

# Panel@Spatial Omics 2021: Human Reference Atlas

**April 15, 2021: 15:30-16:30 BST (UTC+1)**

# Spatial Biology Europe: **ONLINE**

## LIVE & INTERACTIVE CONTENT SCHEDULE

Please see the full programme for the conference below. Where possible, sessions will be made available OnDemand after the scheduled time slot.

*Please note: Access to OnDemand sessions will only be available to delegates who purchase a full access pass*

DAY TWO: 15 APRIL 2021

### Panel Discussion: Human Reference Atlas

PROFILING & IMAGING

**Moderator:** KATY BÖRNER, Victor H. Yngve Distinguished Professor of Engineering and Information Science, **Indiana University**

#### **Panellists:**

JAMES GEE, Associate Professor of Radiologic Science in Radiology. Director, Penn Image Computing and Science Laboratory, Department of Radiology, Perelman School of Medicine, **University of Pennsylvania**

XUEGONG ZHANG, Professor of Pattern Recognition and Bioinformatics, Director, Bioinformatics Division, TNLIST (Tsinghua National Laboratory for Information Science & Technology), Department of Automation, **Tsinghua University**

AMY BERNARD, Director, Science & Technology Strategy, **Allen Institute**

BERNARD DE BONO, Principal Investigator, Associate Professor, **University of Auckland**

15:30  
-  
16:00



**James Gee**





Amy Bernard



# Brain Reference Atlases

The **Allen Institute** has a history of making open datasets, standards and reference resources in bioscience

- A planar **human brain reference atlas** was developed to support a brain-wide map of gene expression (2012)
- Refinement of this planar map extended to a **3D volume** as an anatomical common coordinate framework for **brain structure** and **cell types** (2016) - and spatial -omics

An anatomically comprehensive atlas of the adult human brain transcriptome (2012) <https://www.nature.com/articles/nature11405>

**ALLEN BRAIN ATLAS**  
DATA PORTAL

[HOME](#) [DATA](#) [REFERENCE ATLASES](#)

<http://atlas.brain-map.org/>

### Allen Brain Reference Atlases

The Allen Institute for Brain Science has generated multiple reference atlases, to use with our online datasets or as stand-alone resources. Refer to our [Citation Policy](#) for information on how you may use these images in your work.

#### Adult Mouse

These anatomical reference atlases illustrate the adult mouse brain in coronal and sagittal planes of section. They are the spatial framework for datasets such as in situ hybridization, cell projection maps, and in vitro cell characterization.

(3D Viewer) (Coronal Sec) (SAGITTAL)

[DOCUMENTATION](#) | [REFERENCE HISTOLOGICAL DATA](#) | [SDK](#) | [API](#) | [COMMUNITY FORUM](#) | [ADDITIONAL REFERENCE DATA](#)

#### Adult Human

These anatomical reference atlases illustrate the adult human brain, using modified Brodmann or gyral annotation.

(Modified Brodmann) (Gyral)

[DOCUMENTATION](#) | [ONTOLOGY](#) | [SUPPLEMENTAL HISTOLOGICAL DATA](#) | [CITATION](#)

#### Developing Mouse

These anatomical reference atlases illustrate the developing mouse brain, covering seven stages of embryonic (E) and postnatal (P) development. Dr. Luis Puelles used a custom developmental taxonomy for annotation of the Allen Developing Mouse Brain Reference Atlases.

E11.5 E13.5 E15.5 P56 E18.5 P4 P14

# Human Brain Atlas

## Goals:

- **Computable**
- Accompanied by methods and metadata
- Useful to researchers
- Serve out robust standard references (ontology, taxonomy, spatial)
- Integration or compatibility with **other human and/or neuro datasets & standards**

## BRAINSPAN

ATLAS OF THE DEVELOPING HUMAN BRAIN

<https://www.brainspan.org/static/atlas>

Home Developmental Transcriptome Prenatal LMD Microarray ISH **Reference Atlas** Download Documentation Help

### BrainSpan Reference Atlases

The BrainSpan Reference Atlases are full-color, high-resolution, Web-based digital brain atlases accompanied by a systematic, hierarchically organized taxonomy of developing human brain structures.

For more information, please refer to the [documentation](#).

