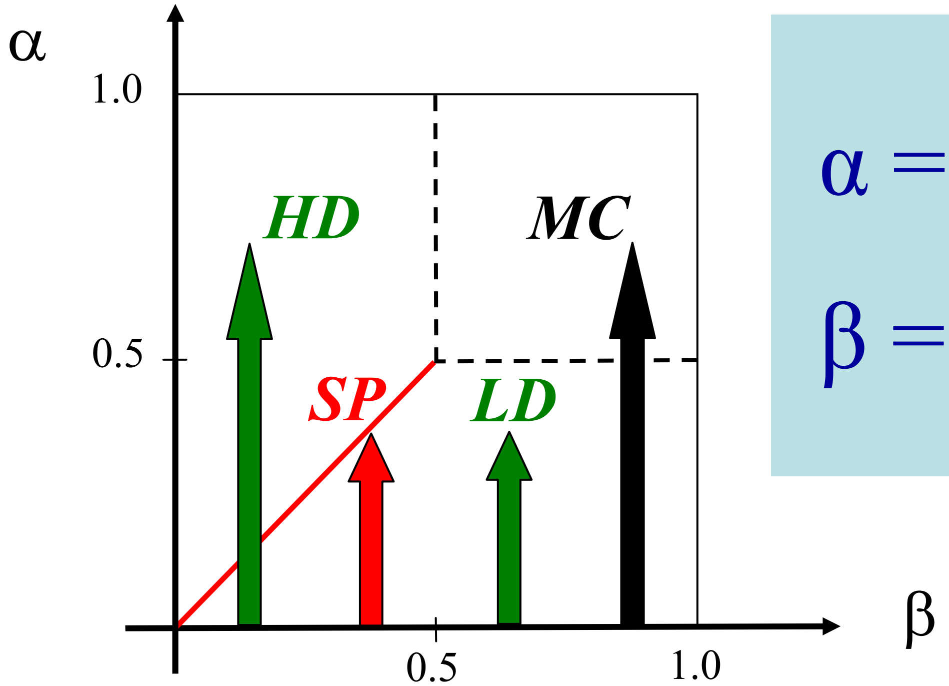
- Summary of parameters and fixed choices:
  - L, α, β, N_{tot}
  - $N_{\times}$ (=ρ*L) , *tanh* function
- Regions studied: *MC*, *HD*, *LD*
- Quantities of interest, as N_{tot} is varied:
  - steady state current: ***J*** (~ protein levels in a cell)
  - total occupancy: N *or* $\rho \equiv N/L$

No * here!!!
constrained
TASEP

Constrained TASEP

ASZ, *JSTAT* P06009 (2008)

Since the on-rate varies from 0 to α, the four possibilities are:

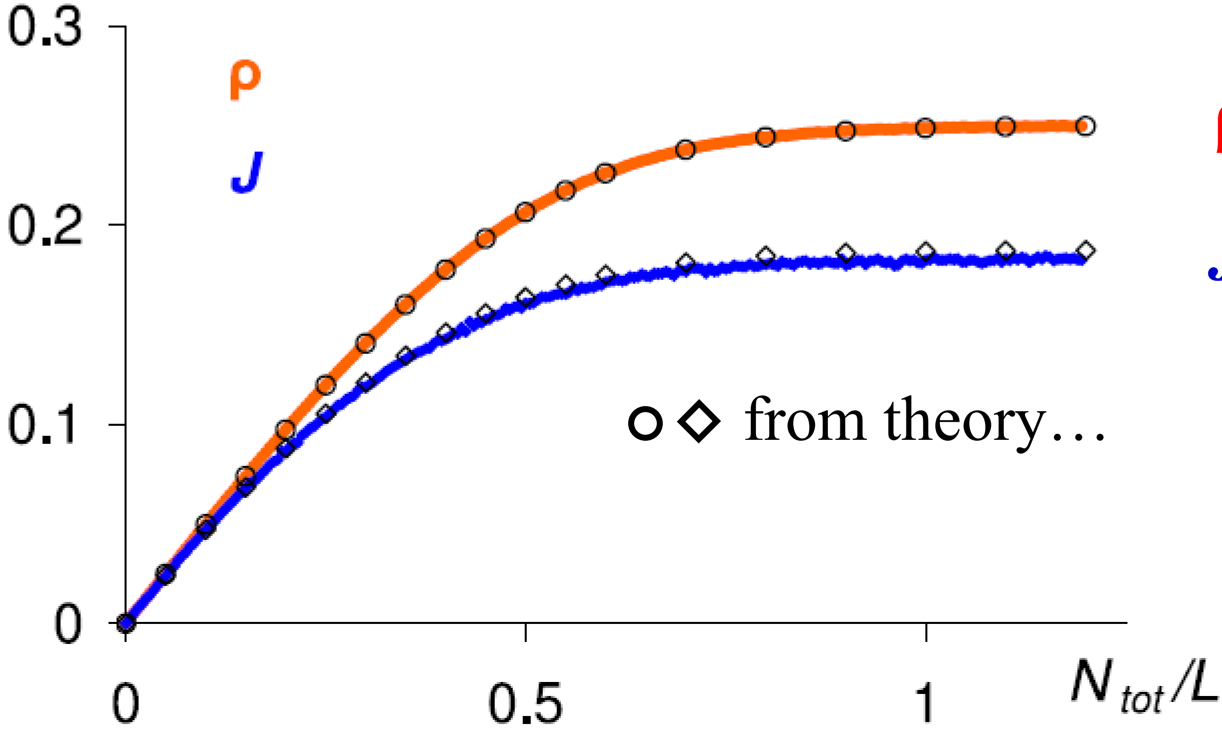


α = 1/4, 3/4

β = 1/4, 3/4

Constrained TASEP: *LD*

ASZ, *JSTAT* P06009 (2008)



$\rho^* = 0.25$

$J^* = \rho^*(1-\rho^*)$

***LD*:** α=1/4, β=3/4, L=1000, $N_\times/L$=0.25

Constrained TASEP: *LD*

ASZ, *JSTAT* P06009 (2008)

- In ordinary *LD* TASEP, we have $\rho^* = \alpha;\ N_\times = \alpha L$
- Set self-consistent condition:

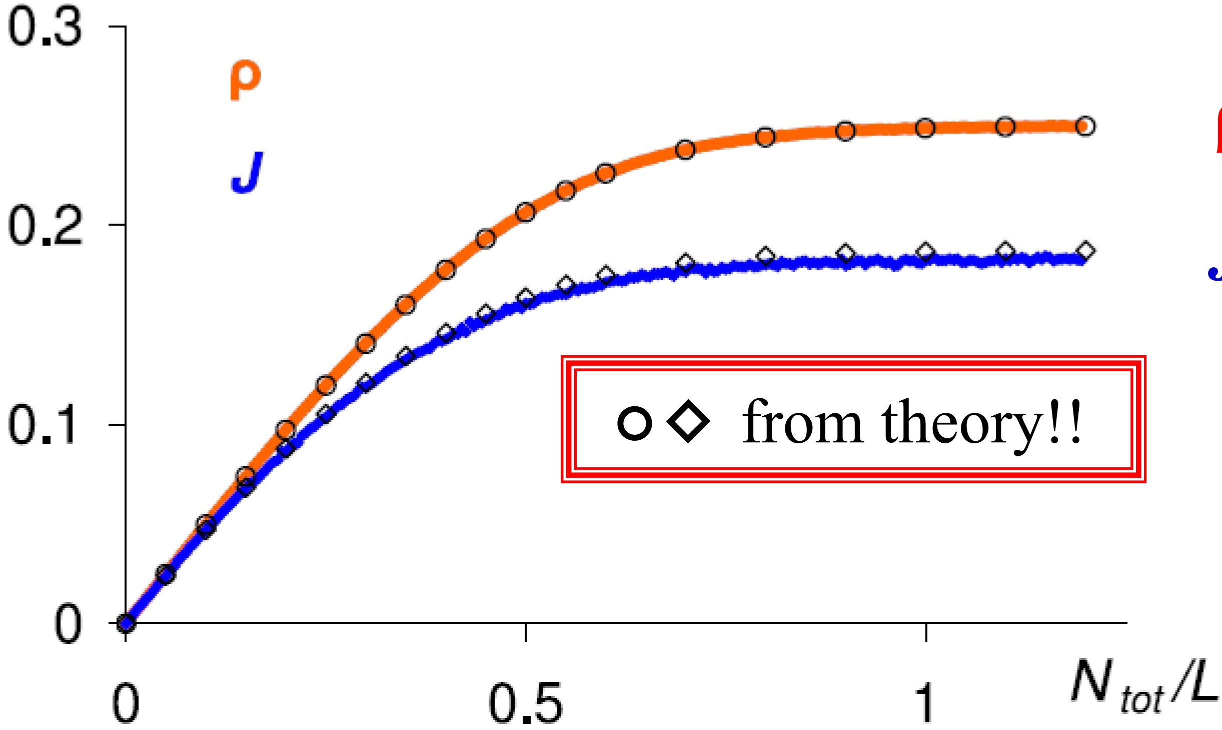
$$\rho/\alpha = tanh(\rho_{tot}/\alpha - \rho/\alpha)$$

$$\rho \rightarrow \begin{cases} \rho_{tot}/2 & \rho_{tot} \rightarrow 0 \\ \alpha & \rho_{tot} \rightarrow \infty \end{cases}$$

- Current from the usual: $\boldsymbol{J} = \rho(1-\rho)$

Constrained TASEP: *LD*

ASZ, *JSTAT* P06009 (2008)



