



Spatially resolved transcriptomics

Method of the Year 2020 @ *Nature Methods*

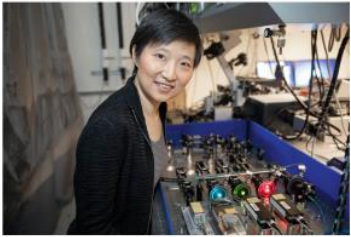
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February 26, 2021

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Ohio State University

Spatially resolved single-cell genomics and transcriptomics by imaging



Xiaowei Zhuang @ Harvard & HHMI

STORM

-- stochastic optical reconstruction microscopy

Super-resolution Microscopy

Method of the Year 2008 @ *Nature Methods*

The Nobel Prize in Chemistry 2014



© Nobel Media AB. Photo: A. Mahmoud

Eric Betzig

Prize share: 1/3

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Stefan W. Hell

Prize share: 1/3

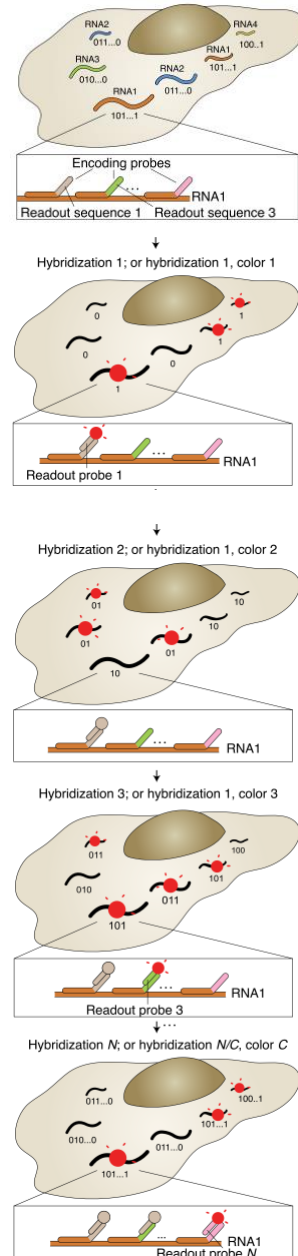
© Nobel Media AB. Photo: A. Mahmoud

William E. Moerner

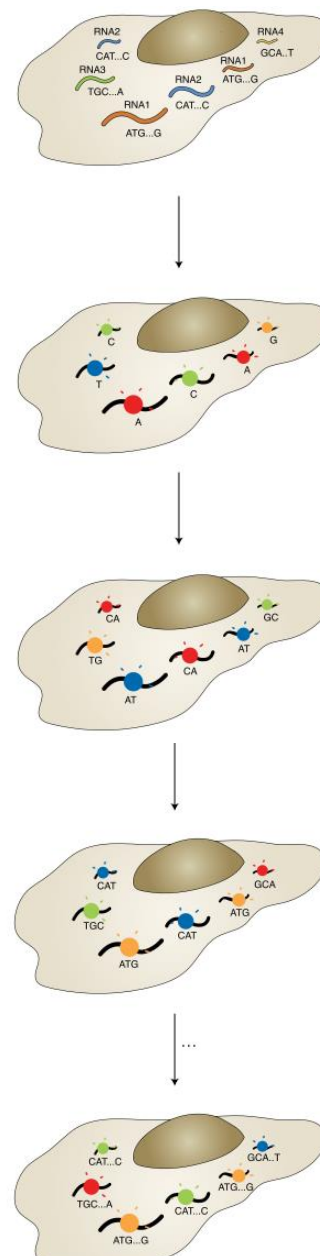
Prize share: 1/3

Betzig: Aug 10, 2006; Mar13, 2006; *PALM Science*; idea in 1995
Zhuang: Aug 9, 2006; Jul 7, 2006; *Nature Methods*

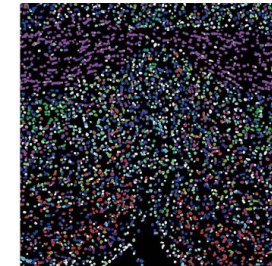
Multiplexed FISH



In situ sequencing

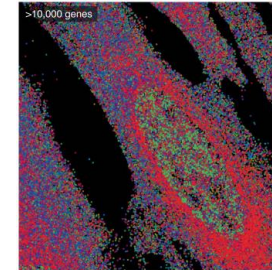


Cell atlas of a complex tissue



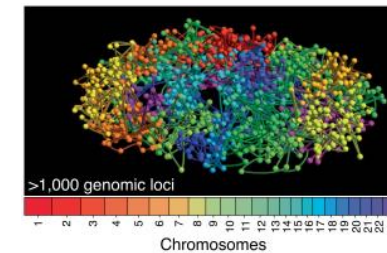
- Single-cell
- In a tissue (brain)
- >1 M cells