Atlas	Annotation	Supporting Data
<a href="#">15 pcw - Whole Brain</a>	46 sections (0.5 - 1.0 mm intervals)	<a href="#">Nissl</a> , <a href="#">AChE</a> , <a href="#">ISH</a>
<a href="#">21 pcw - Cerebrum</a>	81 sections (0.5 - 1.2 mm intervals)	<a href="#">Nissl</a> , <a href="#">AChE</a> , <a href="#">ISH</a>
<a href="#">21 pcw - Brainstem</a>	41 sections (0.25 - 0.5 mm intervals)	<a href="#">Nissl</a> , <a href="#">AChE</a> , <a href="#">ISH</a>
<a href="#">34 yrs - Whole Brain</a>	Featuring two cortical views: <a href="#">Sulcal - Gyral</a> <a href="#">Modified Brodmann</a>  106 sections (0.4 - 3.4 mm intervals)	<a href="#">Nissl</a> , <a href="#">Parvalbumin</a> , <a href="#">3T structural MRI (47MB)</a> , <a href="#">7T structural MRI (5GB)</a> , <a href="#">3T 1200 micron diffusion (880MB)</a> , <a href="#">3T 900 micron diffusion (1GB)</a>



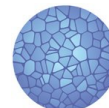
Brain/MINDS



EBRAINS



BICCN



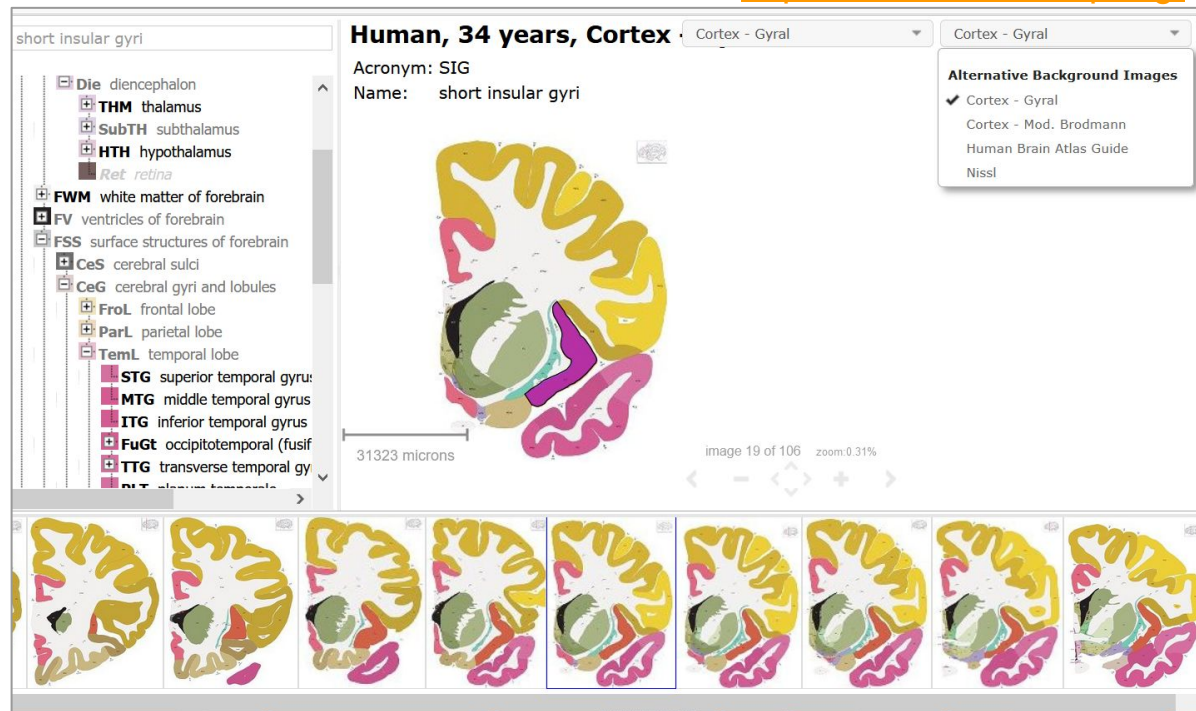
HUMAN  
CELL  
ATLAS

# Adult Brain Atlas

<https://atlas.brain-map.org/>

## Resources

- Open, online atlas portal
- Software development toolkit (SDK and API)
- Applications to build extensible nomenclature from taxonomies ([GitHub](#))

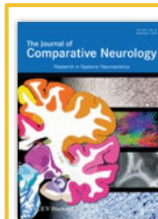


Common cell type nomenclature for the mammalian brain. (2020)

<https://elifesciences.org/articles/59928>

Comprehensive cellular resolution atlas of the adult human brain.