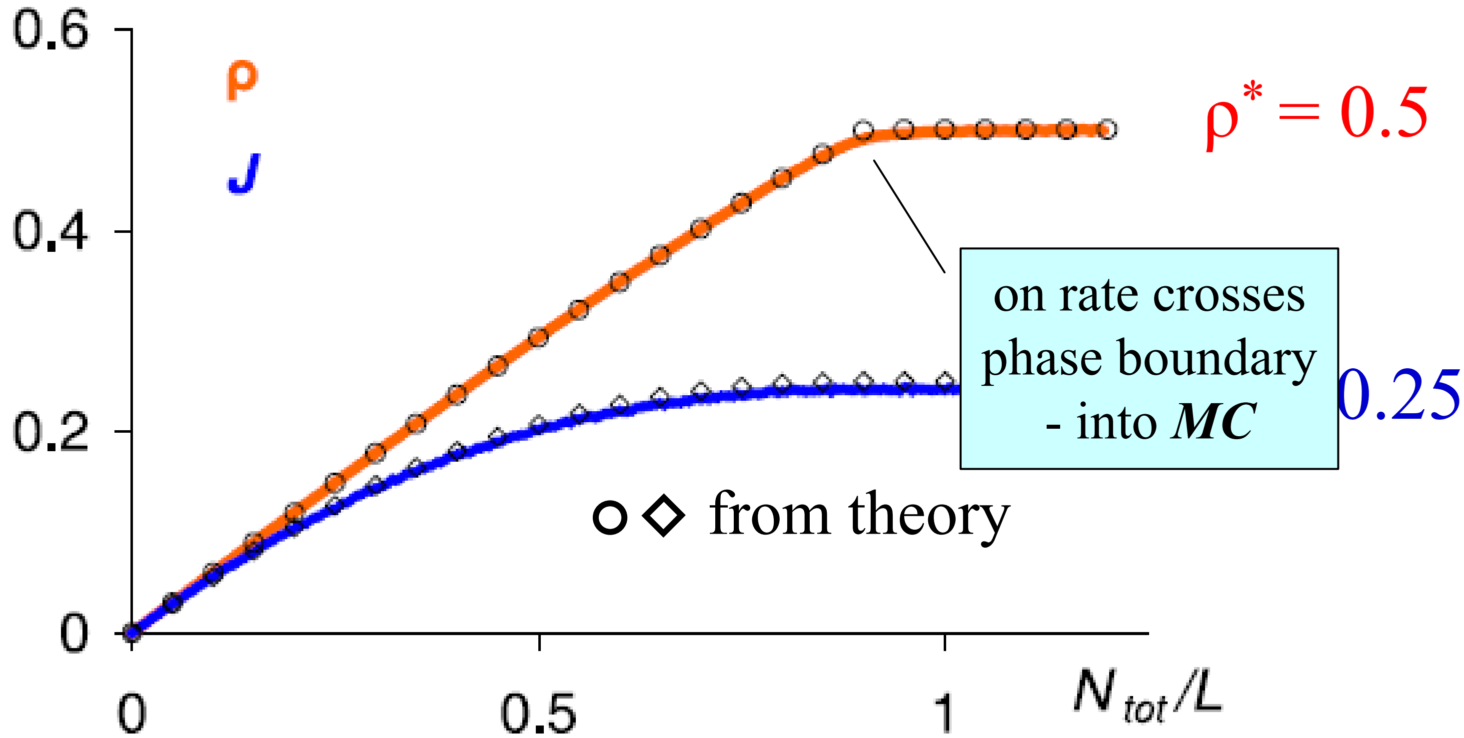
$\rho^* = 0.25$

$J^* = \rho^*(1-\rho^*)$

***LD*:** α=1/4, β=3/4, L=1000, $N_\times/L$=0.25

Constrained TASEP: ***MC***

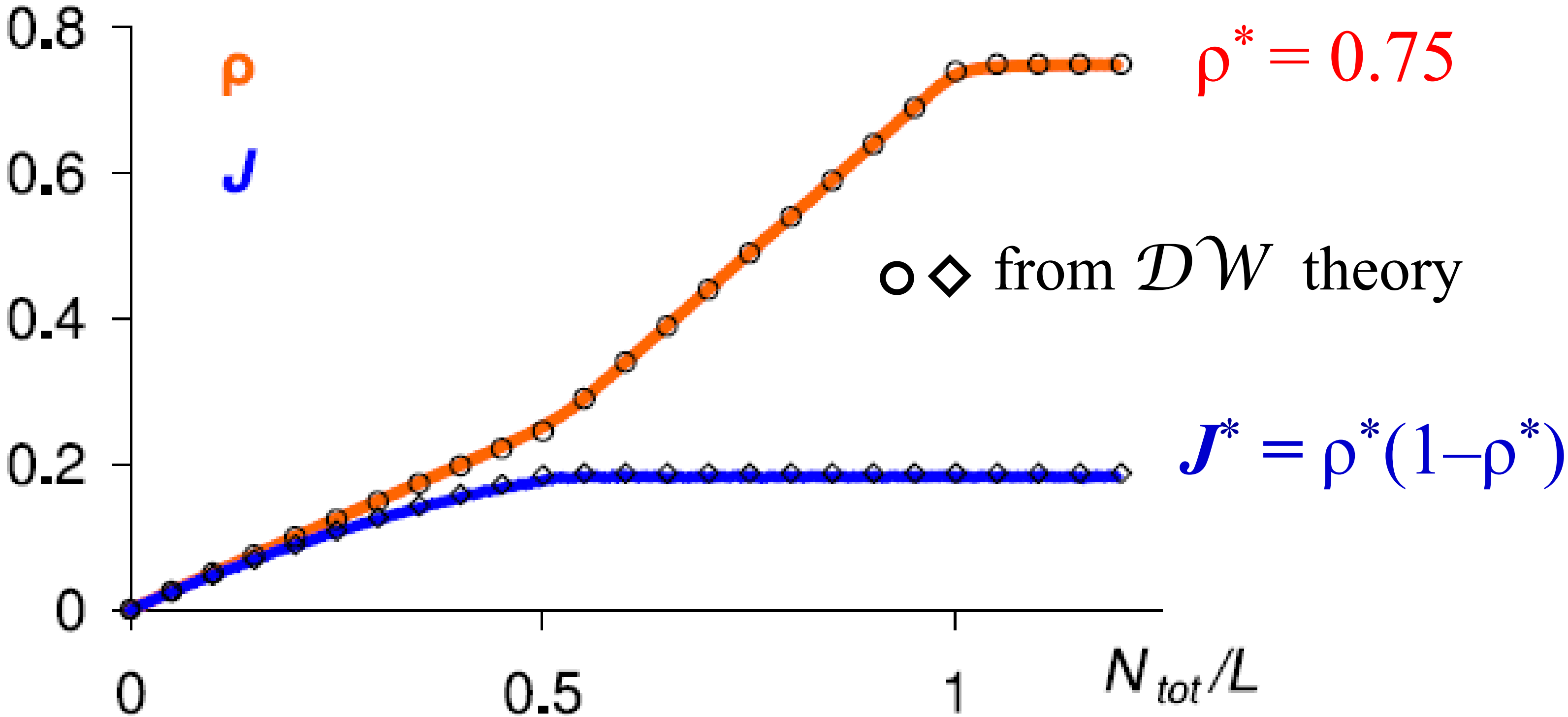
ASZ, *JSTAT* P06009 (2008)



MC**:** $\alpha=3/4$, $\beta=3/4$, $L=1000$, $N_\times/L=0.5$

Constrained TASEP: ***HD***

ASZ, *JSTAT* P06009 (2008)



Why *two* kinks for ρ ? but only *one* for ***J*** ?

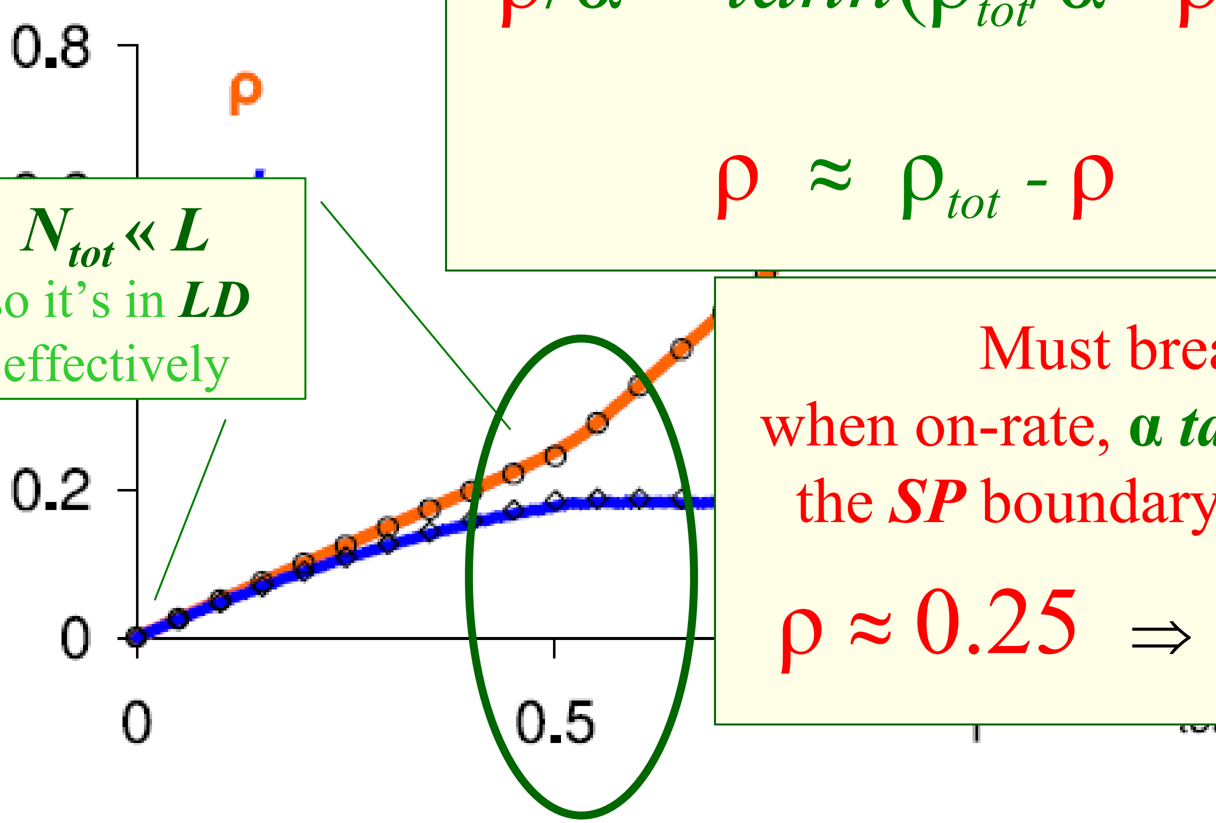
(when crossing only one phase boundary)

