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CIRCLE
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A molecular communications model for local drug delivery applications

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Summary

- Motivations & Scenario
- Proposed model
- Performance evaluation
- Conclusion and future work

Introduction & Motivations

- Targeted and local drug delivery system
  - deploying a number of biological nanomachines (NMs) close to a biological target
  - NMs able to deliver drug molecules in the diseased area.
    - TX are designed to release a continuous flow of drug molecules in the surrounding environment,
    - they diffuse and reach the target (RX).
- Drug molecules are received when they chemically react with compliant receptors deployed on the RX surface.

Introduction & Motivations

- Assumptions:
  - The release rate can be relatively high
  - the drug absorption (trafficking) time is significant
- → congestion may occur at the receiver site.
  - This phenomenon limits the drug absorption rate
  - It makes the signal transmission ineffective
    - an undesired diffusion of drug molecules elsewhere in the body.

Contribution

- Contributions of this talk consists of
  - analysis of the causes of congestion in diffusion-based molecular communications
  - a novel reception model consisting of a set of pure loss queuing systems

Reference model

- From the diffusion equaition, upon a single pulse of *Q* molecules, we get at distance *r*

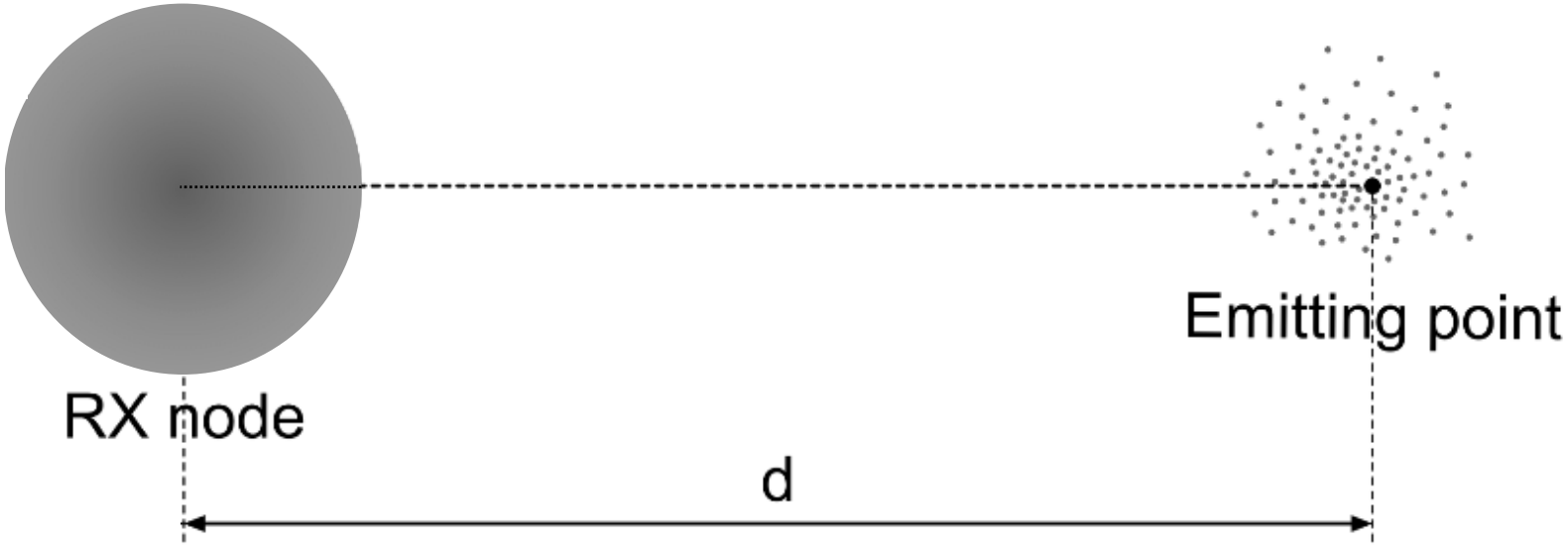
$$h_Q(t,r) = \frac{Q}{(4\pi Dt)^{\frac{3}{2}}} e^{\left(-\frac{r^2}{4Dt}\right)}$$

