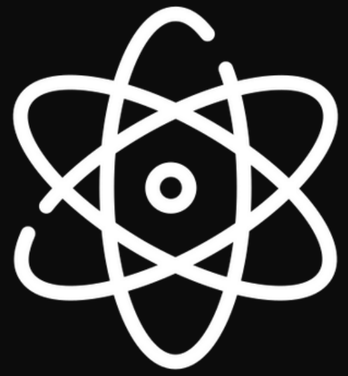
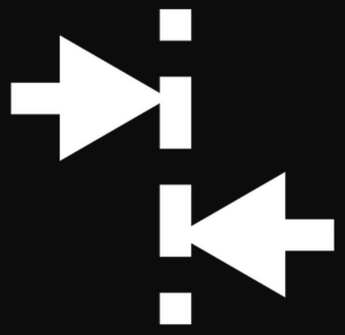
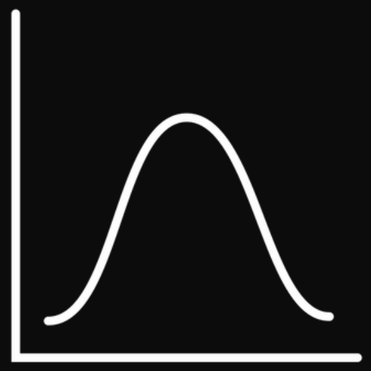
Raspodjela molekularnih motora na rastućem mikrotubulu

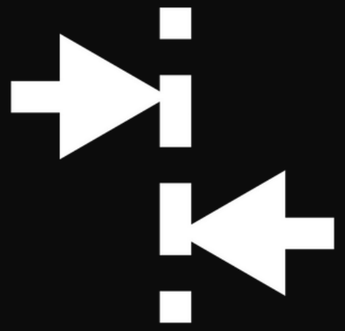
Antonio Parunov

Zašto biofizika?