<https://onlinelibrary.wiley.com/doi/10.1002/cne.24080>



Volume 524, Issue 16  
Special Issue: The Allen Human Brain Reference Atlas

Pages: Spc1, 3125-3481  
November 1, 2016



Xuegong Zhang





# Xuegong Zhang

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## **The organization of cell atlases: apparent coordinates vs. latent representations**

### Multiple apparent coordinates of a cell atlas

- Spatial: anatomic parts, spatial locations, ...
- Temporal: developmental trajectory, cell cycle, ...
- Functional: cell types/states, stemness, malignancy, marker gene expression, ...

The coordinates are of three major types: discrete, continuous, structured

Multifaceted heterogeneity in a cell atlas: multiple intertwined coordinates

# Signal or noise?

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When multiple coordinates intertwined, specific studies usually take one as signal and the rest as noise

But they should be all signals in a reference atlas

	Cell types	Cell cycle	Pseudotime	Other
Cell type study	Signal	Confounder	Confounder	Confounder
Cell cycle study	Confounder	Signal	Confounder	Confounder
Development study	Confounder	Confounder	Signal	Confounder
Reference Atlas	Signal	Signal	Signal	Signal

# A general representation framework for the information structure is desirable

— — —

- To provide a the full portraiture of cells
- To represent the multifaceted cell heterogeneity in an atlas
- To analyze relations across multiple coordinates
- To measure the intrinsic complexity of a cell population
- To find hints for unknown factors
- ...

# UniCoord:

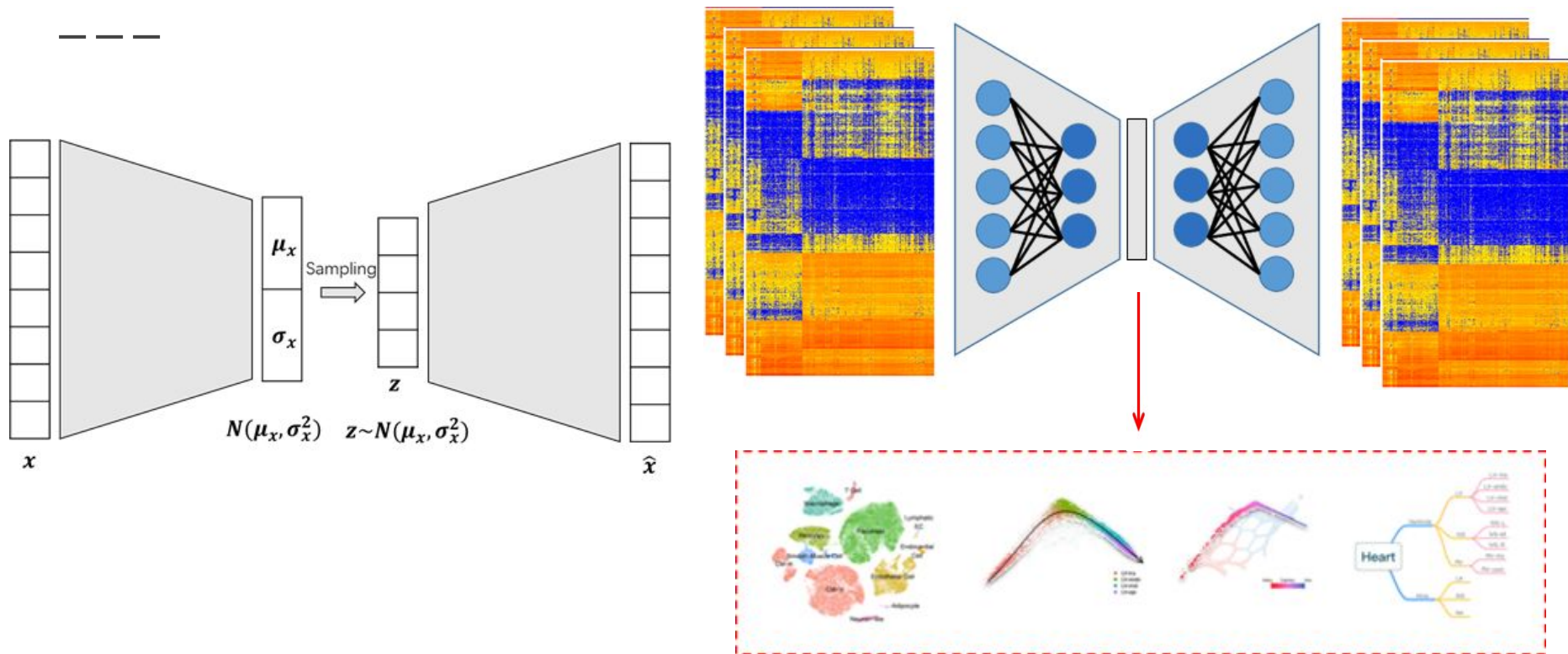
## An unified coordinate system for cell atlases