75

Constrained TASEP: ***HD***

$$\rho/\alpha = tanh(\rho_{tot}/\alpha - \rho/\alpha)$$

$$\rho \approx \rho_{tot} - \rho$$



N**$_{tot}$* « ***L
so it's in ***LD***
effectively

Must breakdown
when on-rate, **α *tanh*(…)**, reaches
the ***SP*** boundary: β = 0.25, i.e.,

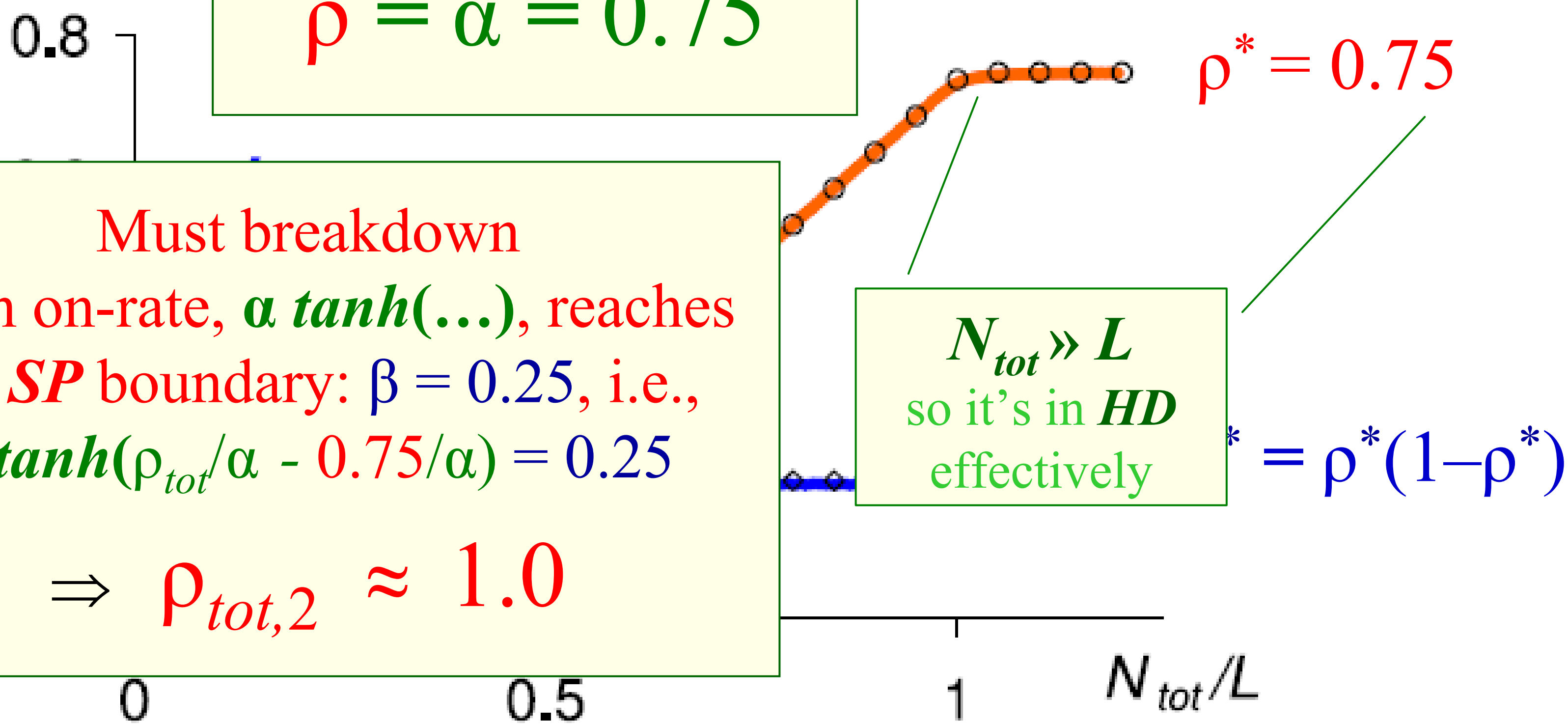
$$\rho \approx 0.25 \;\Rightarrow\; \rho_{tot,1} \approx 0.5$$

***HD*:** α=3/4, β=1/4, *L*=1000, $N_{\times}/L$=0.75

Constrained TASEP: ***HD***

ASZ, *JSTAT* P06009 (2008)

$\rho = \alpha = 0.75$



Must breakdown
when on-rate, **α *tanh*(…)**, reaches
the ***SP*** boundary: $\beta = 0.25$, i.e.,
$\boldsymbol{\alpha}\ \textbf{\textit{tanh}}(\rho_{tot}/\alpha - 0.75/\alpha) = 0.25$

$\Rightarrow \rho_{tot,2} \approx 1.0$

$N_{tot} \gg L$
so it's in ***HD***
effectively

***HD*:** $\alpha=3/4$, $\beta=1/4$, $L=1000$, $N_{\times}/L=0.75$

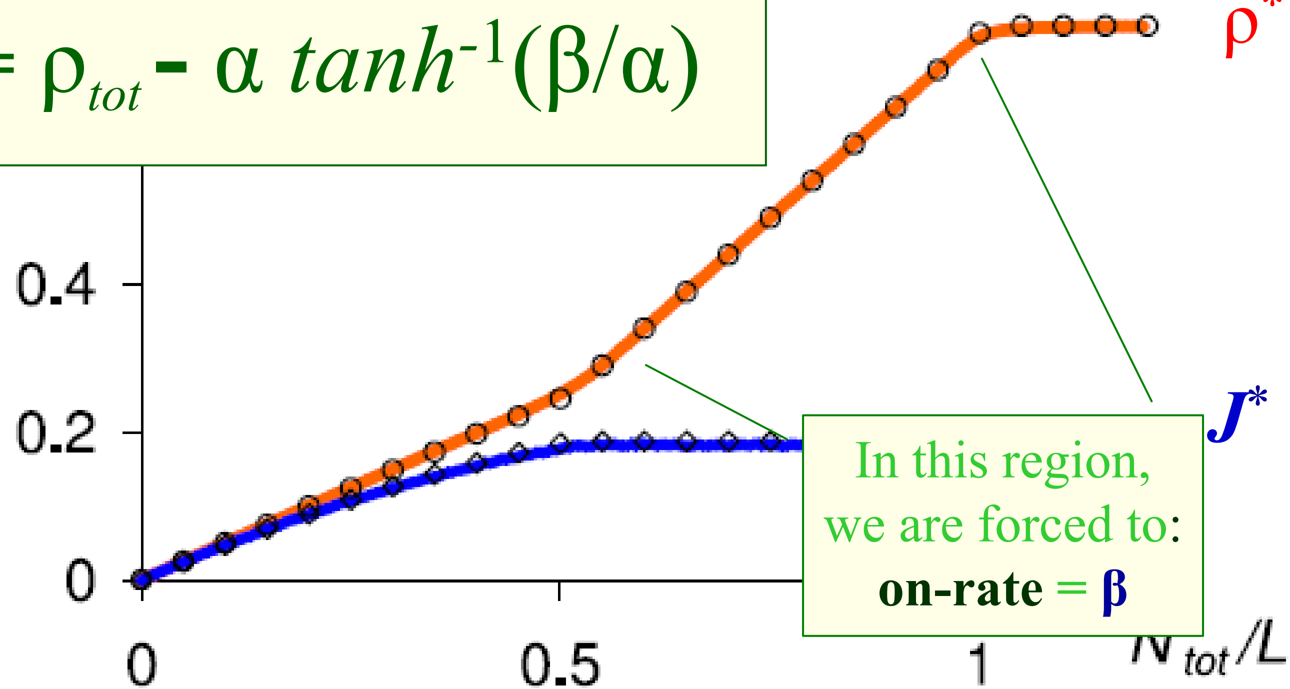
TASEP: ***HD***

009 (2008)

$$\alpha\, tanh(\rho_{tot}/\alpha - \rho/\alpha) = \beta$$

$\Rightarrow$ *linear relationship*!