Intracellular transcriptome organization

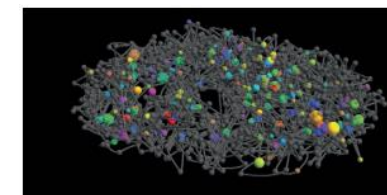


- Single-molecule
- In a single cell
- >10 K genes

3D genome organization & transcriptional bursts



- Single-molecule
- In a single nucleus
- >1000 genomic loci

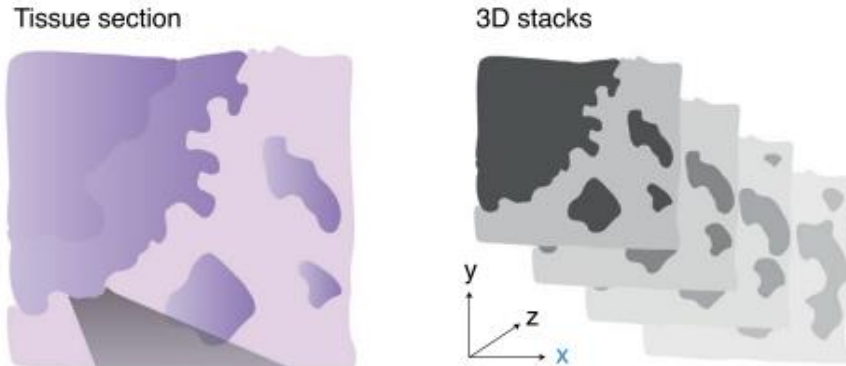


- Single-molecule
- In a single nucleus
- >1000 genes

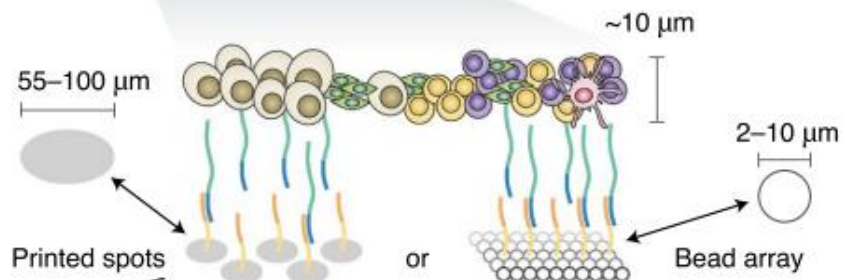
Spatially resolved transcriptomics adds a new dimension to genomics

-- Joakim Lundeberg @ KTH Royal Institute of Technology, Sweden

Sequencing-based spatial transcriptomics



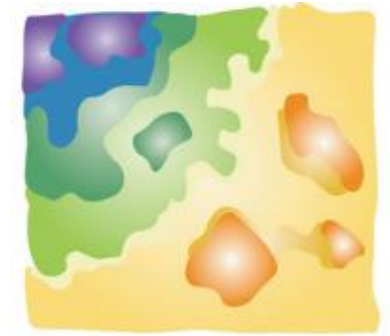
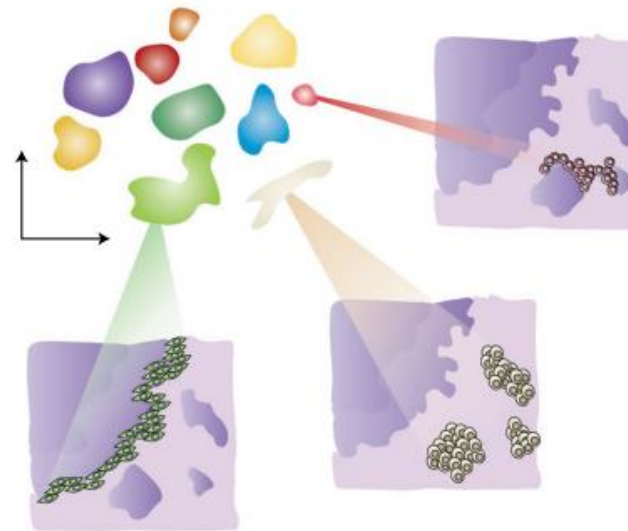
Cryosectioned tissue slices are placed atop the microarray



