Imaging and analysis strategies in the era of spatial omics

Clayton W. Seitz, Ph.D.

February 3, 2025

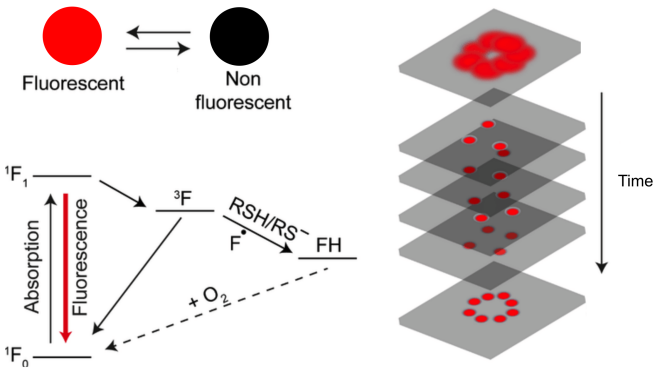
Outline of the talk

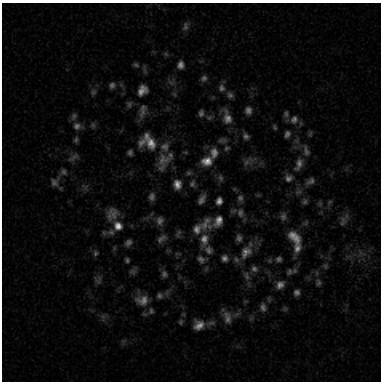
Part I: Localization microscopy for spatial biology

Part II: ML algorithms for spatial biology

Part I: Localization microscopy for spatial biology

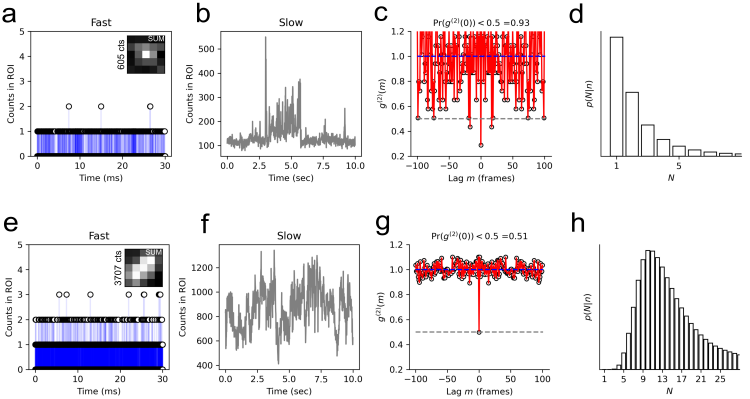
Single molecule localization microscopy



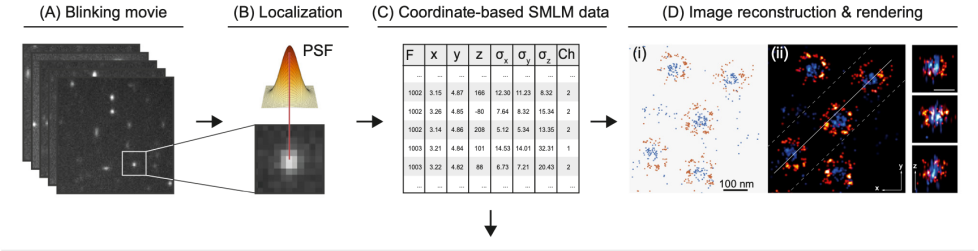


- STORM and similar nanoscopy techniques are limited by localization precision
- Higher lateral/axial resolution than other methods (e.g., SIM,STED,Confocal)
- Poor time resolution

Quantitative single molecule localization microscopy

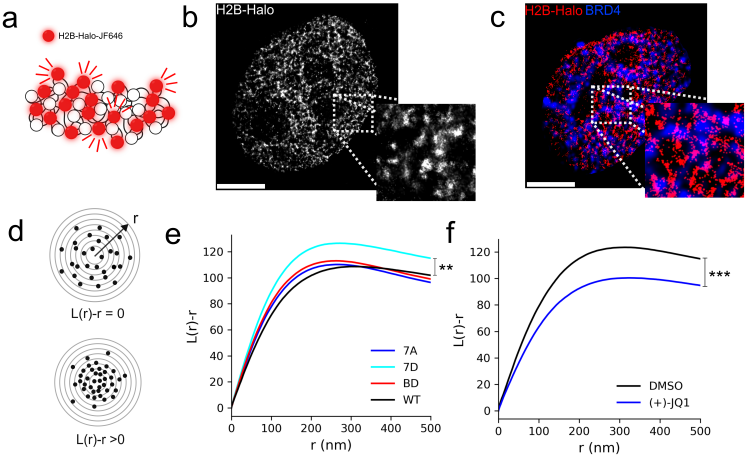


Applications of single molecule localization microscopy



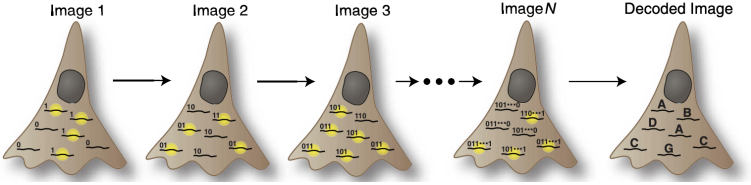
Wu et al. Trends in Cell Biology. **30** (2020)