$$\rho = \rho_{tot} - \alpha\, tanh^{-1}(\beta/\alpha)$$



$\rho^* = 0.75$

$J^* = \rho^*(1-\rho^*)$

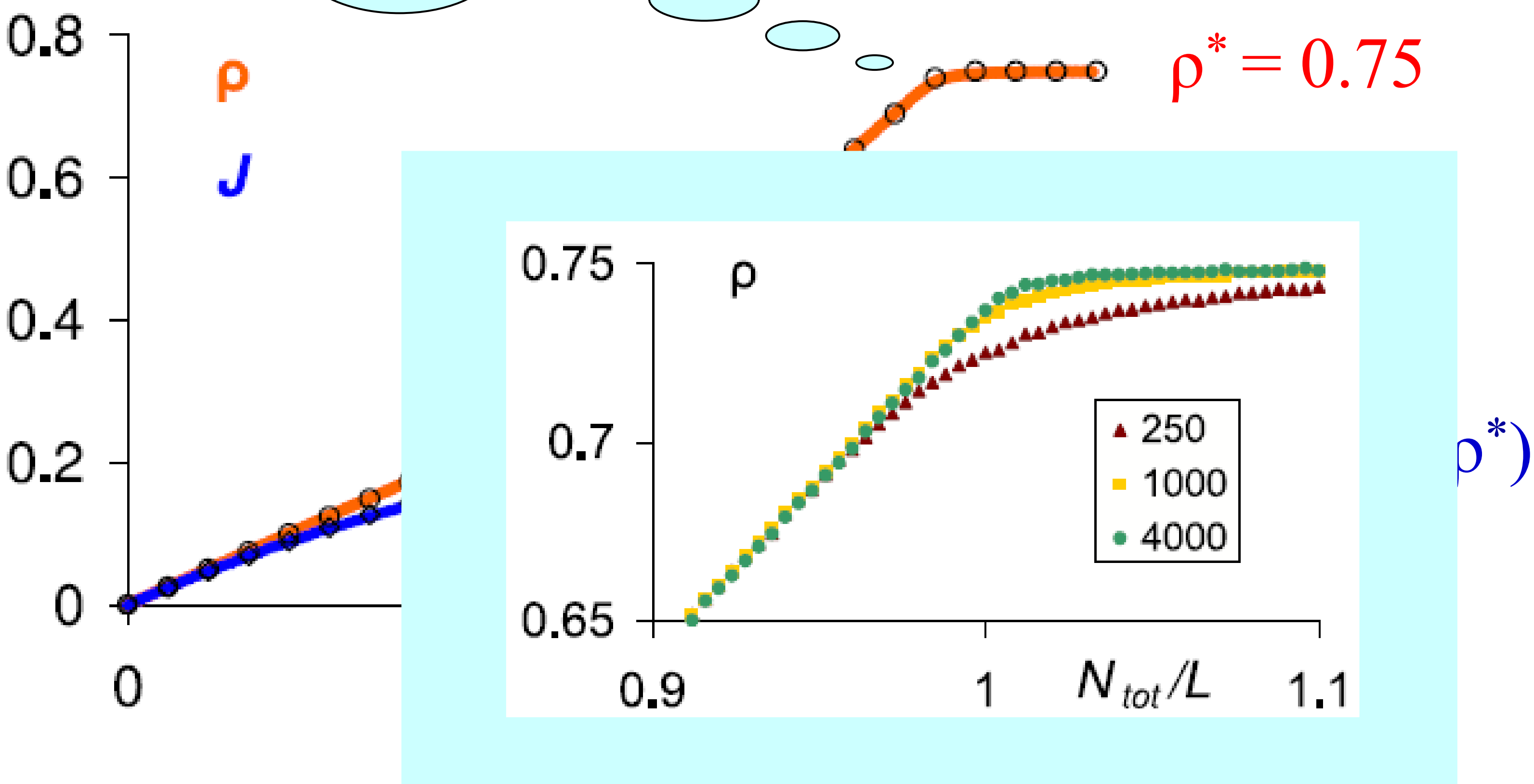
In this region, we are forced to: **on-rate** = β

HD: α=3/4, β=1/4, L=1000, $N_\times/L$=0.75

C … TASEP: *HD*

Finite size rounding

…5009 (2008)



HD: α=3/4, β=1/4, *L*=1000, $N_\times/L$=0.75

Constrained TASEP: *SP*

ASZ, *JSTAT* P06009 (2008)

Two cross-overs!

Most challenging…

Need very large N_{tot}'s to get to asymptotic average $\rho = 0.5$

and

No simple minded theory produces this!

$\rho^* = 0.5$

n $\mathcal{DW}$ theory

$\boldsymbol{J}^* = (1/4)(3/4)$

N_{tot}/L

***SP*:** α=1/4, β=1/4, L=1000, $N_\times/L$=0.5

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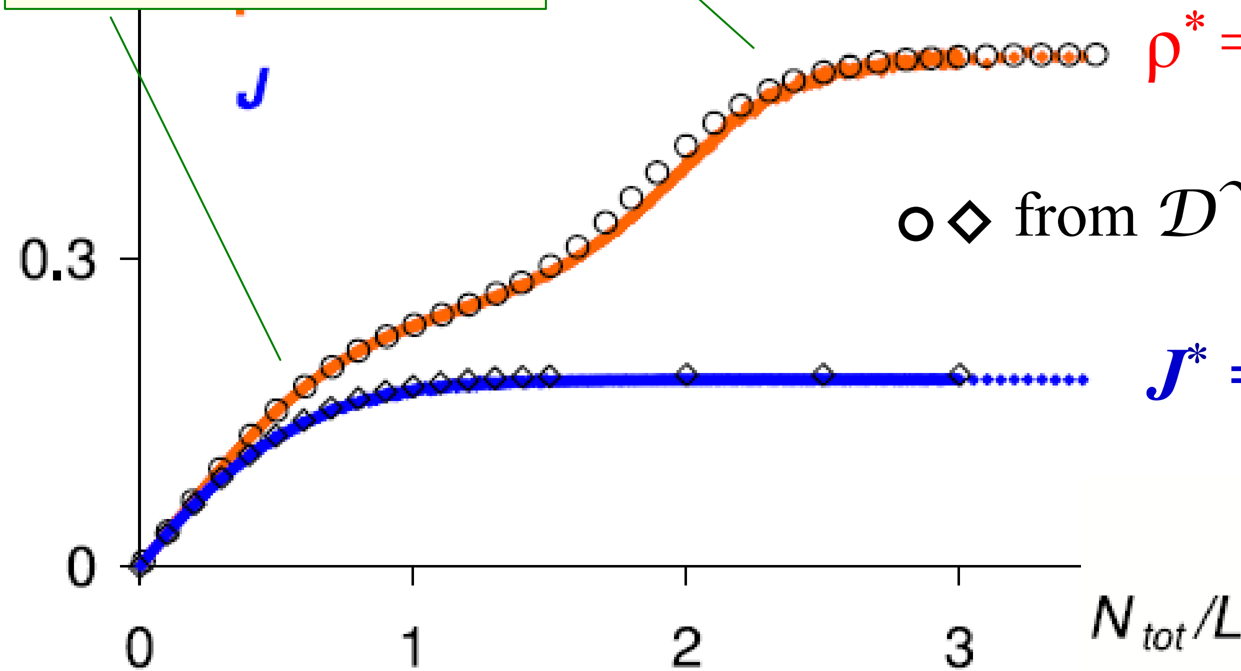
Constrained TASEP: ***SP***

ASZ, *JSTAT* P06009 (2008)

Two cross-overs!
Second ***depends*** on *L*



$\rho^* = 0.5$

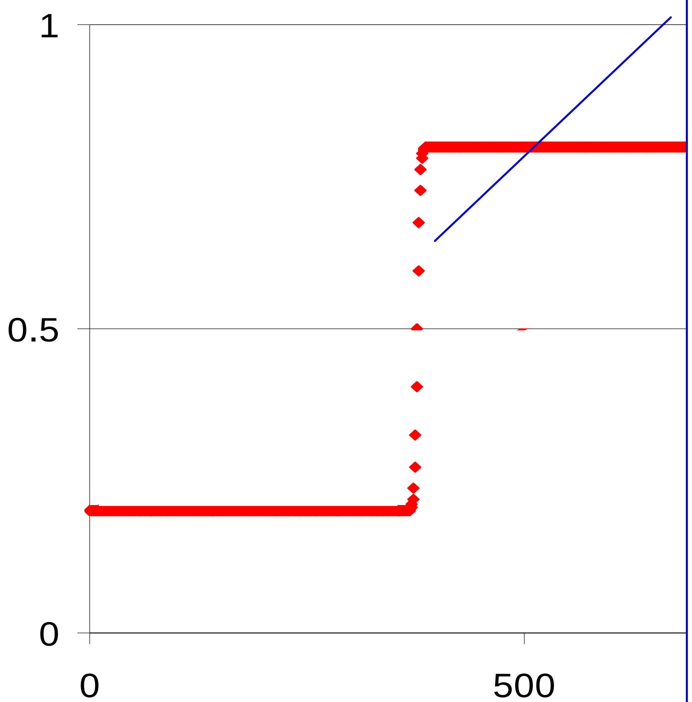
○ ◇ from $\mathcal{DW}$ theory

$J^* = (1/4)(3/4)$

***SP*:** α=1/4, β=1/4, L=1000, $N_\times/L$=0.5

Domain Wall Theory

based on Santen+Appert, *JSP* **106**,187 (2002)



"domain wall"

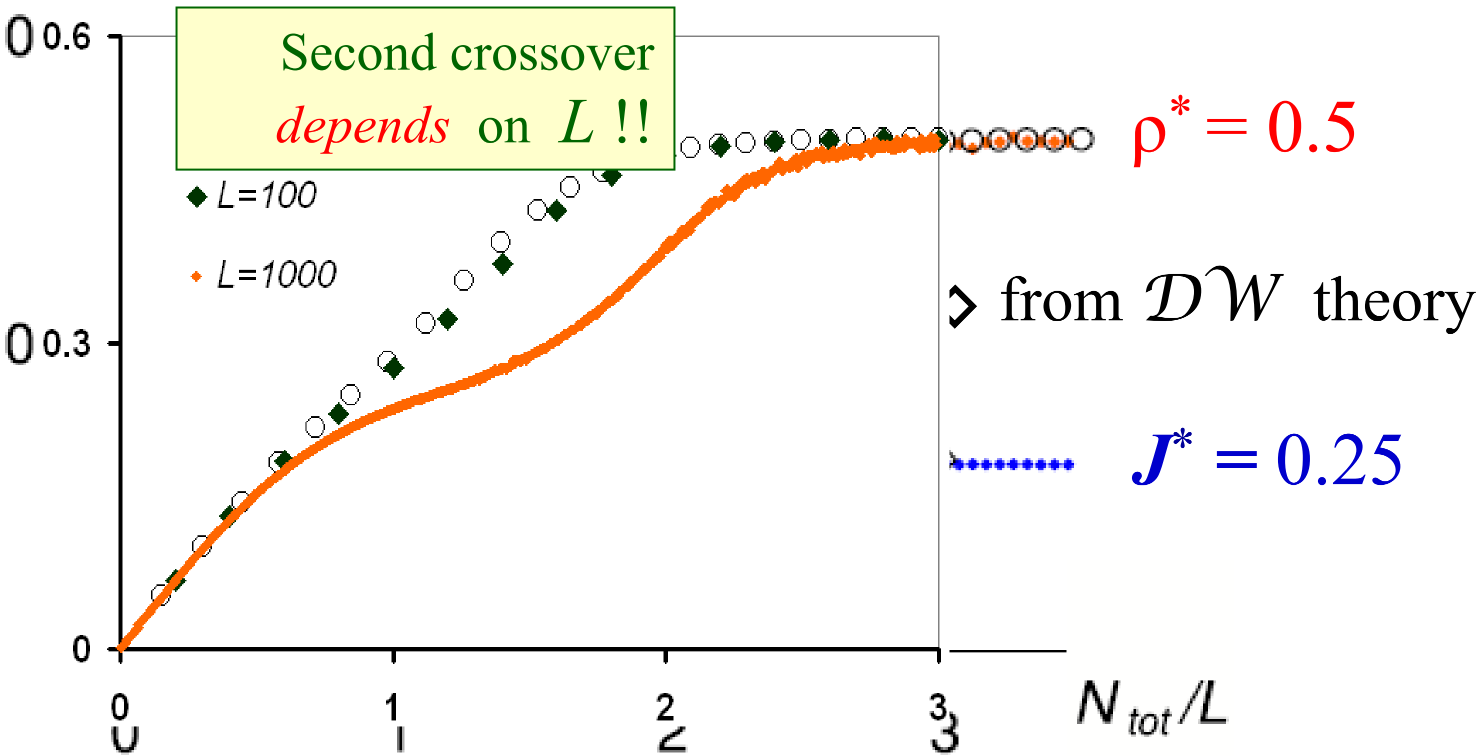
- located at k, but wanders
- driven left/right by currents via α/β