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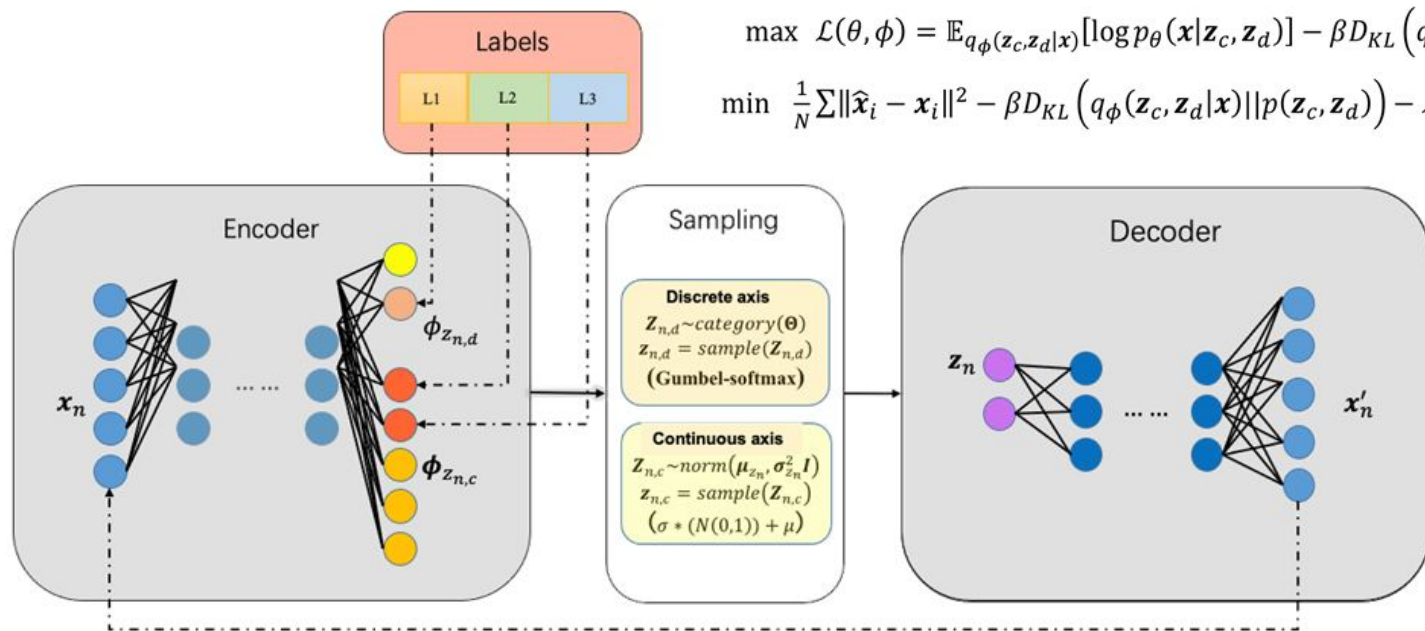
An universal latent CCF (common coordinate framework)

- A low-D vector representation of the hi-D data
- Preserves multifaceted intrinsic coordinates
- Explainable and computable
- Potential for finding unknown heterogeneity
- Individual invariant
- Full annotation of new query cells
- Can generate pseudo-cells