- Upon a train of pulses spaced by Δt, we get at distance *r* for large *t*

$$c(t,r) = \sum_{i=1}^{\lfloor t/\Delta t \rfloor} h_Q(t - i\Delta t, r) \approx \frac{1}{\Delta t} \int_0^t h_Q(\tau, r) d\tau \xrightarrow[t\to\infty]{} \frac{Q}{\Delta t 4\pi Dr}$$

- Concentration is depending on just on TX rate and distance
  - On the RX surface, front receptors receive more “hits”

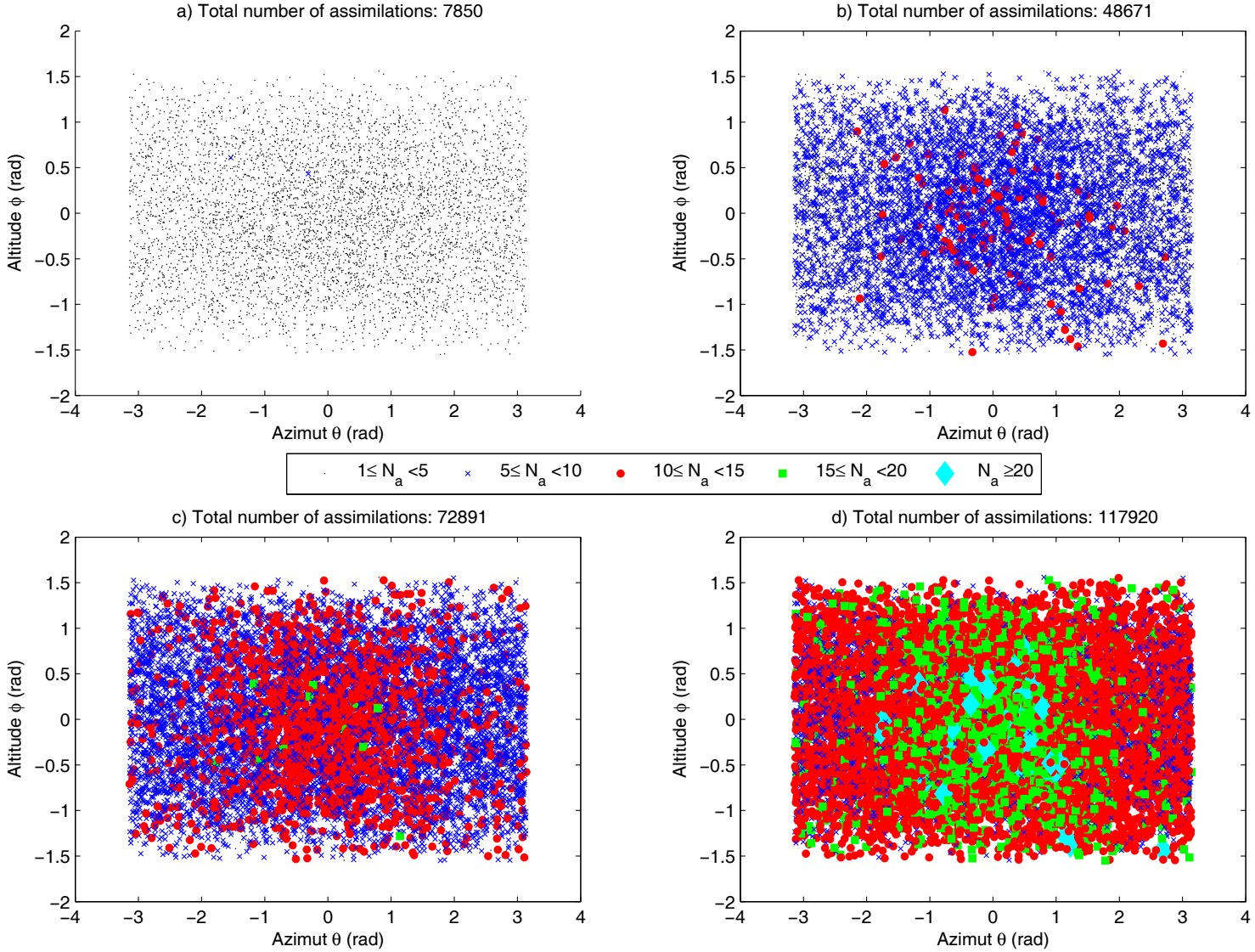
Reference model



Key idea

- Each receptor has to be modeled independently, not like a server pool
  - Queuing model M/M/1/1
    - Account for the trafficking time
    - Design a delivery system able to optimize the amount of locally released drug
    - Take congestion into the game
      - A busy receptor can cause a rejection