for domain wall theory

- write drift in terms of α,β
- write master eqn for $P(k,t)$
- steady state solution is simple *exp*
- get $<N>$ in terms of **α *tanh*(…)** and β
- replace N in (…) by $<N>$, then
- solve self consistent eqn for $<N>$

Constrained TASEP: ***SP***

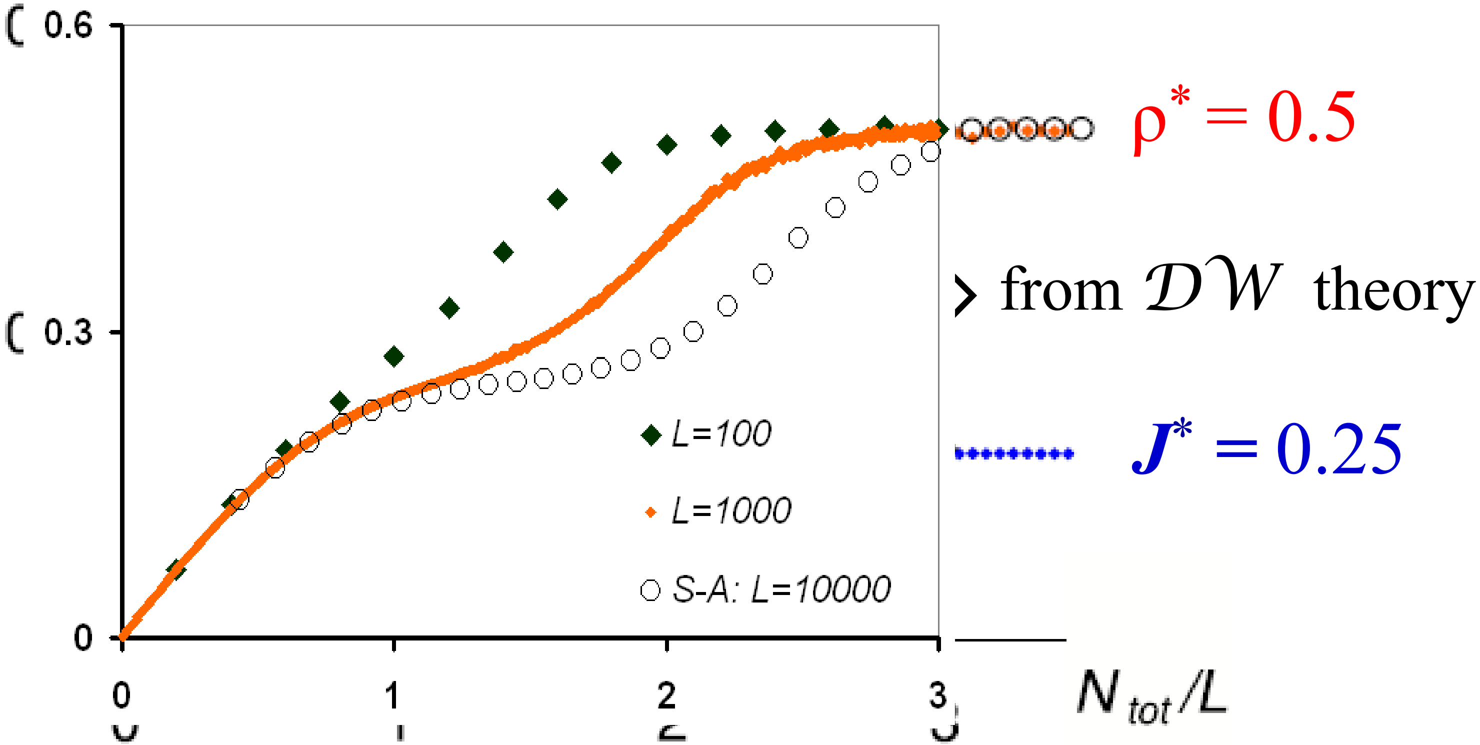
ASZ, *JSTAT* P06009 (2008)



***SP*:** α=1/4, β=1/4, L=1000, $N_{\times}/L$=0.5

Constrained TASEP: ***SP***

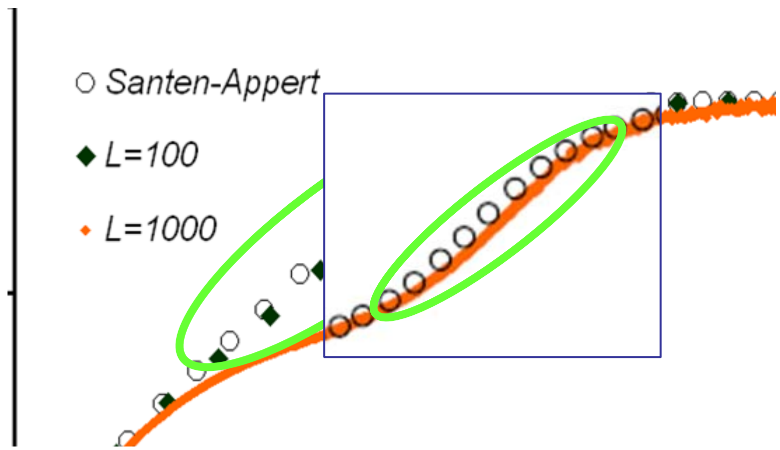
ASZ, *JSTAT* P06009 (2008)



***SP*:** α=1/4, β=1/4, L=1000, $N_\times/L$=0.5

Constrained TASEP: ***SP***

ASZ, *JSTAT* P06009 (2008)



- Such small disagreements seem trivial…

Constrained TASEP: ***SP***

CZ, *JSTAT* P02012 (2009)

- Fluctuations are clearly important for ***SP***
- …but they must be ***suppressed*** by the overall constraint.
- Suppression comes about through the feedback mechanism, i.e., $\boldsymbol{\alpha}(N_{tot} - N)$
- Can see this even in the *LD* regime: Gaussians of $P(N)$ have narrower widths.
- Closer to *SP*, it leads to ***shock localization***.

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Constrained TASEP: ***HD SP***

CZ, *JSTAT* P02012 (2009)

- Generalize DW to account for feedback…

$$\partial_t P(k,t) = D_+ P(k-1,t) + D_- P(k+1,t) - (D_+ + D_-) P(k,t)$$

plus ***reflecting*** boundary conditions

$$D_+ = \frac{j_+}{\rho_+ - \rho_-} = \frac{\beta(1-\beta)}{1-\beta-\alpha}$$

$$D_- = \frac{j_-}{\rho_+ - \rho_-} = \frac{\alpha(1-\alpha)}{1-\beta-\alpha}.$$

position of DW: $\in [1, L]$

Constrained TASEP: ***HD SP***

CZ, *JSTAT* P02012 (2009)

- Generalize DW to account for feedback by
- a simple approximation:
- Promote

$$\boldsymbol{\alpha}(N_{tot} - \langle N \rangle) \Rightarrow \boldsymbol{\alpha}(N_{tot} - N)$$

- Relate N to k, the DW position
- Have k dependent drift coefficients

Constrained TASEP: *HD* *SP*

CZ, *JSTAT* P02012 (2009)

$$\alpha_{\text{eff}} = \alpha \tanh\left[\left(\rho_{\text{tot}} - \rho_{-}\left(k/L\right) - \rho_{+}\left(1-k/L\right)\right)/\alpha\right] \qquad \Rightarrow$$

$$\alpha_{\text{eff},k} = \alpha \tanh\left[\left(\rho_{\text{tot}} - \alpha_{\text{eff},k}\left(k/L\right) - \left(1-\beta\right)\left(1-k/L\right)\right)/\alpha\right].$$

This self consistent equation is solved (numerically) to arrive at the k dependence in $\alpha_{\text{eff},k}$

… and inserted into

$$D_{+,k} = \frac{\beta(1-\beta)}{1-\beta-\alpha_{\text{eff},k}}$$

$$D_{-,k} = \frac{\alpha_{\text{eff},k}(1-\alpha_{\text{eff},k})}{1-\beta-\alpha_{\text{eff},k}}.$$

These are then inserted into the master equation:

Constrained TASEP: ***HD SP***

CZ, *JSTAT* P02012 (2009)

$$\partial_t P(k) = D_{+,k-1}P(k-1) + D_{-,k+1}P(k+1) - (D_{+,k} + D_{-,k})P(k)$$

$$P^*(k) = \left(\sum_{m=k_{\min}}^{k-1} \prod_{\ell=m+1}^{k} \frac{D_{-,\ell}}{D_{+,\ell-1}} + 1 + \sum_{m=k+1}^{L} \prod_{\ell=k+1}^{m} \frac{D_{+,\ell-1}}{D_{-,\ell}} \right)^{-1}.$$

