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

PROFILING & IMAGING

Panel Discussion: Human Reference Atlas

15:30 - 16:00

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**

James Gee

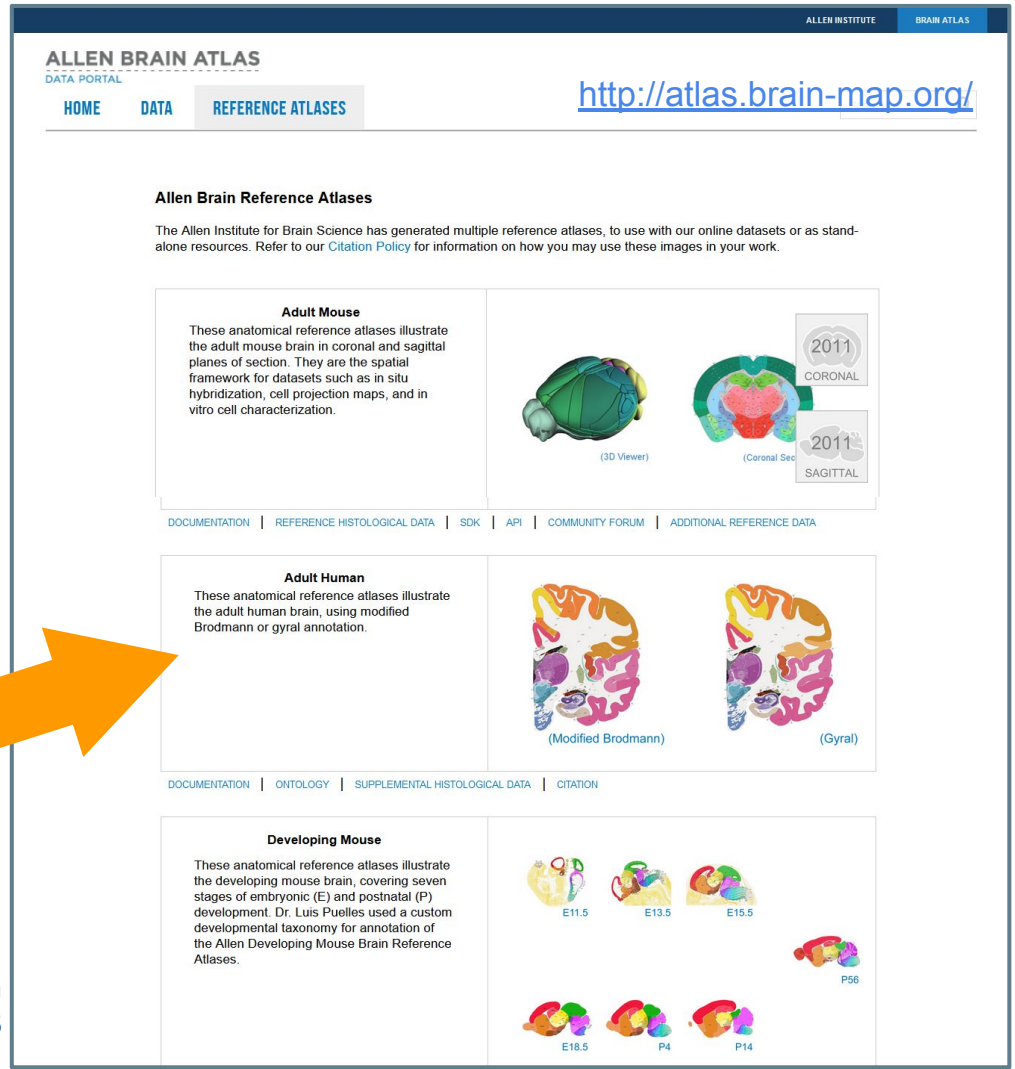
Amy Bernard

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

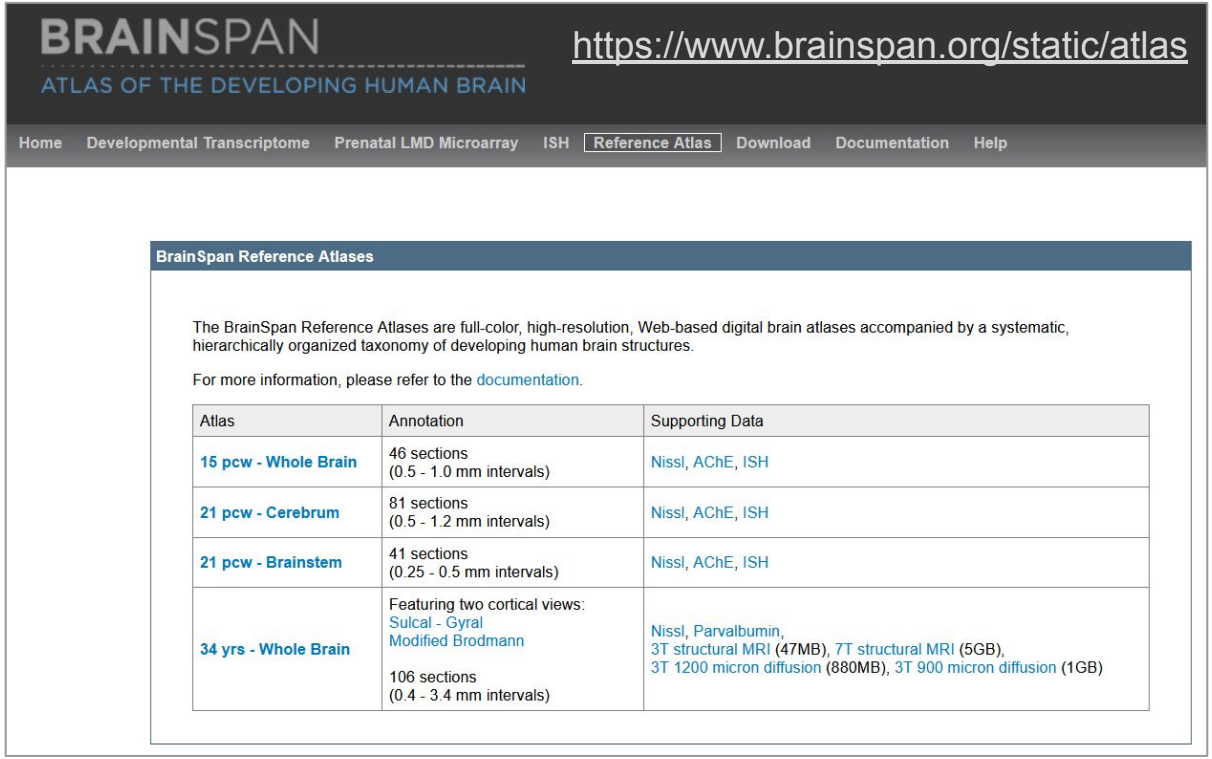
An anatomically comprehensive atlas of the adult human brain transcriptome (2012) https://www.nature.com/articles/nature11405