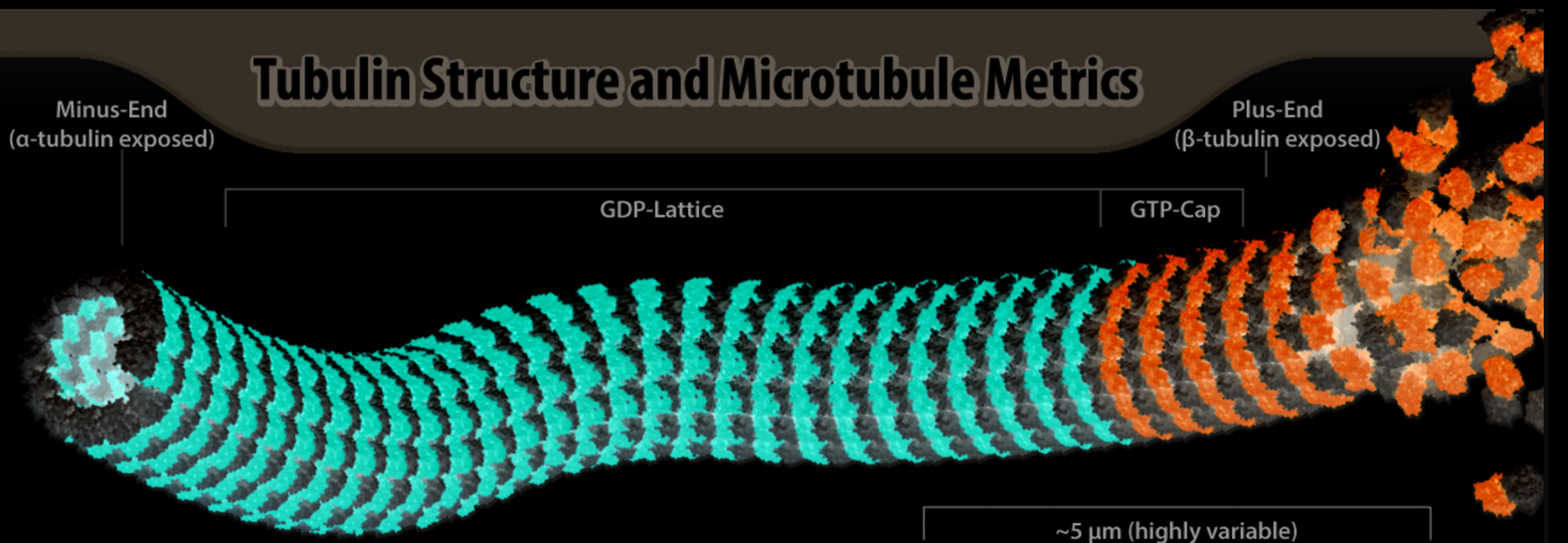






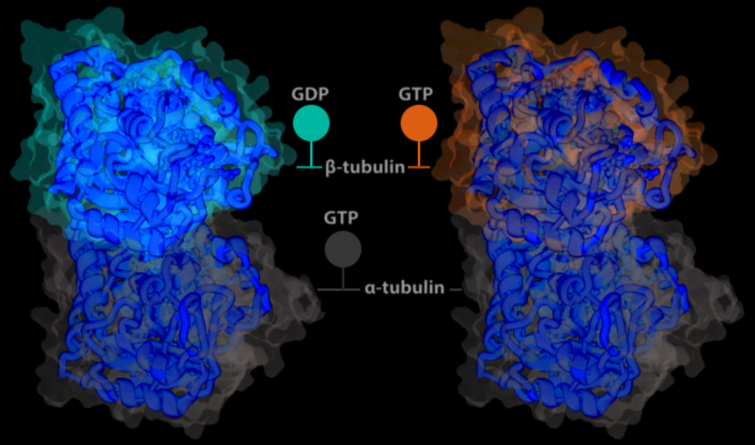


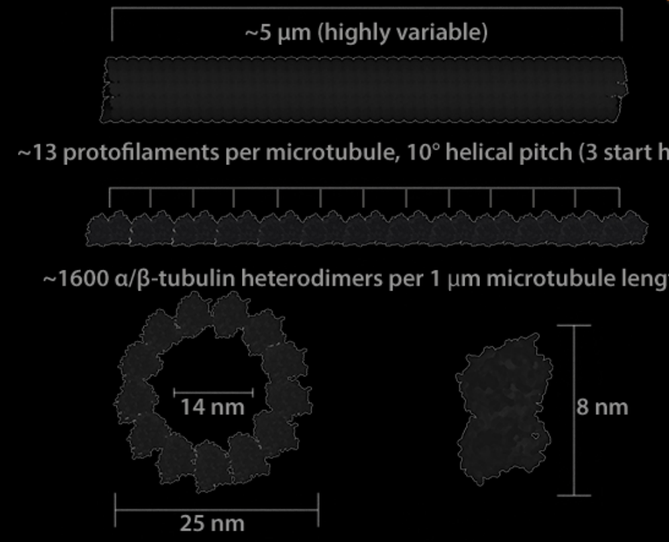
Tubulin Structure and Microtubule Metrics



In Vitro Parameters:

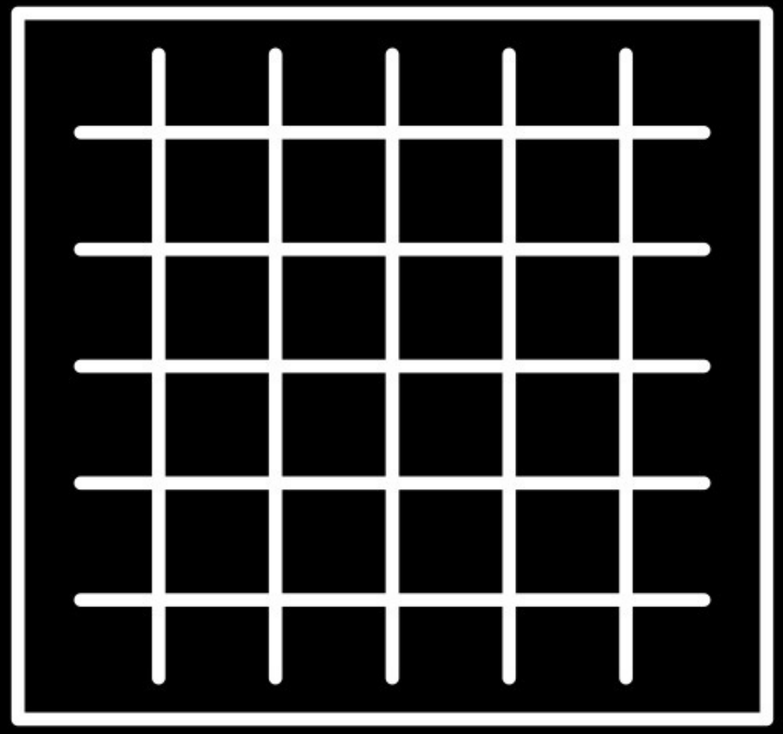
- Growth rate ≈ 0.6-3 µm/min [1,2]
- Shrinkage rate ≈ 20-30 µm/min [1,2]
- Association rate constant ≈ 2–10 μM^{-1} s^{-1} [1,2,3]
- Free energy from GTP hydrolysis ≈ 7.5 kcal mol^{-1} [3]
- Pushing force ≈ 3-4 pN [4]
- Pulling force ≈ 30-65 pN [3,4]
- Persistence length ≈ 5.2 mm [5]
- Critical concentration ≈ 0.1-2 mg/ml [6]
- Molecular weight ≈ 110 kDa (α/β heterodimer)
- Extinction coefficient ≈ 115,000 M^{-1} cm^{-1} at 280 nm
- Concentration Conversion: 1 mg/ml ≈ 10 µM





References
1) Mitchison T, Kirshner M. (1984) Dynamic instability of microtubule growth. Nature 312: 237-242.
2) Walker RA, O'Brien ET, Pryer NK, et al. (1988) Dynamic instability of individual microtubules analyzed by video light microscopy: rate constants and transition frequencies. The Journal of Cell Biology 107:1437-1448.
3) Desai A, Mitchison T. (1997) Microtubule polymerization dynamics. Annual Review of Cell and Developmental Biology 13: 83-117.

Metoda konačnih razlika



Metoda končnih razlika

Konzistentnost + Stabilnost = Konvergentnost

Advekcija

$$\frac{\partial \rho(x,t)}{\partial t} + v_m \frac{\partial \rho(x,t)}{\partial x} = k_{on}\theta(v_g t - x) - k_{off}\rho(x,t)$$

Advekcija

$$\frac{\partial \rho}{\partial x} \rightarrow \frac{1}{\Delta x}(u_i^n - u_{i-1}^n)$$

$$\frac{\partial \rho}{\partial t} \rightarrow \frac{1}{\Delta t}(u_i^{n+1} - u_i^n)$$