Proof


a) Total number of assimilations: 7850
b) Total number of assimilations: 48671
c) Total number of assimilations: 72891
d) Total number of assimilations: 117920
Altitude ϕ (rad)
Azimut θ (rad)
1≤ N_a <5
5≤ N_a <10
10≤ N_a <15
15≤ N_a <20
N_a ≥20

Proposed model

- Poisson model for arrivals
  - Arrival model at each receptor λ_{aj}
    - Inspired by [1]: depending on concentration
    - Depending on RX-TX distance: $r_i \lambda_{ai} = r_j \lambda_{aj}$
- Exponential service model
  - Taken by [2], average equal to T_{traff}
- A model also for rejections $\lambda_{rj} = \frac{T_{traff} \lambda_{aj}^2}{1 - T_{traff} \lambda_{aj}}$

[1] M. Pierobon and I. Akyildiz, "Noise analysis in ligand-binding reception for molecular communication in nanonetworks," *IEEE Trans. on Signal Proc.*, 59(9), Sept., 2011.
[2] D. Lauffenburger and J. Linderman, *Receptors: Models for Binding, Trafficking, and Signalling,*. Oxford University Press, 1996.

Application to drug delivery

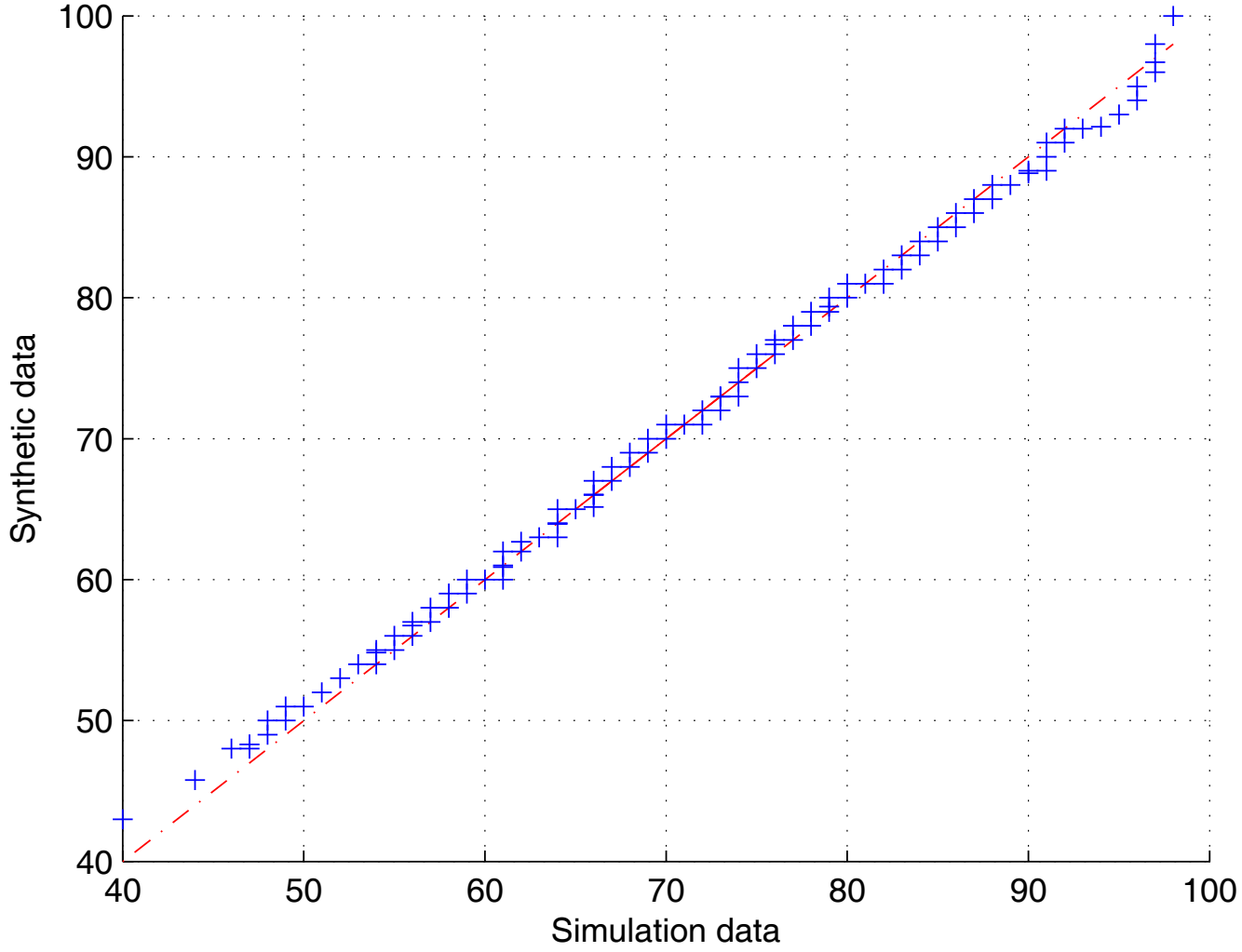
- Find the receptor occupancy f that triggers a full drug response
  - Aggregate arrival model inspired by [3]
    - $\lambda^*_a = \sum_{j=1}^{R_{RX}} \lambda_{aj}$, λ^*_r depends on λ^*_a