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**



HuBMAP ORGANS

SPARC

EBRAINS

HUMAN CELL ATLAS

Brain/MINDS

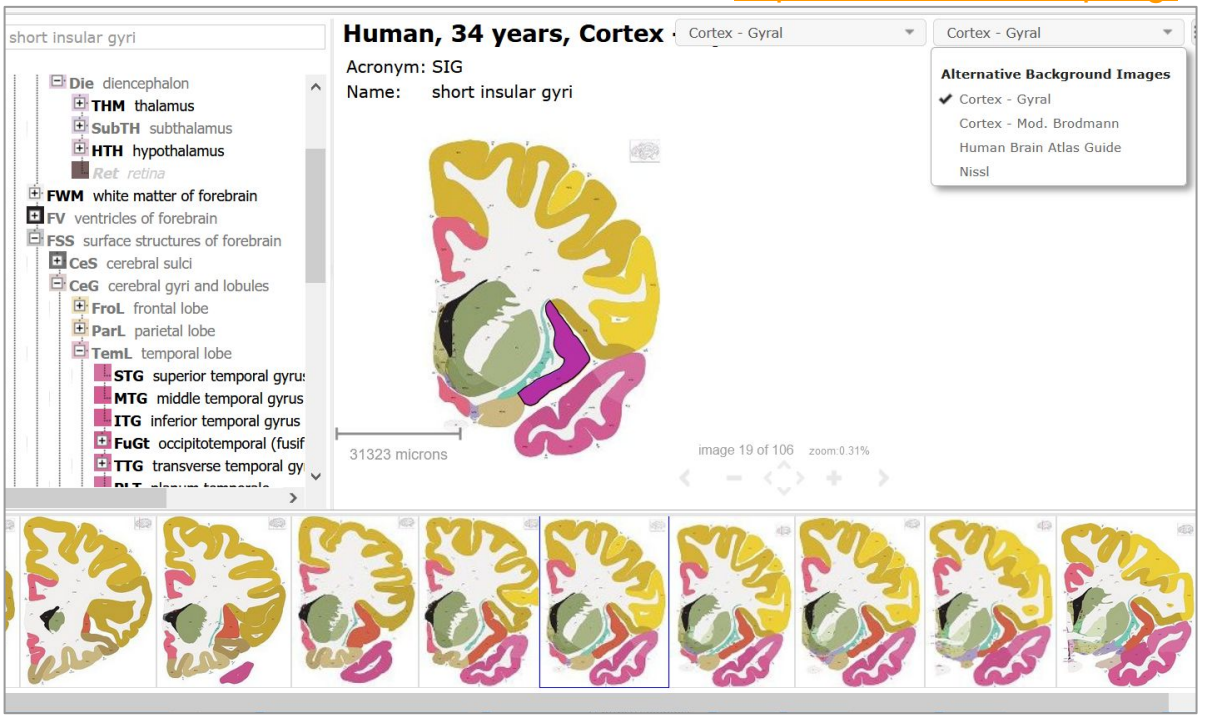
BICCN

Adult Brain Atlas

Resources

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

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

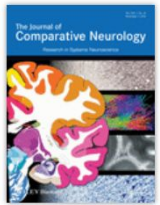


Common cell type nomenclature for the mammalian brain. (2020)