BRD4 binding is necessary for maintenance of nucleosome nanodomains



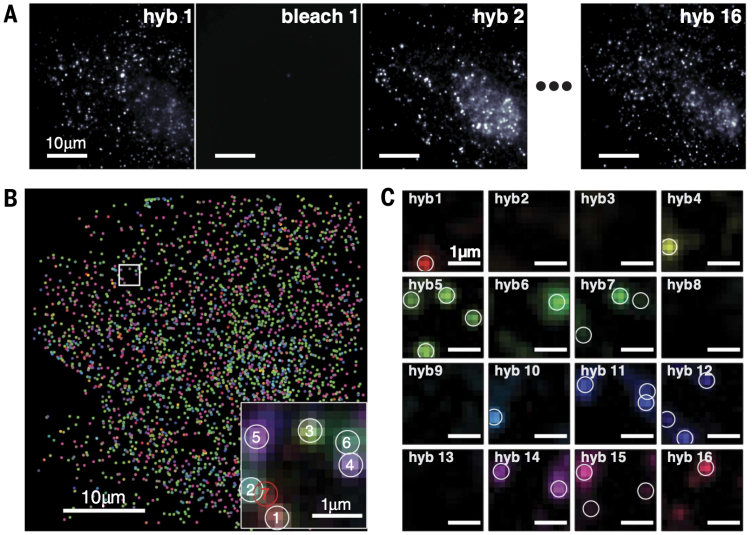
- H2B is densely labeled for super-resolution imaging
- BRD4 chromatin binding activity controls nanodomain density

Multiplexed single molecule localization microscopy



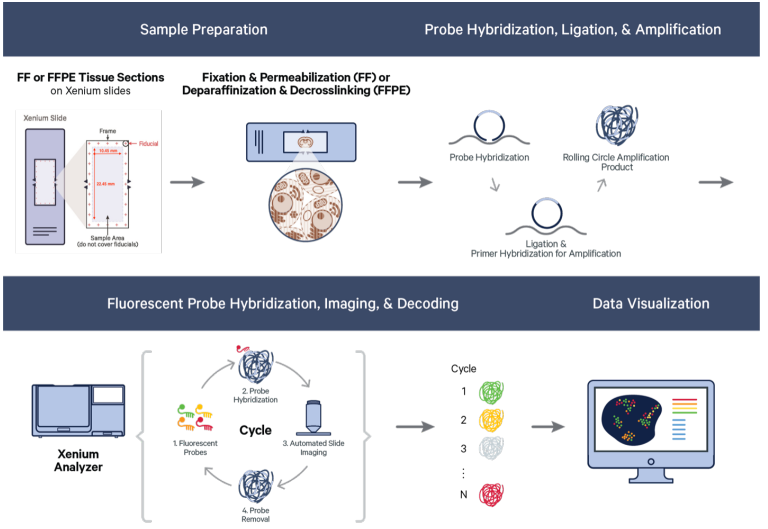
Wu et al. Trends in Cell Biology. **30** (2020)

Multiplexed single molecule localization microscopy



Wu et al. Trends in Cell Biology. **30** (2020)

Multiplexed single molecule localization microscopy

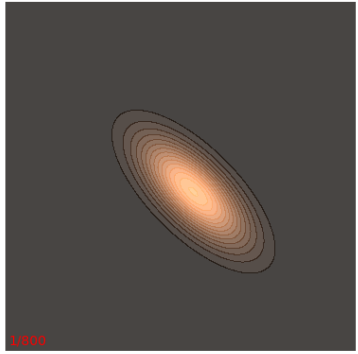


Wu et al. Trends in Cell Biology. **30** (2020)

Part II: Generative models for spatial biology

Approach I: Resolution enhancement with a diffusion model

- Can sample from $p(\theta|\boldsymbol{x})$ using a stochastic process called Langevin dynamics

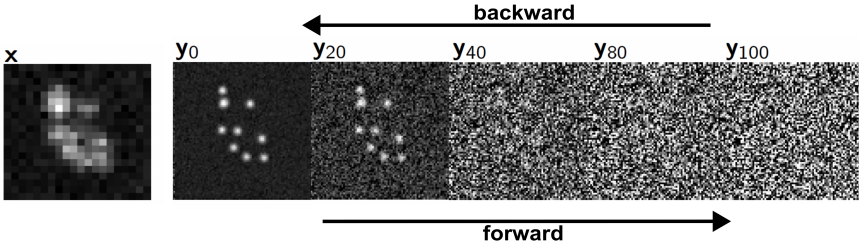


Drift and diffusion: $\theta_t = \overbrace{\theta_{t-1} - \frac{\beta}{2}\nabla f(\theta)}^{\mu} + \sqrt{\beta}\xi \quad \xi \sim \mathcal{N}(0, I)$