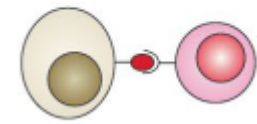
Spatially barcoded probes are printed as microarrays of spots on the surface of glass slides or beads

After enzymatic permeabilization, the released mRNAs hybridize with the surface probes

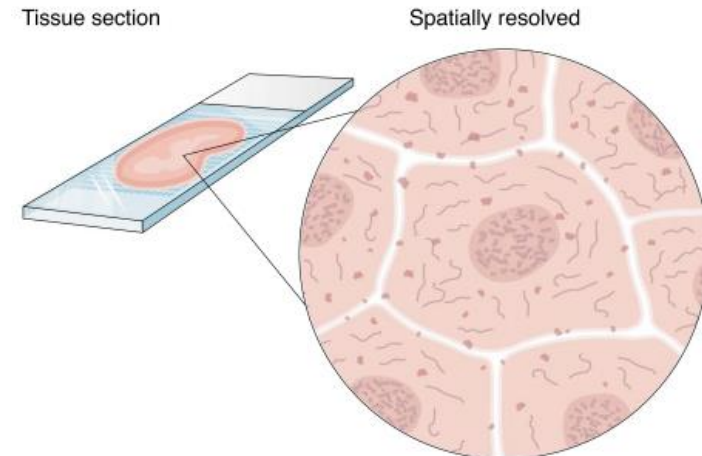
Cell type mapping (scRNA-seq)



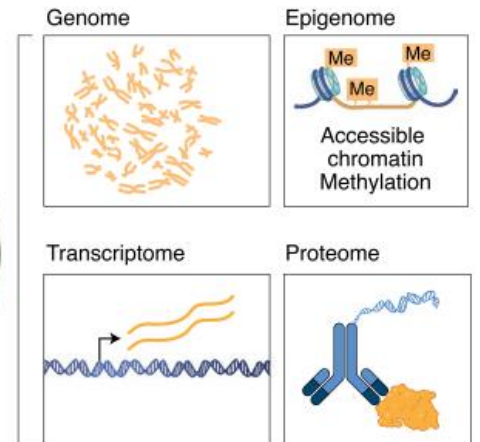
Cell-cell interaction



Networks
cell-cell and gene-gene

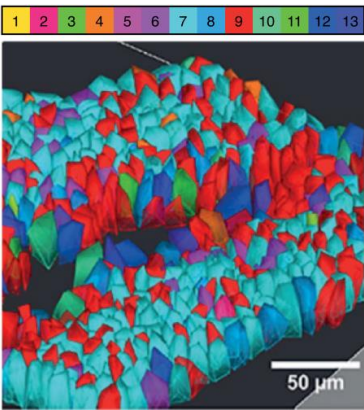


Molecular barcoding

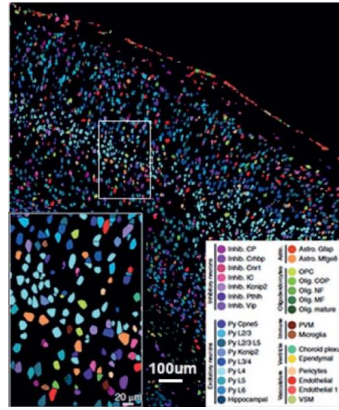


Spatially resolved transcriptomics in neuroscience

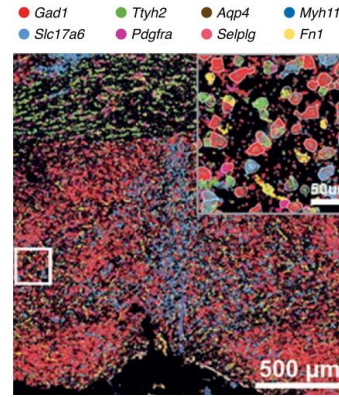
-- Hongkui Zeng @ Director of Allen Institute for Brain Science, USA



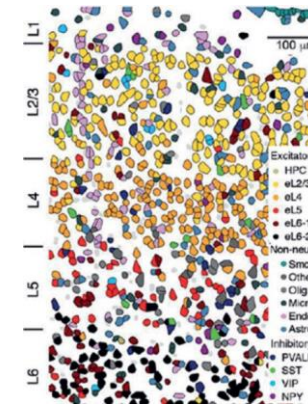
- **seqFISH (Neuron, 2016)**
- dentate gyrus
- 13 genes