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

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?

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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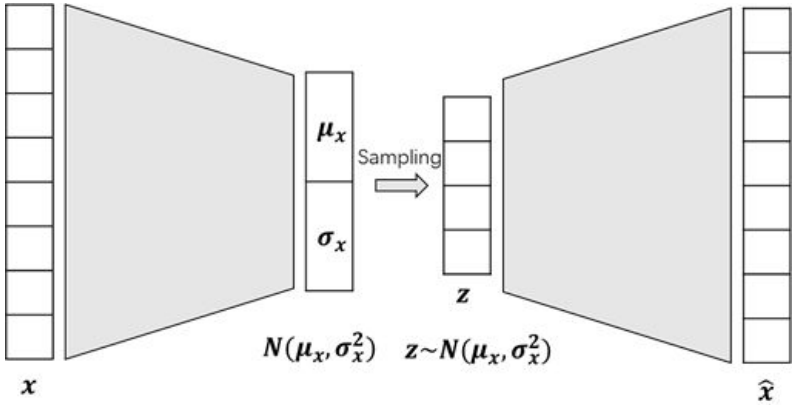
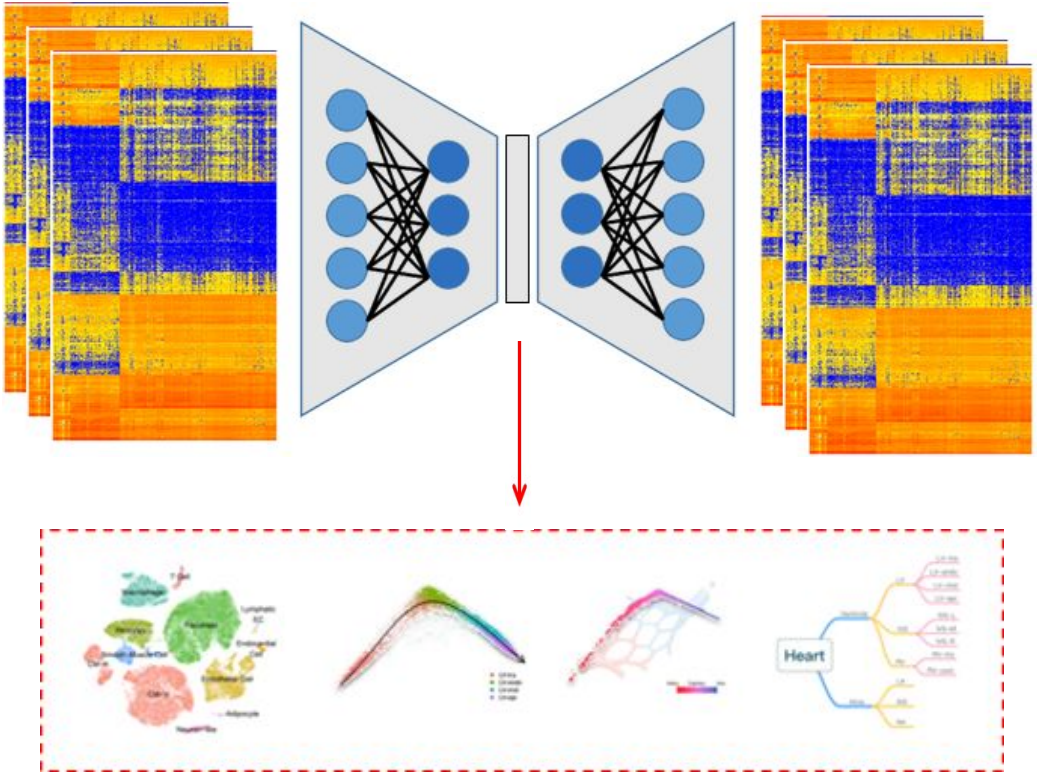
An universal latent CCF (common coordinate framework)