Apart from minor complications, ***P****(***k***), the stationary distribution can be found easily via:

$$P^*(k) \propto \prod_{l=k}^{L-1} \frac{D_{-,\ell+1}}{D_{+,\ell}}$$

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Constrained TASEP: ***HD SP***

CZ, *JSTAT* P02012 (2009)

$$\partial_t P(k) = D_{+,k-1}P(k-1) + D_{-,k+1}P(k+1) - (D_{+,k} + D_{-,k})P(k)$$

$$P^*(k) = \left(\sum_{m=k_{\min}}^{k-1} \prod_{\ell=m+1}^{k} \frac{D_{-,\ell}}{D_{+,\ell-1}} + 1 + \sum_{m=k+1}^{L} \prod_{\ell=k+1}^{m} \right.$$

NB: In this approximation, it's a weighted integral over *P** .

$$\rho_i = \sum_{k=k_{\min}}^{i} (1-\beta)P^*(k) + \sum_{k=i+1}^{L} \alpha_{\mathrm{eff},k} P^*(k)$$

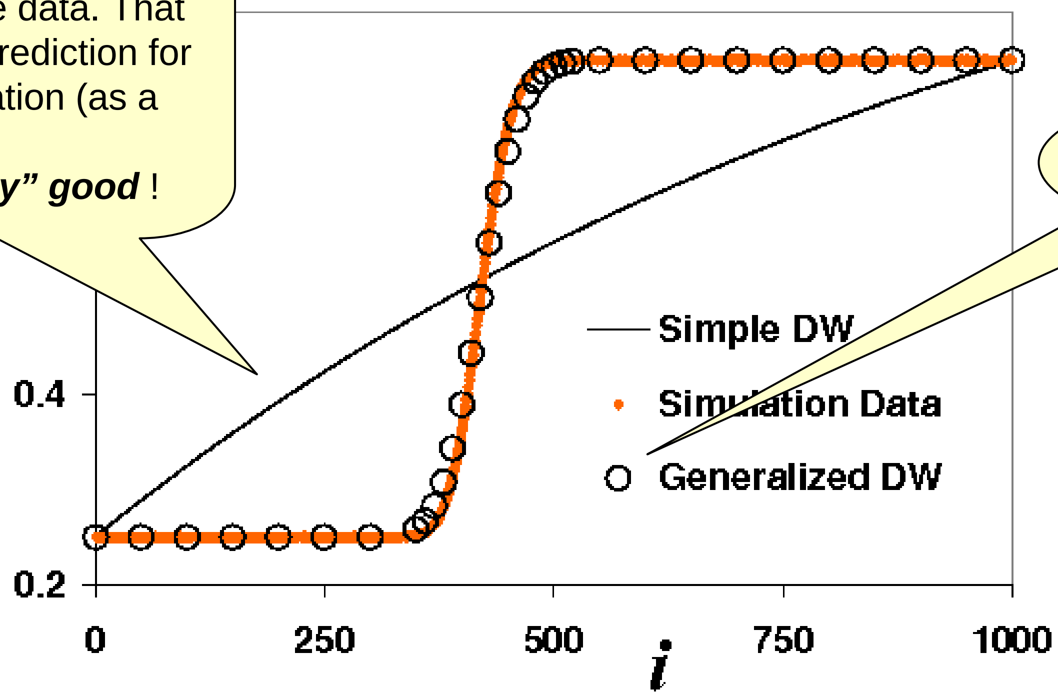
From here, we can find the density profile $\boldsymbol{\rho_i}$ …

Constrained TASEP: ***HD***

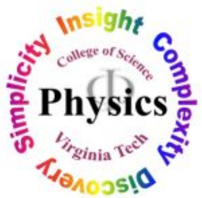
CZ, *JSTAT* P02012 (2009)

The area under this curve is close to that of the data. That is why the SDW prediction for the overall occupation (as a function of N_{tot}) is ***“deceptively” good*** !

This is a zero parameter fit !



This GDW theory captures the essence of ***shock localization.***



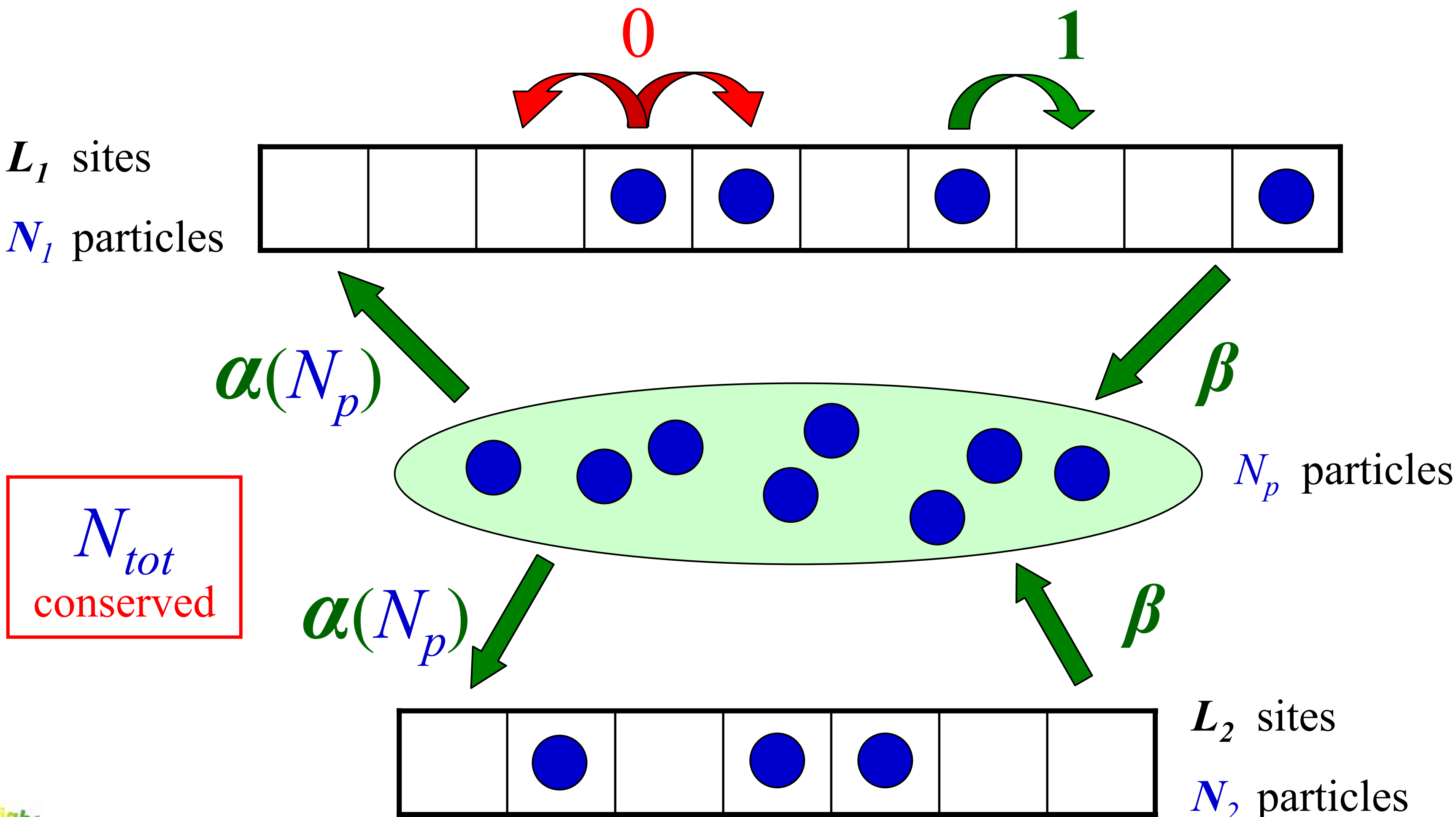
Constrained ***single*** TASEP

- Generalized DW theory is excellent at predicting properties of the stationary state.
- Dynamics remains more challenging, e.g., new puzzles associated with the Power Spectrum of $N(t)$.

…any questions before moving onto competition amongst ***many*** TASEPs?

Constrained two TASEPs

Cook, Zia, Schmittmann, tbp (2009)



Constrained two TASEPs

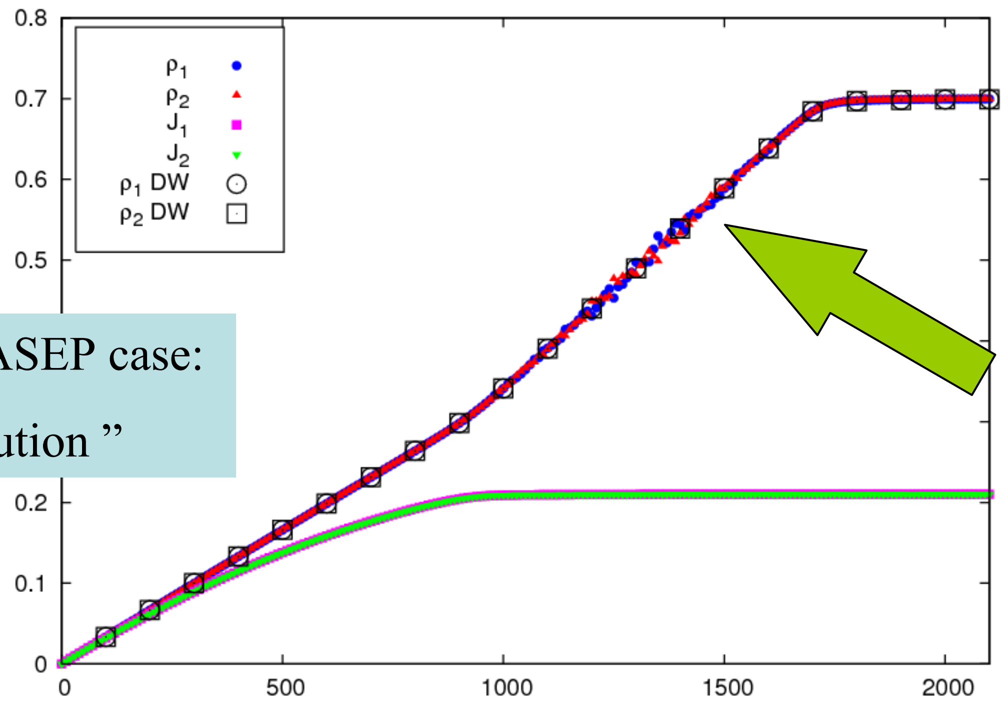
CZS, tbp (2009)

