A **Field–Theoretic** Approach to Microtubule Growth

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Introduction
- Reaction-diffusion equations
- Master equation
- Field-theory

Field theory of microtubule growth
- Model
- Tubulin probe in vicinity of MT cap
- Discrete microtubule movement
- Bath of tubulin

Conclusion

Two components

- Chemical reactions

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- Combination of reactions and movement

$$A_i(\vec{x}) + A_j(\vec{x}) \xrightarrow{\lambda} A_i(\vec{x} + \vec{h}) \tag{3}$$

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- Example 1: Reaction

$$2A \xrightarrow{\lambda} B \tag{4}$$

$$\begin{aligned}\partial_t \mathcal{P}(\{m\},\{n\},t) &= \text{gain} - \text{loss} \\ &= \lambda \sum_x \left(\binom{m_x+2}{2} \mathcal{P}(\{m_x+2\},\{n_x-1\},t) + \right. \\ &\qquad \left. - \binom{m_x}{2} \mathcal{P}(\{m_x\},\{n_x\},t) \right)\end{aligned}$$

- Example 2: Diffusion

$$\partial_t \mathcal{P}(\{m\},t) = \frac{D}{h^2} \sum_x \sum_{|x-y|=1} \Big((m_x+1)\mathcal{P}(\{m_x+1, m_y-1\},t) + \\ - m_x \mathcal{P}(\{m_x\},t) \Big) \qquad (5)$$

Miraculous transformation (Doi [1], Peliti[2], Wijland[3])

- $2A \xrightarrow{\lambda} B$

$$H = \int_{\mathbb{R}} \int_{\mathbb{R}^d} \frac{\lambda}{2} \left(\varphi(t,x)^2 \psi^\dagger(t,x) - \varphi^\dagger(t,x)^2 \varphi(t,x)^2 \right) d^d x dt \quad (6)$$

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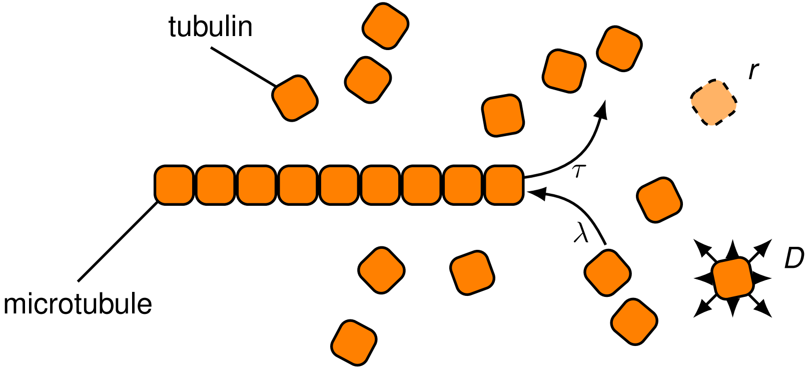
- Diffusion

$$H = \int_{\mathbb{R}} \int_{\mathbb{R}^d} D \varphi^\dagger(t,x) \Delta \varphi(t,x) d^d x dt \quad (7)$$

Simple Model of Microtubule Growth



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- Take probabilities of interest: $\varphi(t,x), \psi(t,x), \ldots$

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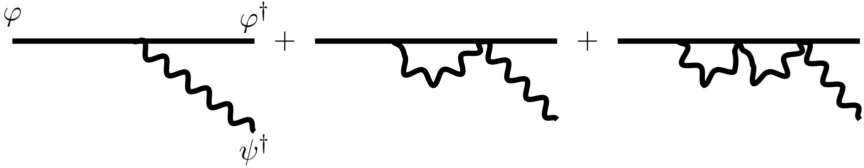
- Consider ALL corresponding Feynman diagrams
- Write their integral representation
- Calculate...

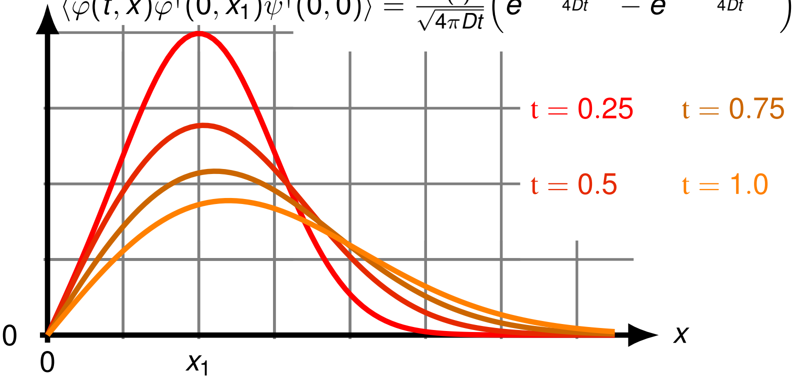
How to find single tubulin probability densities

