Transcription on Crowded DNA



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Bionanoscience Department Think big about life at the smallest scale



Central dogma of molecular biology



Image from wikipedia.org

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Image from wikipedia.org

DNA has to be both accessible and structured





RNA Polymerase transcribing DNA

DNA and nucleosomes

RNAP can evict nucleosome and nucleosomes are roadblocks for RNAP



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Central questions



1. How do roadblocks like nucleosomes on DNA affect transcription?

2. How do RNAP's affect nucleosome occupancy?

A model for transcription

Totally Asymmetric Exclusion Process¹ (TASEP), exactly solvable²:



¹MacDonald 1968, ²Derrida 1992, many more

A model for transcription with roadblocks

Totally Asymmetric Exclusion Process¹ (TASEP) with roadblocks²:





¹MacDonald 1968, ²Loan 1998

TASEP with roadblocks= Bus Route Model (BRM)

- The BRM can be solved in the mean-field limit
- A jamming transition for the BRM has been studied (Loan 1998)



Effective attraction between motors due to roadblocks



















Solving the TASEP with roadblocks



Heuristic arguments agree well with Monte Carlo simulations



K_{rb}=0.2, k_b=0.05, 0.5, 0.1

Open boundary conditions

 Heuristic arguments for open boundary conditions

The initiation-limited (Low Density) phase

For the TASEP the input and output dynamics are the same

With slow roadblock binding input and output dynamics are different

Boundary conditions

- Conservation of flux: $\alpha(1-\rho_1)$ =Flux_{in}=Flux_{out}
- In boundary region, motors distribution is partially set by initiation dynamics

Simulations with typical parameters on highly transcribed gens

Position along gene

Bursting in gene expression

Open boundaries under physiological conditions, compare to experiments

Open boundaries under physiological conditions, compare to experiments

Conclusions

- **1.** We have a heuristic understanding of BRM with open boundary conditions for low initiation
- **2.** Bursty dynamics can be generated during transcription elongation, due to peloton formation
 - **3**. The BRM gives an explanation for observed RNAP and nucleosome profiles

Thank you for your attention!

Outlook

- Billions of extension possible for a more accurate model for transcription:
 - Include backtracking (pausing) of RNAP
 - Multiple roadblock species

Thanks Martin Depken, the theory group and BN for the discussions and you for your attention!

Approximate k(d) by step function for bursty dynamics

• Heuristic arguments valid when

Predictions(black)+simulations(red) for bulk density vs initiation rate α

Slow roadblock binding

Fast roadblock binding

- Roadblocks on a track
- Make motors pack,
- when many motors on a gene
- No roadblocks can be seen

Map our model onto zero-range process to obtain solution in meanfield limit

Evans (1998, 2005)

Determine the density at the first site, p1, and in the bulk, p