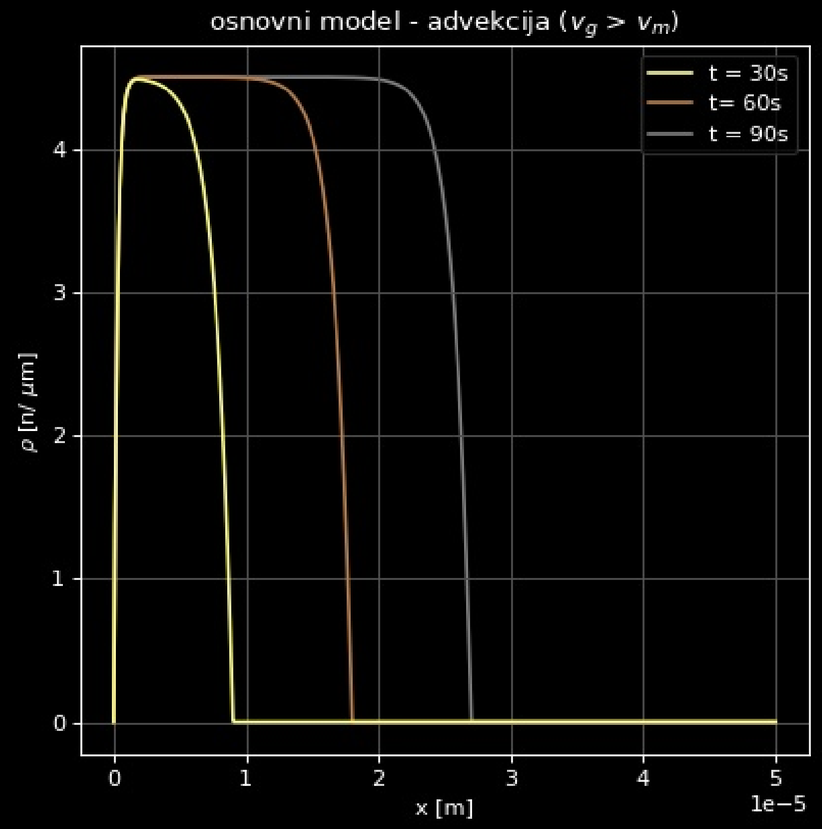
Advekcija

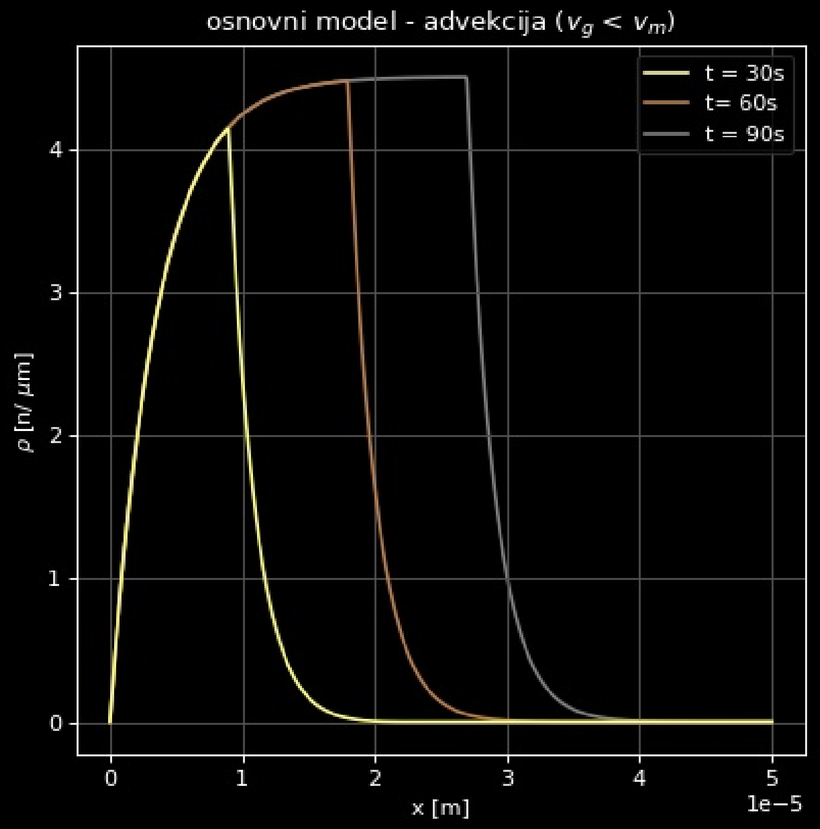
$$\frac{\partial \rho}{\partial x} \to \frac{1}{\Delta x}(u_i^n - u_{i-1}^n)$$