Approach I: Resolution enhancement with a diffusion model

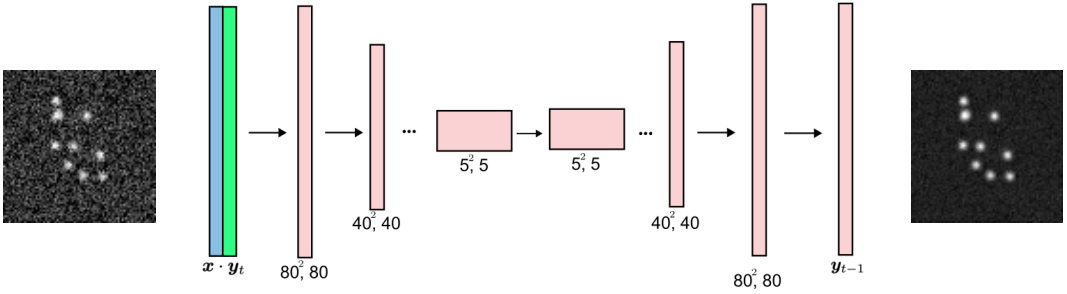
- Task: infer a high resolution image $\mathbf{y}_0$ from low resolution $\mathbf{x}$
- Drift is not available for image data, but can be learned from pairs $(\mathbf{x}, \mathbf{y}_0)$

$$p_\psi(\mathbf{y}_{t-1}|\mathbf{y}_t, \mathbf{x}) = \mathcal{N}(\mu_\psi, \beta_t I)$$



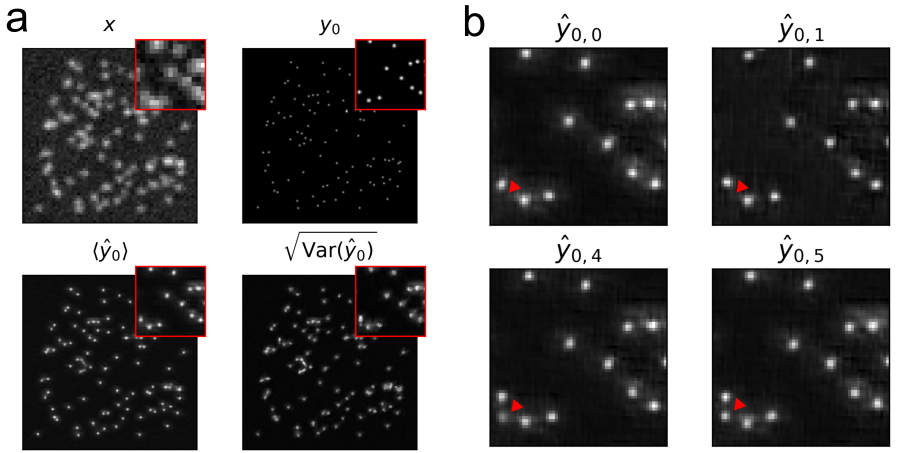
$$q(\mathbf{y}_t|\mathbf{y}_{t-1}) = \mathcal{N}\left(\sqrt{1-\beta_t}\mathbf{y}_{t-1}, \beta_t I\right)$$

Approach I: Resolution enhancement with a diffusion model



- A convolutional neural network ψ estimates the drift μ_ψ
- Denoising step: $y_{t-1} \sim p_\psi(\mathbf{y}_{t-1}|\mathbf{y}_t, \mathbf{x}) = \mathcal{N}(\mu_\psi, \beta_t I)$

Super resolution with a diffusion model



Selected Publications

- **C. Seitz**, D. Fu, M. Liu, H. Ma, and J. Liu. *BRD4 phosphorylation regulates the structure of chromatin nanodomains*. In Review. Phys Rev Lett. 2024
- **C. Seitz** and J. Liu. *Uncertainty-aware localization microscopy by variational diffusion*. In Progress. 2024
- **C. Seitz** and J. Liu. *Quantum enhanced localization microscopy with a single photon avalanche diode array*. In Progress. 2024
- M. Locatelli†, J. Lawrimore†, H. Lin†, S. Sanaullah, **C. Seitz**, D. Segall, P. Kefer, S. Moreno Naike, B. Lietz, R. Anderson, J. Holmes, C. Yuan, G. Holzwarth, B. Kerry, J. Liu, K. Bonin, P. Vidi. *DNA damage reduces heterogeneity and coherence of chromatin motions*. PNAS 12 July 2022; 119 (29): 1-11
- M. Zhang, **C. Seitz**, G. Chang, F. Iqbal, H. Lin, and J. Liu *A guide for single-particle chromatin tracking in live cell nuclei*. Cell Biology International 15 January 2022; 46 (5): 683-700

Temporary page!

LaTeX was unable to guess the total number of pages correctly. As there was some unprocessed data that should have been added to the final page this ex page has been added to receive it.
If you rerun the document (without altering it) this surplus page will go away because LaTeX now knows how many pages to expect for this document.