Imaging and analysis strategies in the era of spatial omics

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About Me

Education

- PhD @ Purdue University, MS @ University of Chicago

Research interests

- Bioimaging, Machine learning methods for live cell imaging
- Quantitative single molecule localization microscopy
- Generative models, statistical physics, theory of deep learning

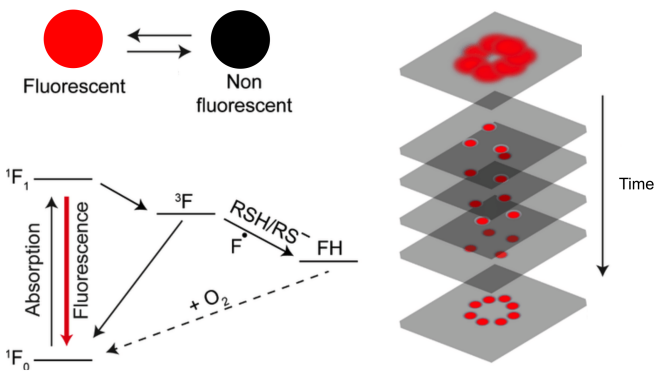
Outline of the talk

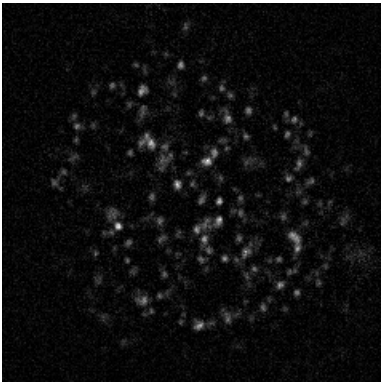
Localization microscopy for spatial biology

Modeling and analysis approaches in spatial transcriptomics

Localization microscopy for spatial biology

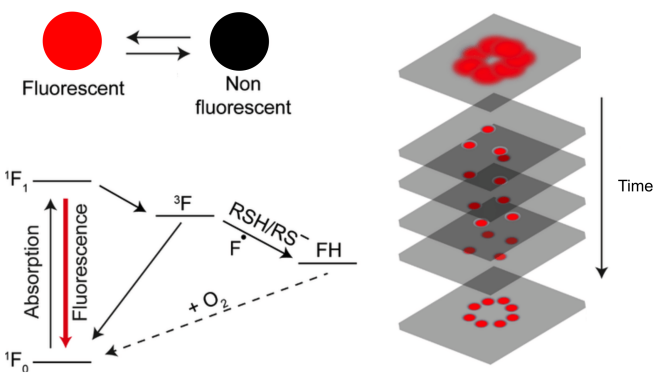
Single molecule localization microscopy

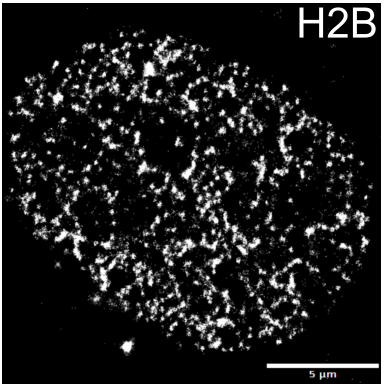




- STORM and similar nanoscopy techniques are limited by localization precision
- Higher lateral/axial resolution than other methods (e.g., SIM,STED,Confocal)
- Poor time resolution

Stochastic optical reconstruction microscopy (STORM)





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Nanoscopy by localizing isolated fluorescent emitters

- Modeling the point spread function permits sub-pixel localization

$$\mu_k = i_0 \int\int O(u,v)dudv + \lambda$$

$$i_0 = g_k \eta \zeta \Delta$$

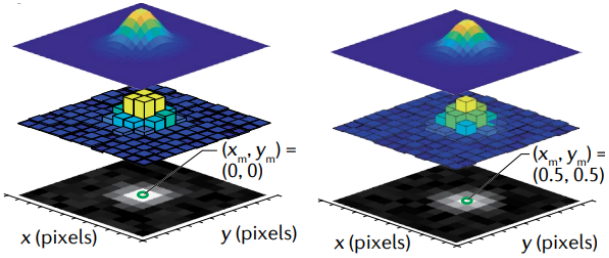
g_k – pixel gain

η – quantum efficiency

ζ – photon emission rate

Δ – exposure time

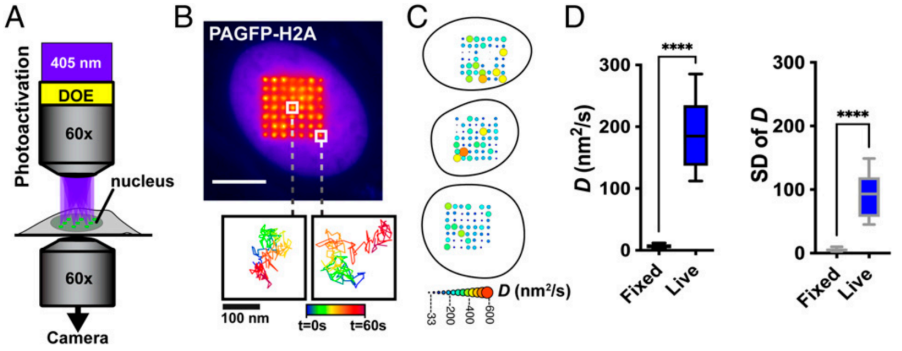
λ – background rate



Maximum likelihood localization:

$$\theta^* = \underset{\theta}{\operatorname{argmax}} \prod_k p(\mathbf{x}_k|\theta) = \underset{\theta}{\operatorname{argmin}} - \sum_k \log p(\mathbf{x}_k|\theta)$$

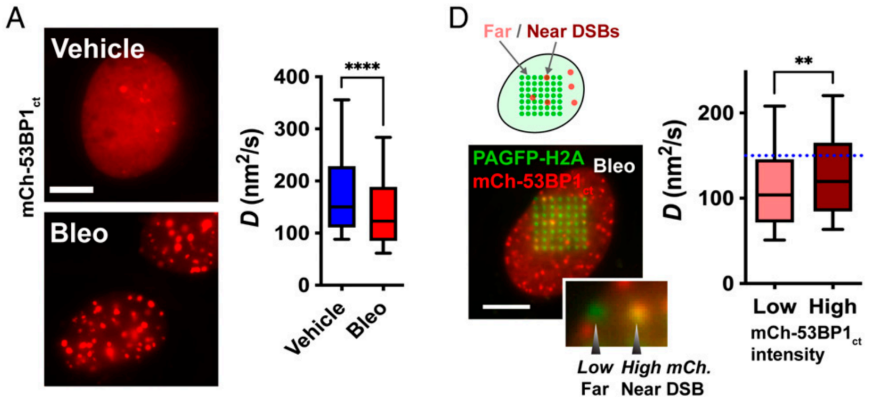
Tracking chromatin loci with photoactivated localization microscopy



Locatelli, Seitz et al. PNAS **29** (2022)

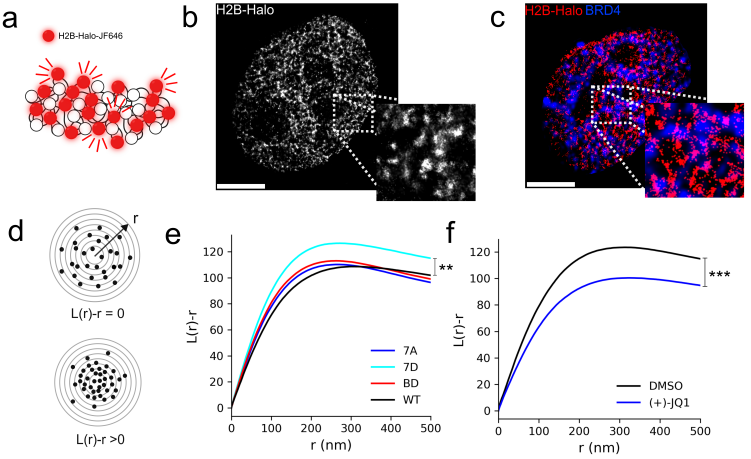
- A diffractive optical element (DOE) is used to photoactivate chromatin microdomains
- Used for understanding the spatial correlations of chromatin diffusion

Tracking chromatin loci with photoactivated localization microscopy



Locatelli, Seitz et al. PNAS **29** (2022)

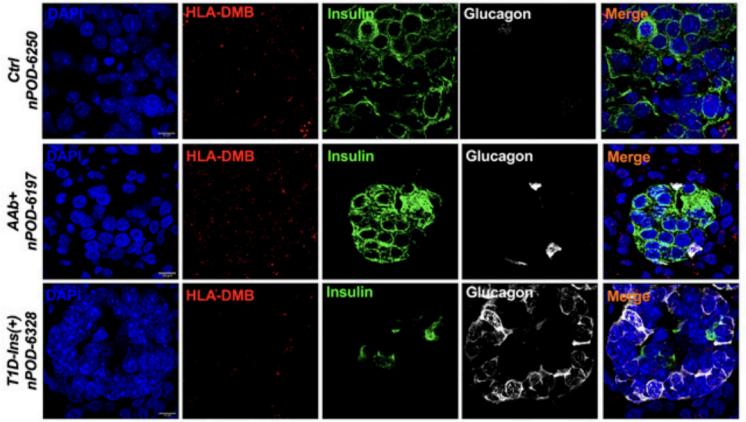
Analyzing the structure of nucleosome nanodomains with SMLM