$$\lambda_o = \lambda_a^* + \lambda_r^* = \frac{r_{RX}}{d} \frac{R_{RX} r_{r,rx}}{\pi r_{RX} + R_{RX} r_{r,rx}} \frac{Q}{\Delta t}$$

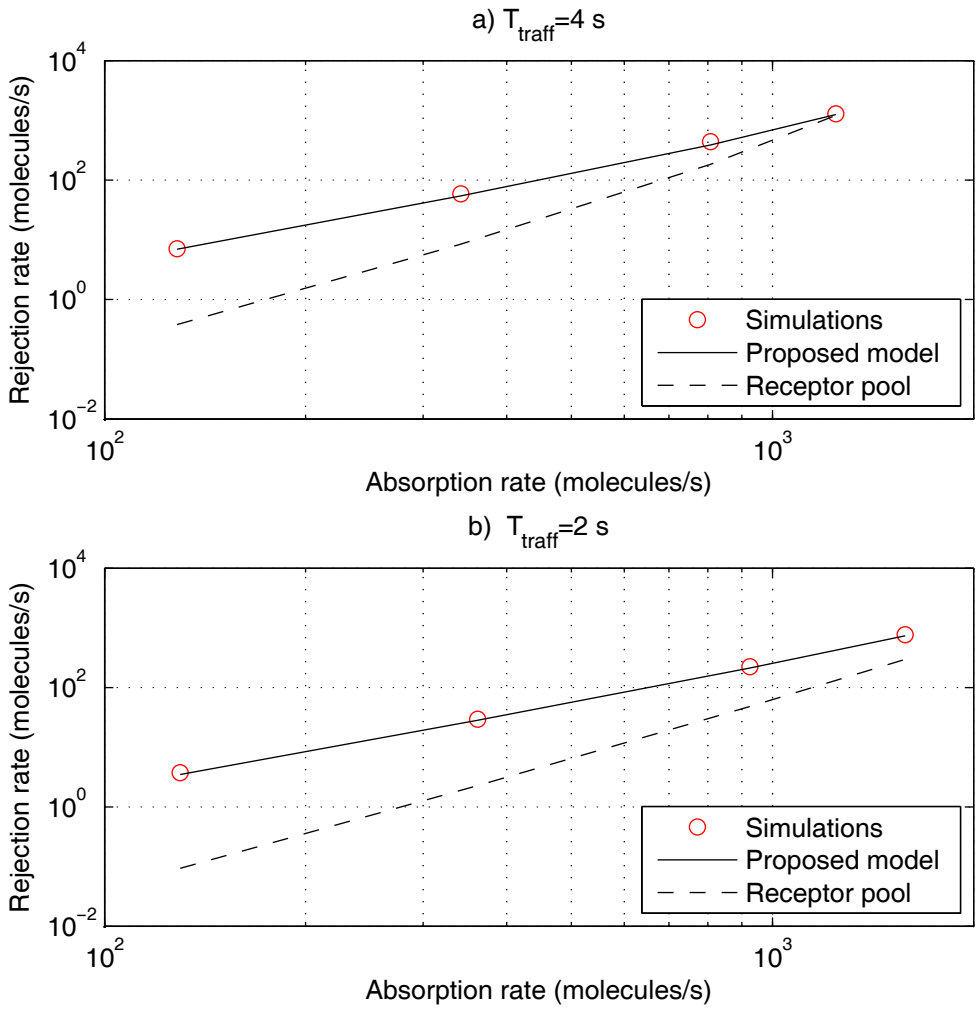
  - Target fraction: $f = \frac{T_{traff} \lambda^*_a}{R_{RX}}$