# An Expanded VAE Model for Learning Multifaceted Coordinates



# The expanded VAE model of UniCoord

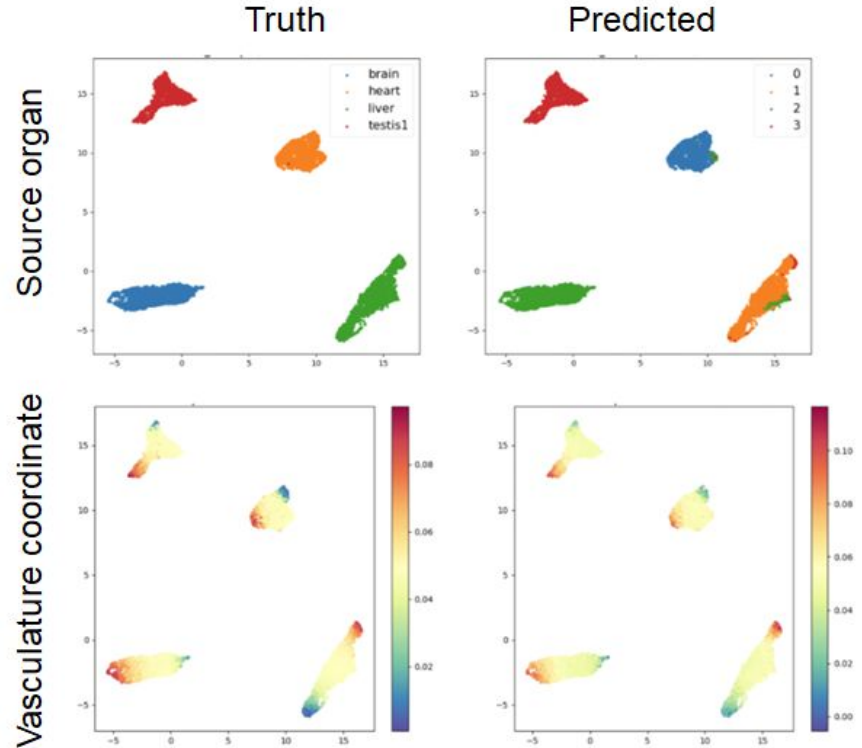
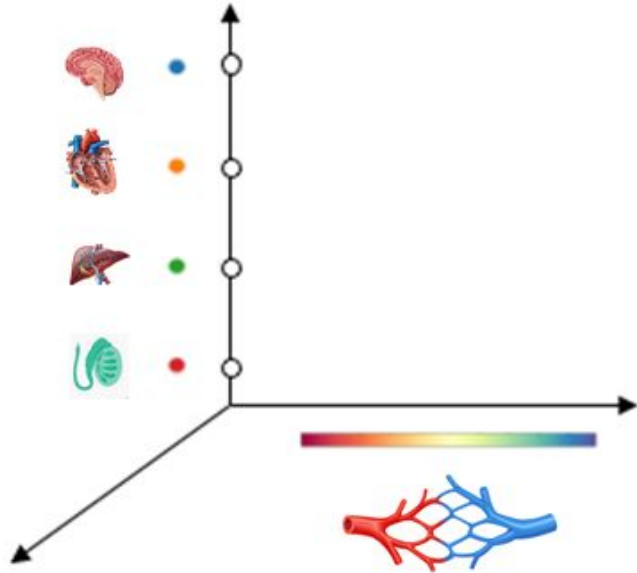


$$\max \mathcal{L}(\theta, \phi) = \mathbb{E}_{q_{\phi}(z_c, z_d | x)} [\log p_{\theta}(x | z_c, z_d)] - \beta D_{KL}(q_{\phi}(z_c, z_d | x) || p(z_c, z_d)) + \mathcal{L}_{reg}$$

$$\min \frac{1}{N} \sum \|\hat{x}_i - x_i\|^2 - \beta D_{KL}(q_{\phi}(z_c, z_d | x) || p(z_c, z_d)) - \mathcal{L}_{reg} \quad \text{when data are Gaussian}$$



# Example of UniCoord Experiments





# Bernard de Bono





# Bernard de Bono

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Q&A