$$\langle \varphi(t,x)\varphi^\dagger(0,x_1)\psi^\dagger(0,0)\rangle \tag{8}$$

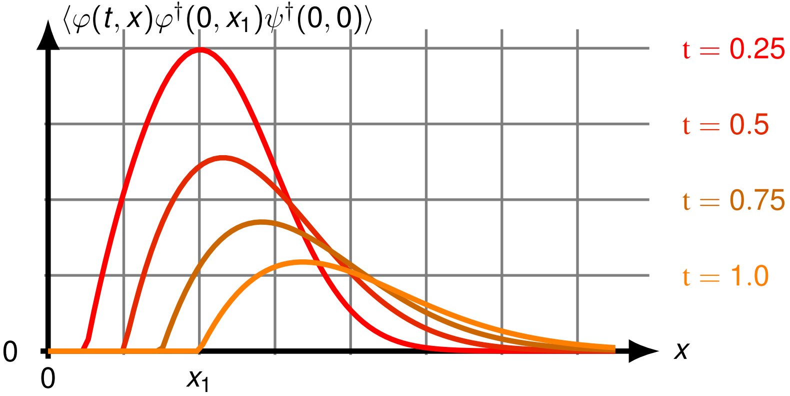


Single tubulin close to stationary microtubule tip

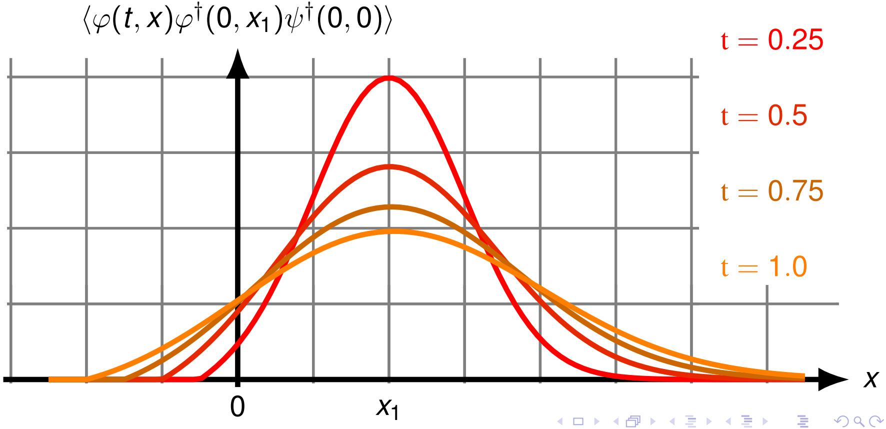
$$\langle \varphi(t,x)\varphi^\dagger(0,x_1)\psi^\dagger(0,0)\rangle = \frac{H(t)}{\sqrt{4\pi Dt}}\left(e^{-\frac{(x-x_1)^2}{4Dt}} - e^{-\frac{(|x|+|x_1|)^2}{4Dt}}\right)$$



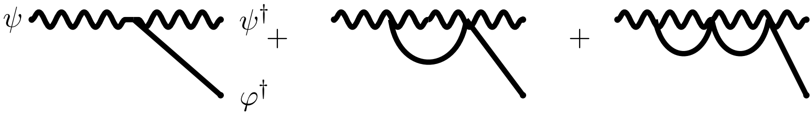
Single tubulin close to moving microtubule tip I



Single tubulin close to moving microtubule tip II



MT cap movement induced by tubulin absorption



$$\langle \psi_j(t)\psi_{j_0}^\dagger(0)\varphi^\dagger(0,x_2)\rangle = \delta_{j,j_0} + \mathrm{erfc}\left(\frac{|x_2 - hj_0|}{\sqrt{4Dt}}\right)\left(\delta_{j,j_0+1} - \delta_{j,j_0}\right)$$

How to incorporate large numbers of tubulin?

Homogenous tubulin density ζ

$$\varphi = \check{\varphi} + \zeta$$

Without decay

$$\langle \psi_j(t)\psi^\dagger_{j_0}(t_0)\rangle_T = \begin{cases} e^{-\lambda\zeta(t-t_0)}\frac{\left(\lambda\zeta(t-t_0)\right)^{j-j_0}}{(j-j_0)!} & j-j_0 \geq 0 \\ 0 & j-j_0 < 0 \end{cases}$$

With decay

$$\langle \psi_j(t)\psi^\dagger_{j_0}(t_0)\rangle_T = e^{-(\lambda\zeta+\tau)(t-t_0)}\sum_{m=\max\{0,j_0-j\}}^{\infty}\frac{(\tau(t-t_0))^m}{m!}\frac{(\lambda\zeta(t-t_0))^{j-j_0+m}}{(j-j_0+m)!} \tag{9}$$

Depletion of tubulin

1 dim

$$\langle \varphi(t,x)\psi_0^\dagger(0)\rangle_{t\to\infty} = \zeta + (\tau - \lambda\zeta)\frac{e^{-\sqrt{\frac{r}{D}}|x|}}{2\sqrt{Dr}}\left(1 - \frac{\lambda}{2\sqrt{Dr}+\lambda}\right)$$

3 dim

$$\langle \varphi(t,x)\psi_0^\dagger(0)\rangle_{t\to\infty} =$$

$$\zeta + \frac{(\tau - \lambda\zeta)e^{-\sqrt{\frac{r}{D}}|x|}}{4\pi D|x|}\left(1 - \frac{\lambda(2\Lambda - \pi\sqrt{r/D})}{4\pi^2 D + \lambda(2\Lambda - \pi\sqrt{r/D})}\right)$$

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2. From microscopic & short-time behaviour it can predict behaviour in any spatial and time scale
3. It can predict fluctuations and correlations of any order

Thank you!

- Masao Doi, *Second quantization representation for classical many-particle system*, J. Phys. A: Math. Gen., Vol. 9. No. 9.1976.
- L. Peliti, *Path integral approach to birth-death processes on a lattice*, Journal de Physique 1985, 46 (9), pp.1469-1483. 10.1051/jphys:0198500460901469OO
- Frédéric van Wijland, *Field theory for reaction-diffusion processes with hard-core particles*, PHYSICAL REVIEW E, VOLUME 63, 022101,2001.