$$\frac{\partial \rho}{\partial t} \to \frac{1}{\Delta t}(u_i^{n+1} - u_i^n)$$

$$u_i^{n+1} = u_i^n - C(u_i^n - u_i^{n-1}) + \Delta t f_i^n,$$

Advekcija


osnovni model - advekcija ($v_g > v_m$)
t = 30s
t= 60s
t = 90s
ρ [n/ μm]
x [m]
1e−5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Advekcija + difuzija + ograničenje

$$\frac{\partial \rho(x,t)}{\partial t} + v_m \frac{\partial \rho(x,t)}{\partial x} = D \frac{\partial^2 \rho(x,t)}{\partial x^2} + k_{on}\left(1 - \frac{\rho(x,t)}{\rho_{max}}\right)\theta(v_g t - x) - k_{off}\rho(x,t)$$

Advekcija + difuzija + ograničenje

$$\frac{\partial \rho}{\partial t} = \frac{1}{\Delta t}(u_i^{n+1} - u_i^n)$$

$$\frac{\partial^2 \rho}{\partial x^2} = \frac{1}{2\Delta x^2}(u_{i+1}^{n+1} - 2u_i^{n+1} + u_{i-1}^{n+1}) + (u_{i+1}^n - 2u_i^n + u_{i-1}^n))$$

$$\frac{\partial \rho}{\partial x} = \frac{1}{4\Delta x}(u_{i+1}^{n+1} - u_{i-1}^{n+1}) + (u_{i+1}^n - u_{i-1}^n))$$

$$\rho = \frac{1}{2}(u_{i+1}^n - u_i^n)$$

Advekcija + difuzija + ograničenje

$$\frac{\partial \rho}{\partial t} = \frac{1}{\Delta t}(u_i^{n+1} - u_i^n)$$

$$\frac{\partial^2 \rho}{\partial x^2} = \frac{1}{2\Delta x^2}(u_{i+1}^{n+1} - 2u_i^{n+1} + u_{i-1}^{n+1}) + (u_{i+1}^n - 2u_i^n + u_{i-1}^n))$$