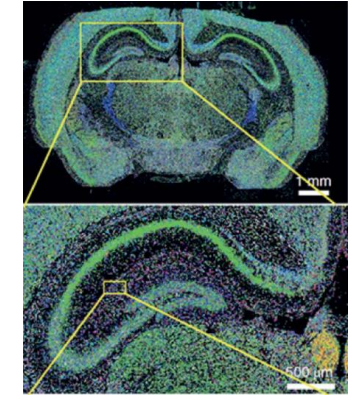
- **osmFISH (Nat Methods, 2018)**
- Somatosensory cortex
- 31 cell types
- 39 genes



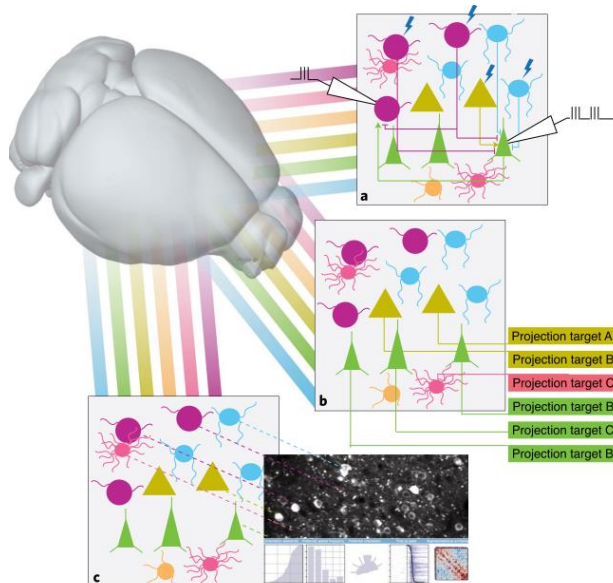
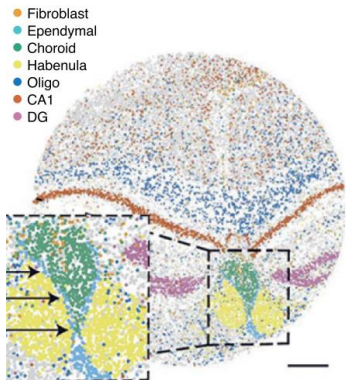
- **MERFISH (Science, 2018)**
- hypothalamic preoptic area
- 70 cell types
- 155 genes



- **STARmap (Science, 2018)**
- visual cortex
- 16 cell types
- 160 genes



- **pciSeq (Nat Method, 2020)**
- hippocampus
- 99 genes



- **Slide-seq (Science, 2019)**
- hippocampus
- large scale
- transcriptome-wide

- **Cell-type-dependent local connectivity**
- **Multi-patch (1991 Nobe Prize)**
- **Optogenetics (Method of the Year 2010)**

- **Long-range projection**
- Barcoded anterograde or retrograde viral labeling

- **Add cell type identities to circuit analysis**
- Spatially resolved transcriptomics
- Calcium imaging

**More opportunities
for both technology
and methodology!**

Method of the Year 2007-2020 @ Nature Methods

- 2007: Next-generation sequencing (**1980 Nobel Prize** for Sanger) (Ray Wu 吴瑞)
- 2008: Super-resolution fluorescence microscopy (**2014 Nobel Prize**) (Xiaowei Zhuang 庄小威)
- 2009: Induced pluripotent stem cells (**2012 Nobel Prize**) (Hongkui Deng 邓宏奎)
- 2010: Optogenetics (Feng Zhang 张锋)
- 2011: Genome editing (ZFN, TALEN) (**2020 Nobel Prize** for CRISPR) (Feng Zhang 张锋, David Liu 刘如谦)
- 2012: Proteomics (**2002 Nobel Prize** for mass spectrometry) (Fuchu He 贺福初)
- 2013: Single-cell sequencing (Fuchou Tang 汤富酬, Xiaoliang Sunney Xie 谢晓亮)
- 2014: Light-sheet fluorescence microscopy
- 2015: Single-particle cryo-electron microscopy (**2017 Nobel Prize**) (Yigong Shi 施一公)
- 2016: Epitranscriptomics (Chuan He 何川)
- 2017: Organoids (Yu Chen 陈宇)
- 2018: Imaging in freely behaving animals (Heping Cheng 程和平)
- 2019: Single-cell multimodal omics (Fuchou Tang 汤富酬)
- 2020: Spatially resolved transcriptomics (Xiaowei Zhuang 庄小威, Long Cai 蔡龙)

Sequencing

Imaging

Thanks