Seitz et al. bioRxiv, Cells, In Review (2025)

- H2B is densely labeled for super-resolution imaging

Spatial organization of HLA-DMB mRNA in T1D



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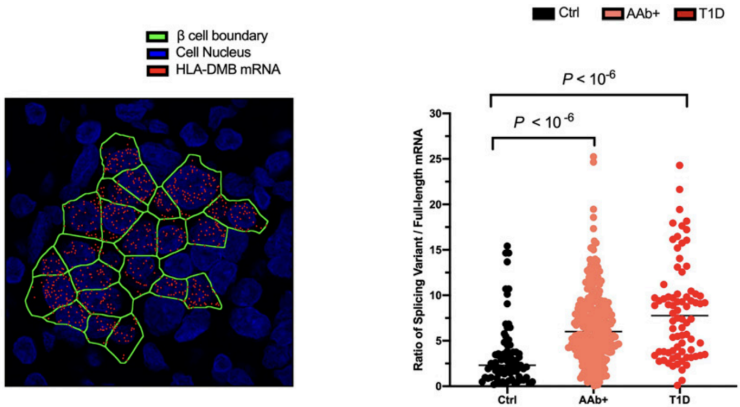

Seitz et al. bioRxiv, Cells, In Review (2025)

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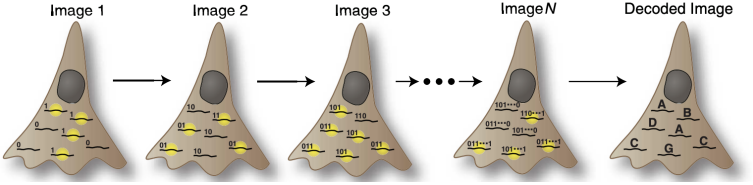
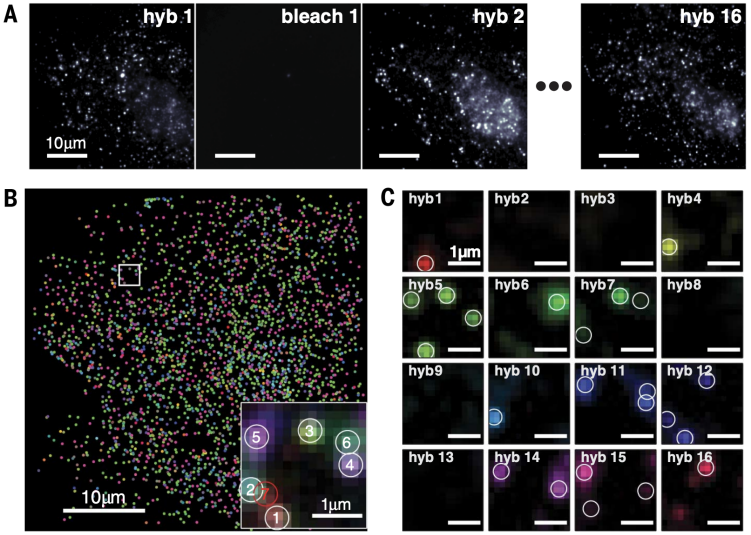
Multiplexed single molecule localization microscopy



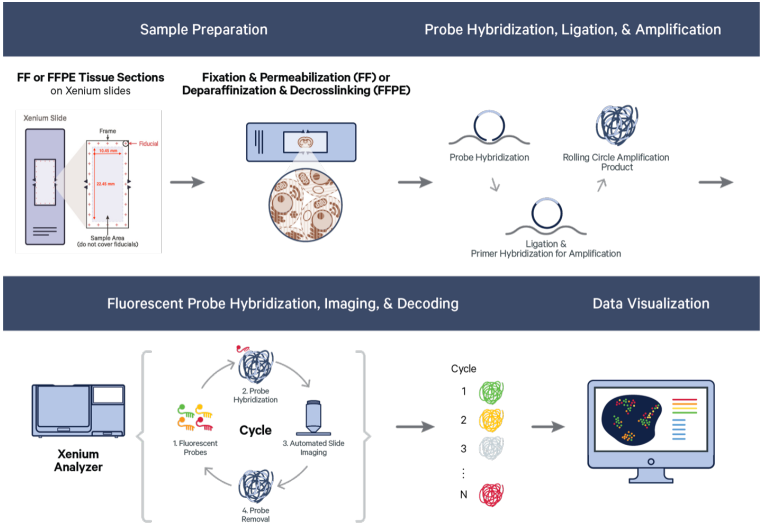
Chen et al. Science. **348** (2015)

Multiplexed single molecule localization microscopy



Chen et al. Science. **348** (2015)

Multiplexed single molecule localization microscopy



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

Multiplexed single molecule localization microscopy

Xenium data example and postprocessing example

Modeling and analysis approaches in spatial transcriptomics

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