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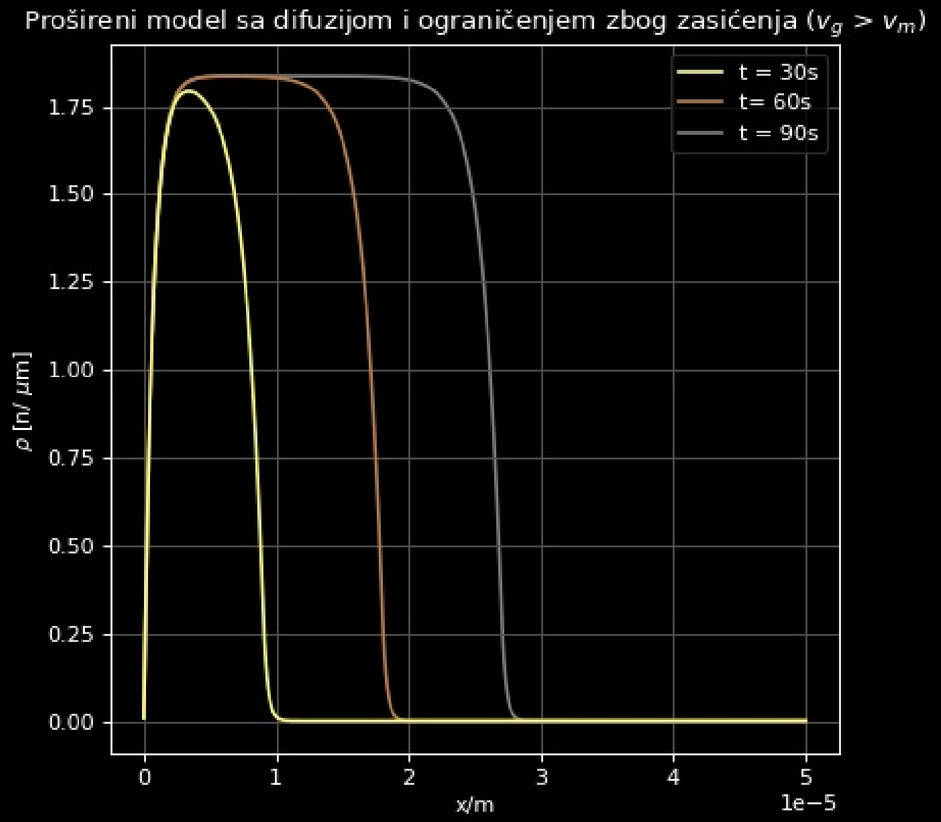
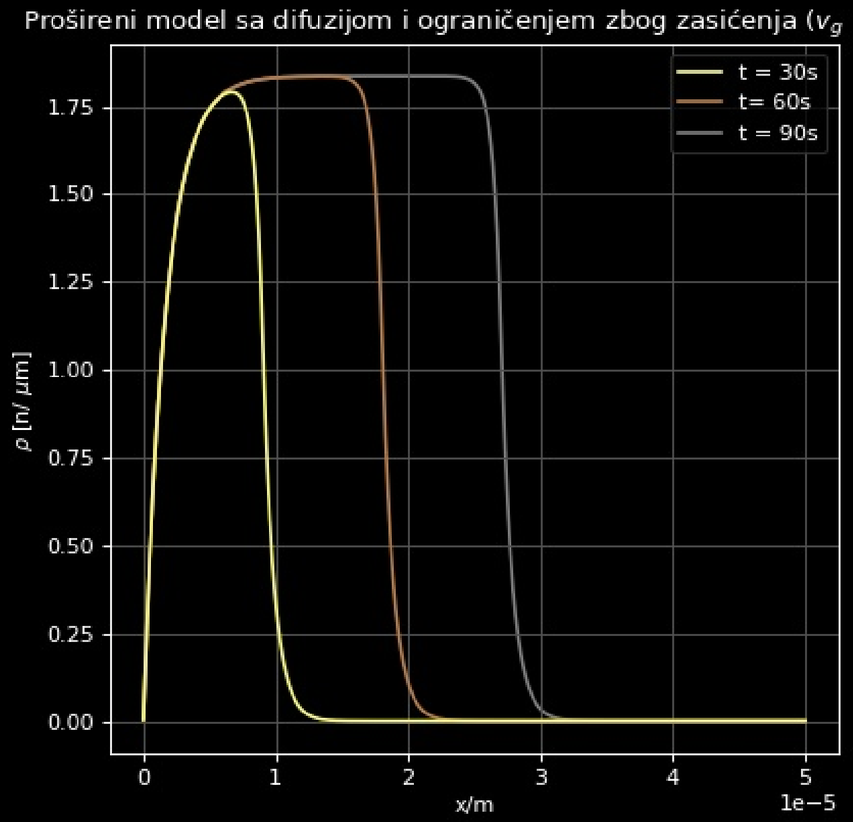
$$\downarrow$$