- For $\alpha(N_p)$, keep *tanh* function with $N_\times = \rho^*(L_1+L_2)/2$
- $L_1 = L_2$ not much different from single case...
  - ***except*** for motion (anticorrelated) of DWs
  - de-localization; flat profiles recovered
  - "intrinsic" profile (from shifted averages) unchanged
- $L_1 \neq L_2$ shows new feature...
  - for ***HD***, there are ***five regimes*** as N_{tot} increases
  - smaller chain has a central plateau + 2 crossovers

Constrained two TASEPs

CZS, tbp (2009)

- $L_1 = L_2 = 1000$ ***HD*** with α=0.7, β=0.3



Like single TASEP case:

“ 3 branch solution ”

Constrained two TASEPs

CZS, tbp (2009)

- $L_1 = L_2 = 1000$ ***HD*** with α=0.7, β=0.3
  - ***except*** for motion (anticorrelated) of DWs
  - de-localization; flat profiles recovered
  - "intrinsic" profile (from shifted averages) unchanged

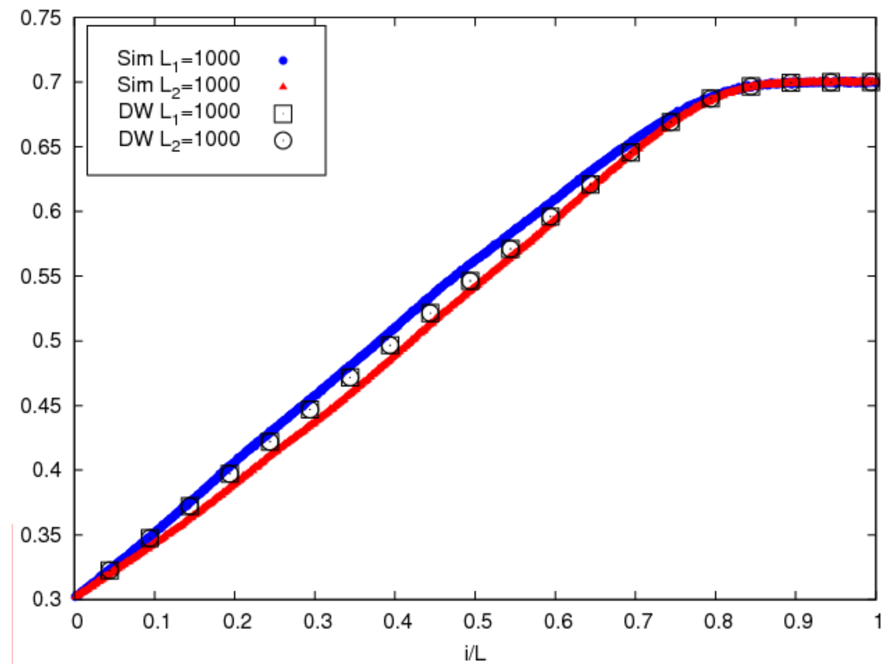
Constrained two TASEPs

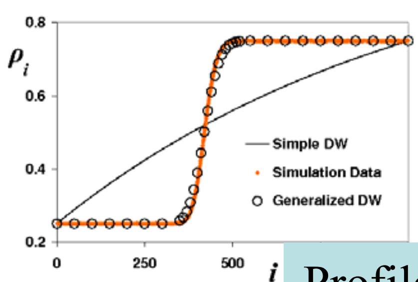
CZS, tbp (2009)

- $L_1 = L_2 = 1000$ ***HD*** with α=0.7, β=0.3
  - ***except***
  - de-loca
  - "intrins unchan

Ws

red



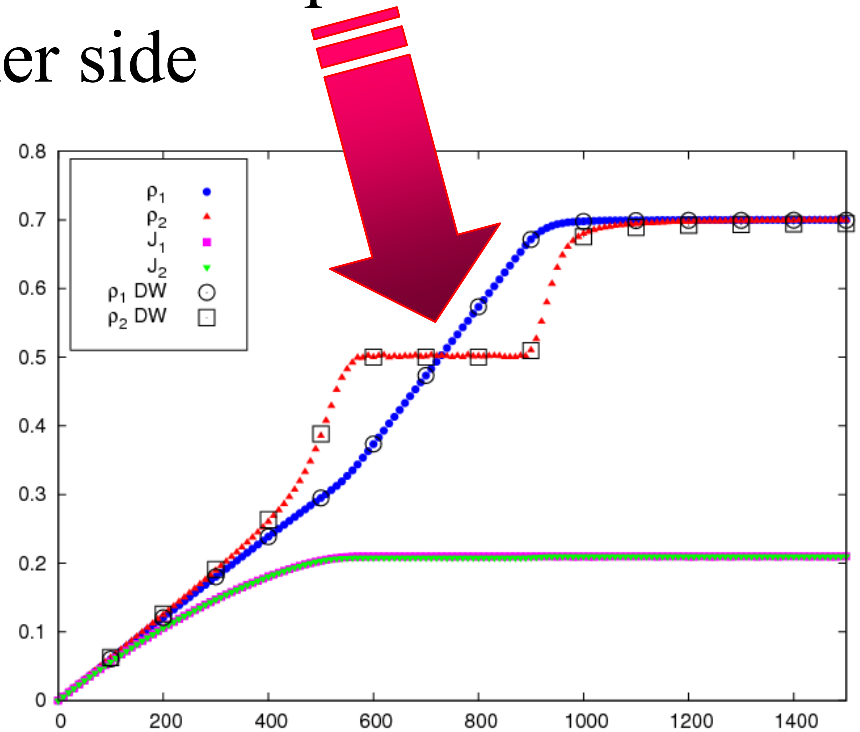


Profile in single TASEP

Constrained two TASEPs

CZS, tbp (2009)

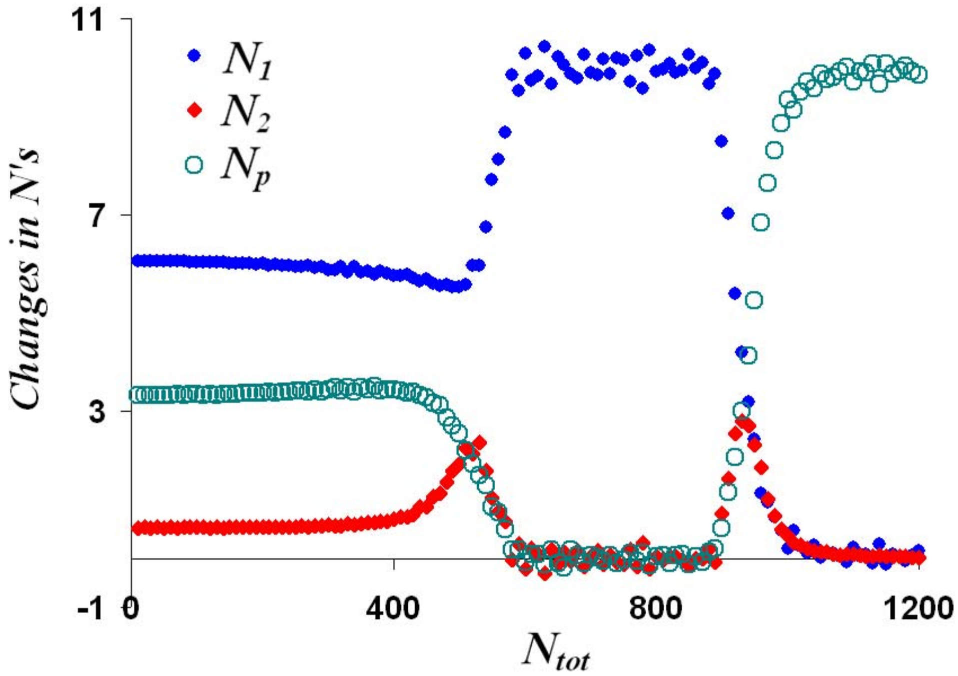
- $L_1 = 10L_2 = 1000$ ***HD*** with α=0.7, β=0.3
  - ***five regimes*** as N_{tot} increases
  - smaller chain has a "central plateau" and crossovers on either side



Constrainec

CZS

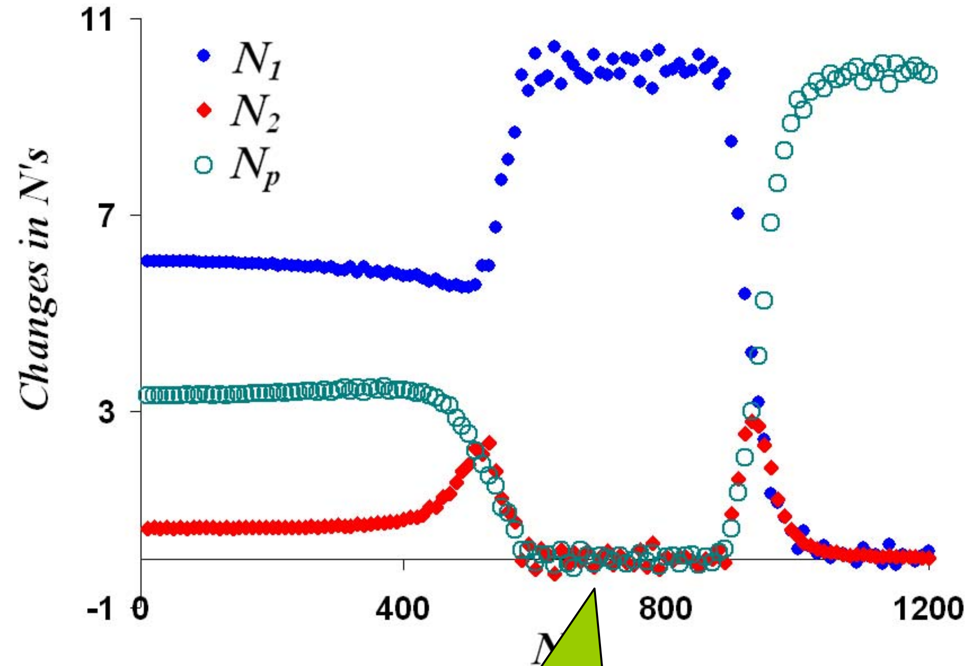
- $L_1 = 10L_2 = 1000$
  - ***five regimes*** as *N*
  - smaller chain ha crossovers
  - highlight via $dN_{1,2,p}/dN$
  - TWO mechanisms for shock de/localization (feedback vs. competition); profiles very different
  - *rough* intuitive picture for new feature
  - *excellent* DW theory for two TASEPs