[3] A. Akkaya, H. Yilmaz, C. Chae, and T. Tugcu, "Effect of receptor density and size on signal reception in molecular communication via diffusion with an absorbing receiver," *IEEE Comm. Letters*, 19(2), 2015.

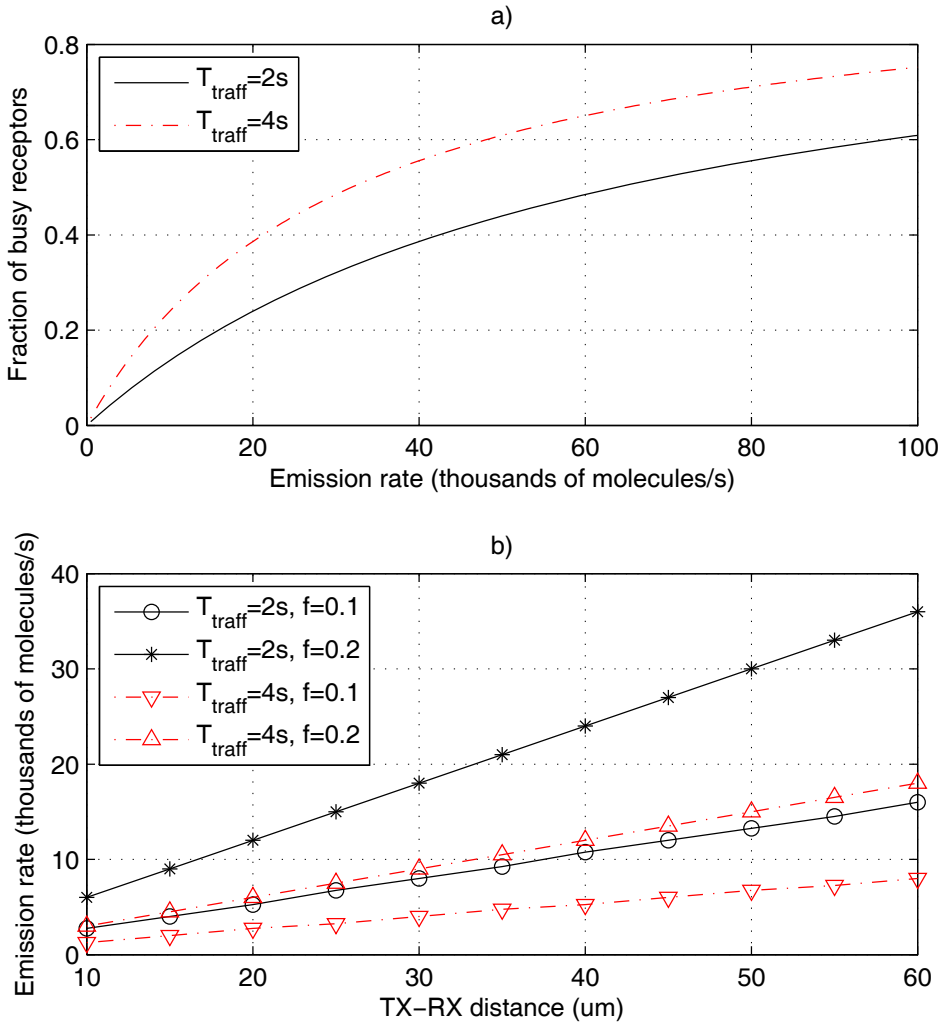
Performance evaluation



Performance evaluation



Performance evaluation



Conclusion & outlook

- Concept of congestion for diffusion-based molecular communication
- How drug delivery could exploit this concept
- Future work:
  - Apply in diffusion + drift scenarios
  - Consider molecules decaying and detachment
  - How should NMs determine the suitable rate?
    - Measurement issues
    - Computing issues