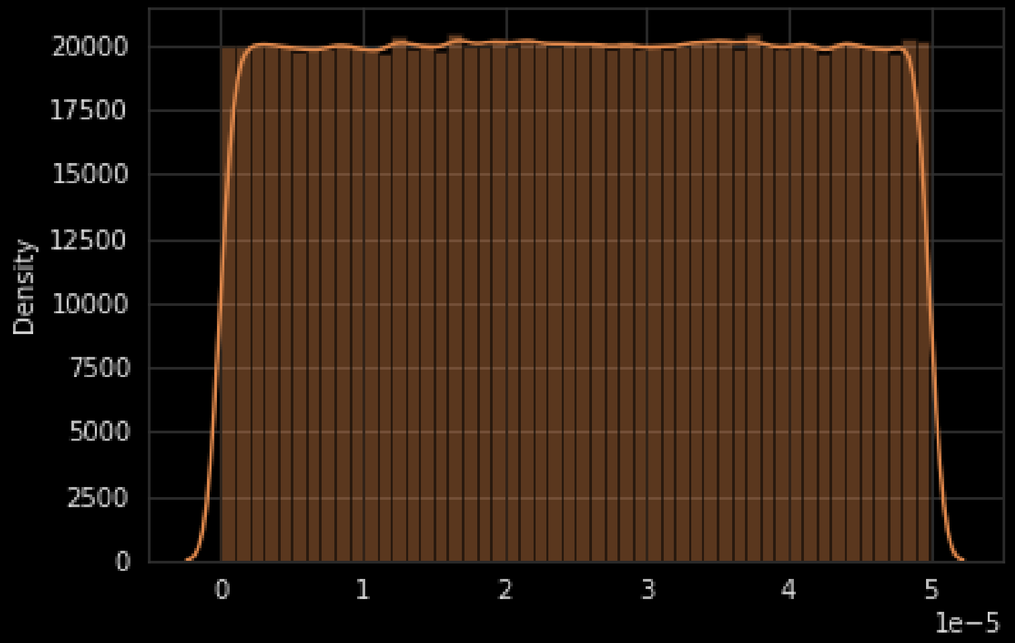
$$\mathbf{A}U = b$$

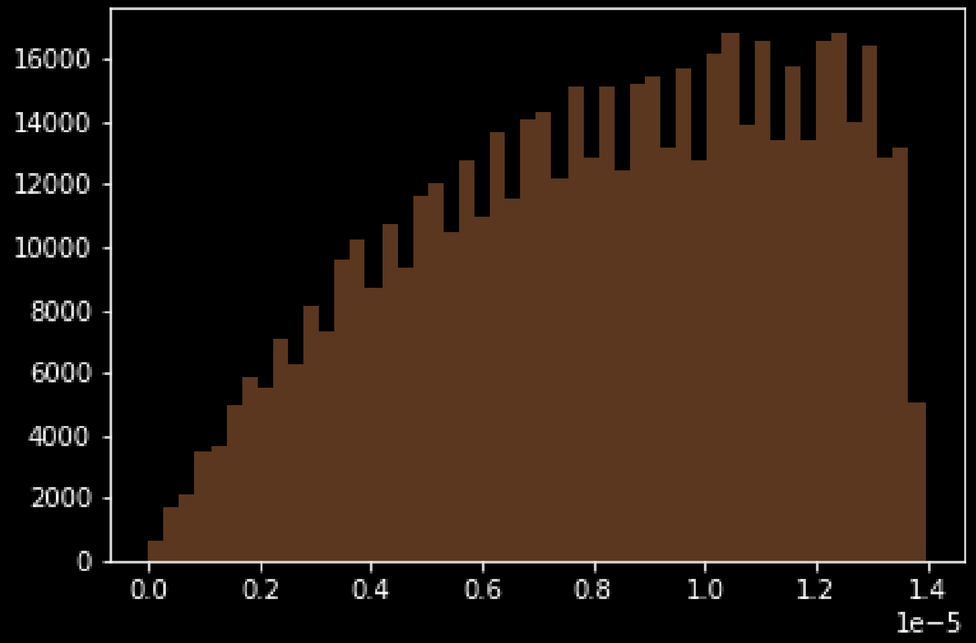
Advekcija + difuzija + ograničenje





Stohastički model





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[1] Howard J. Mechanics of Motor Proteins and the Cytoskeleton, Sunderland, MA: Sinauer Associates, 2001. .
[2] Schliwa, M., Molecular Motors, Weinheim, Wiley-VCH, 2003.
[3] Https://web.stanford.edu/class/cme306/Discussion/Discussion1.pdf.
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[5] H. P. Langtangen, S. Linge, Finite Difference Computing with PDEs.
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[8] Z. Drmač, V. Hari, M. Marušić, M. Rogina, S. Singer, S. Singer, Numerička analiza.