- 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

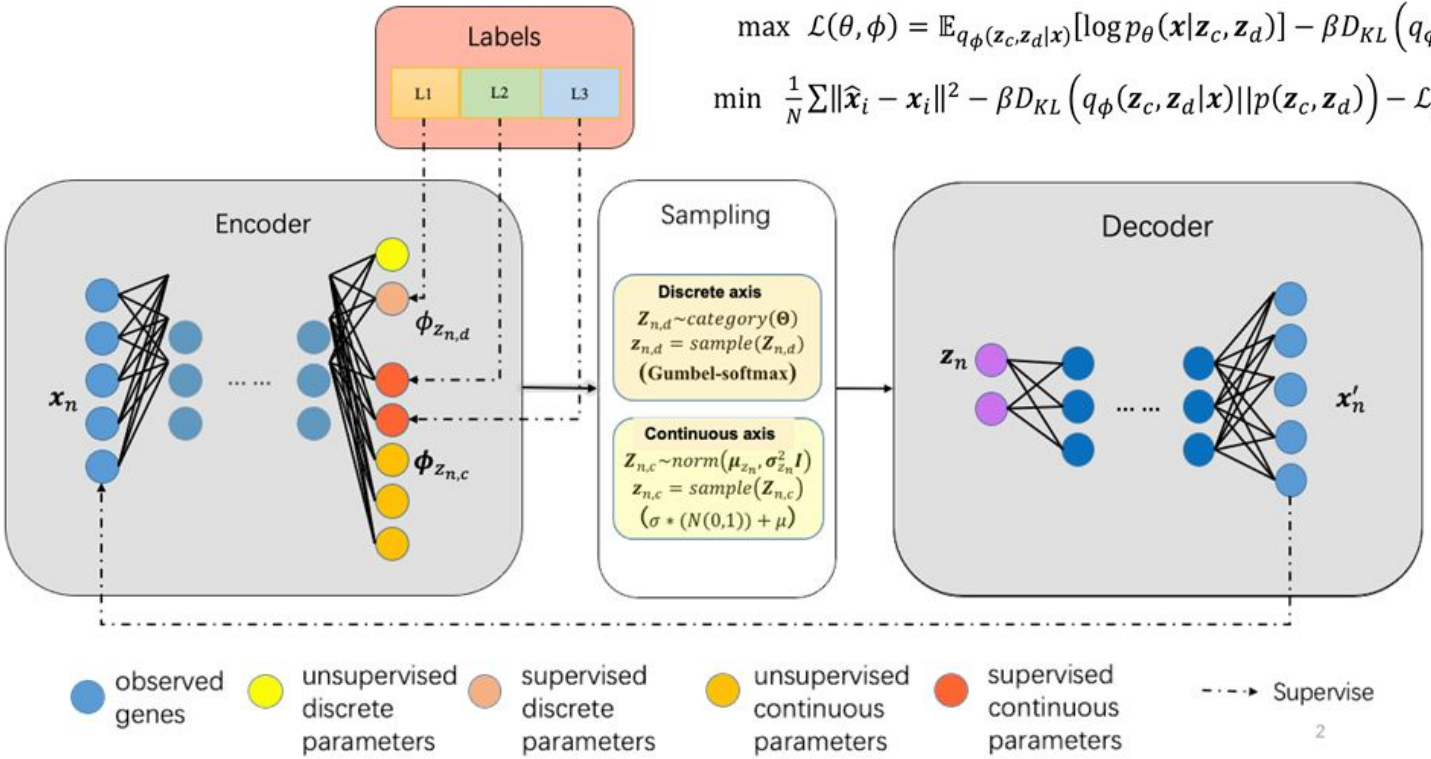




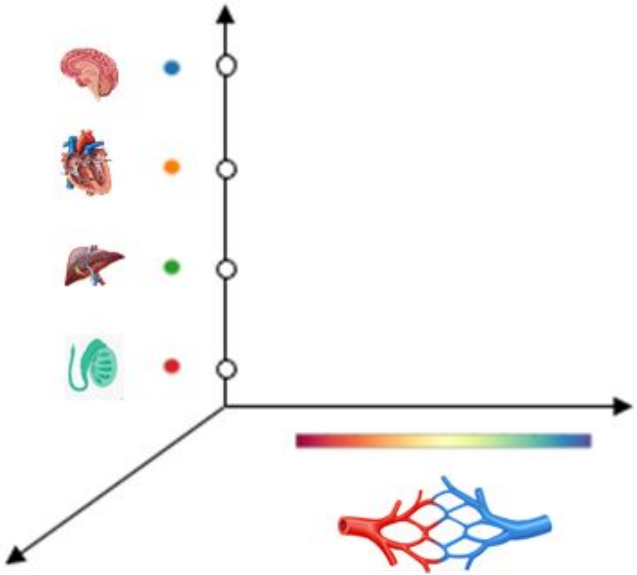
The expanded VAE model of UniCoord

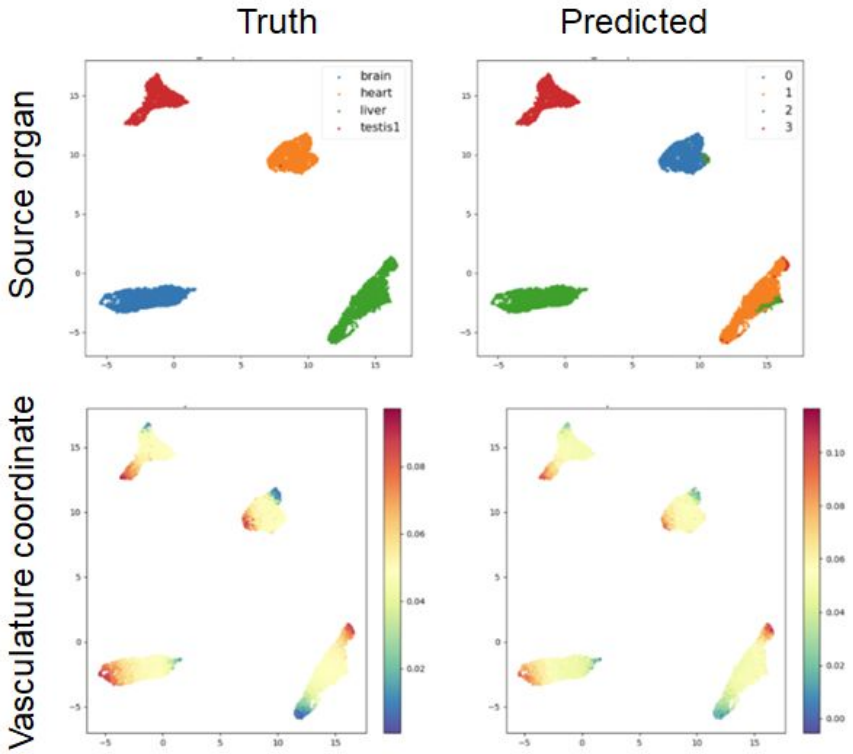
$$\max \ \mathcal{L}(\theta,\phi) = \mathbb{E}_{q_\phi(\boldsymbol{z}_c,\boldsymbol{z}_d|\boldsymbol{x})}[\log p_\theta(\boldsymbol{x}|\boldsymbol{z}_c,\boldsymbol{z}_d)] - \beta D_{KL}\left(q_\phi(\boldsymbol{z}_c,\boldsymbol{z}_d|\boldsymbol{x})||p(\boldsymbol{z}_c,\boldsymbol{z}_d)\right) + \mathcal{L}_{reg}$$

$$\min \ \frac{1}{N}\sum\|\hat{\boldsymbol{x}}_i - \boldsymbol{x}_i\|^2 - \beta D_{KL}\left(q_\phi(\boldsymbol{z}_c,\boldsymbol{z}_d|\boldsymbol{x})||p(\boldsymbol{z}_c,\boldsymbol{z}_d)\right) - \mathcal{L}_{reg}$$ when data are Gaussian



Example of UniCoord Experiments





Bernard de Bono

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Q&A