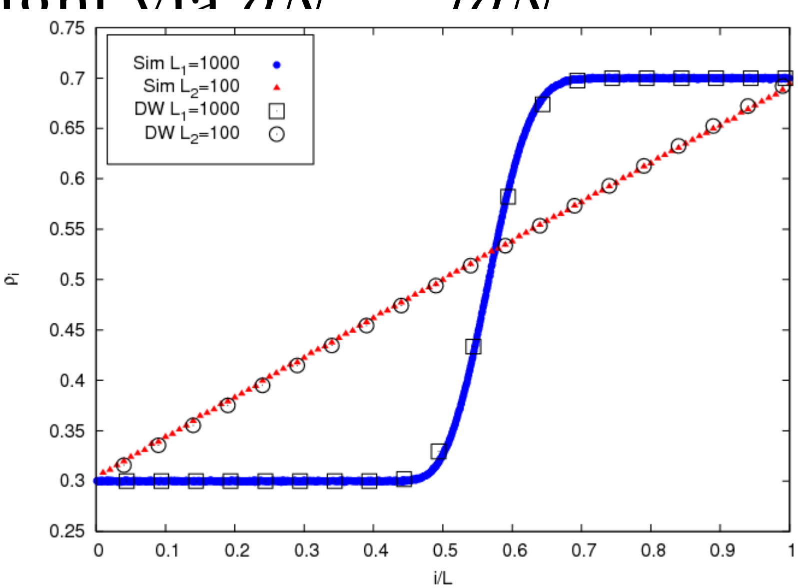


Constrainec

CZS

- $L_1 = 10L_2 = 1000$
  - *five regimes* as *N*
  - smaller chain ha crossovers
  - highlight via dN $/dN$
  - TWC localization (feedba different
  - *rougl* eature
  - *excel* SEPs

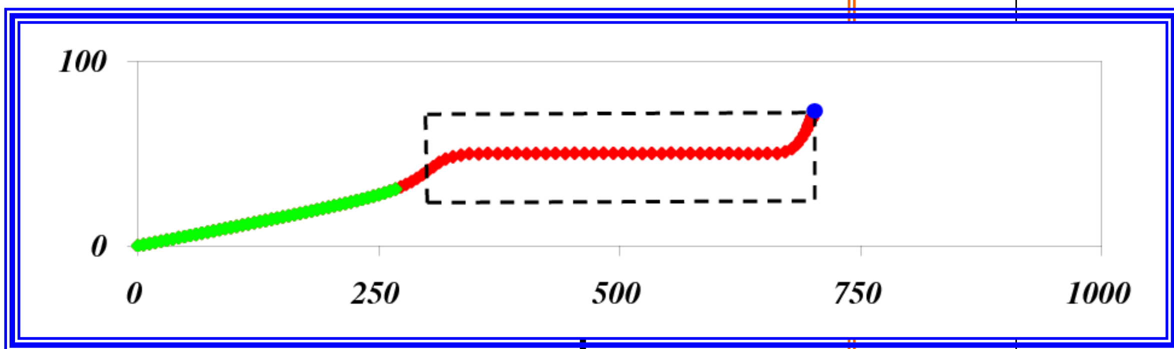


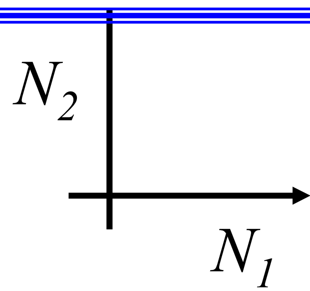


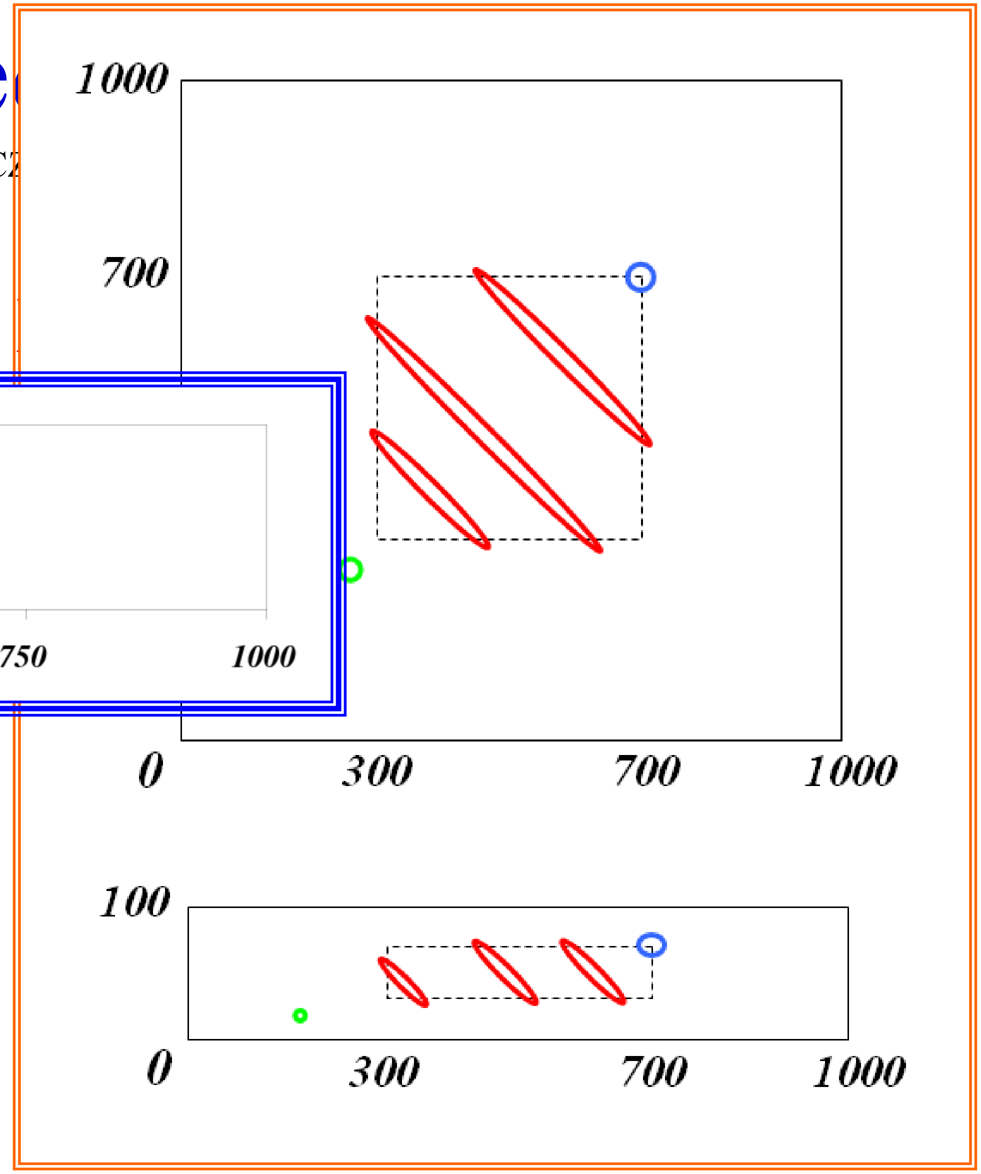
Constraine

CZ

- *Rough* intuitive







Constrained two TASEPs

CZS, tbp (2009)

- *Rough* intuitive picture for new feature
- *Excellent* DW theory for two TASEPs
  - write master equation for $P(k_1, k_2; t)$
  - α_{eff} depends only on N_1+N_2 and so, $K \equiv k_1+k_2$
  - rates in ME satisfy detailed balance
  - stationary $P^*(k_1, k_2)$ "equilibrium-like" and so…
  - exactly solvable (with no fit parameters!)
  - ***predicts*** profiles, overall densities, etc.
  - generalized to ***any number*** of TASEPs

Constrained many TASEPs

CZS, tbp (2009)

- DW theory ***agrees well*** with MC 3 TASEPs
- No qualitatively new features … at least so far!
- Interesting analogy with canonical ensemble
  - – constant K ($\equiv k_1 + k_2 + \ldots + k_M$) sheets have equal P^*
  - – constant E sheets have equal P^* : $E \Leftrightarrow K$?
  - – T controls E $\Leftrightarrow$ N_{tot} controls K ?
- If α of various TASEPs differ, then P^* is a genuinely *nonequilibrium* distribution.

$\vdots$

Summary and Outlook

- "Finite resources" provides many new interesting issues for TASEP
- Some aspects understood; but puzzles remain
- Many immediate extensions e.g., extended particles, non-uniform hopping rates, competition for other resources (e.g., aa-tRNA), …
- Further generalizations e.g., multi-species, multi-lanes
- A long way to go, just to describe one cell
- …let alone many cells that make up one living being!

TASEP and its many off-springs,

within the larger context of non-equilibrium statistical mechanics,

provide many exciting opportunities:

- …full of open questions and surprises,
- …with many potentially important applications,
- …and a wide range of ways to get involved

Come and join the party!

D.A. Adams
(now at U. Michigan)

L.J. Cook

The "Partying" Folks