

# Cytosplore EvoViewer: Visual Analytics of Conserved Evolutionary Patterns in multi-species single-cell sequencing data



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Image Ref. Left: <u>https://phys.org/news/2024-05-chimps-shown-tool-skills-adults.html</u> Image Ref. Middle: <u>https://www.nbcnews.com/id/wbna9535875</u> Image Ref. Right: <u>https://stock.adobe.com/nl/images/a-man-chopping-wood-in-the-forest/115368859</u>









Image Ref.: <u>https://phys.org/news/2024-05-chimps-shown-tool-skills-adults.html</u>









Image Ref.: <u>https://www.nbcnews.com/id/wbna9535875</u>









Image Ref.: <u>https://stock.adobe.com/nl/images/a-man-chopping-wood-in-the-forest/115368859</u>







Image Ref.: <u>https://vocal.media/01/the-evolution-of-human-language-from-grunts-to-global-</u> <u>communication</u>



### Brain Complexity Across Species





Image Ref.: http://www.wiringthebrain.com/2020/08/are-bigger-bits-of-brains-better.html



## Transcriptomic data

- Information about the RNA molecules
- Which genes are expressed

Image Ref.: <u>https://www.nature.com/articles/s41386-019-0484-7</u>









### Brain tissue





Genes



Cell by gene matrix

### Comparative studies



Heuer, et al., Elsevier, 2019



**Pacific Visualization 2025** 

### CORRECTION FOR THIS ARTICLE



**Evolutionary expansion of connectivity between** multimodal association areas in the human brain

compared with chimpanzees

Dirk Jan Ardesch<sup>a</sup>, Lianne H. Scholtens<sup>a</sup>, Longchuan Li<sup>b</sup>, Todd M and Martiin P. van den Heuvel<sup>®</sup>

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Edited by John Morrison, University of California Davis, and accepted by Editorial

The development of complex cognitive functions during human evolution coincides with pronounced encephalization and expan-sion of white matter, the brain's infrastructure for region-toregion communication. We investigated adaptations of the human macroscale brain network by comparing human brain wiring with that of the chimpanzee, one of our closest living primate relatives. White matter connectivity networks were reconstructed using diffusion-weighted MRI in humans (n = 57) and chimpanzees (n = 20) and then analyzed using network neuroscience tools. We demonstrate higher network centrality of connections linking multimodal association areas in humans compared with chimpanzees, to-gether with a more pronounced modular topology of the human connectome. Furthermore, connections observed in humans but not in chimpanzees particularly link multimodal areas of the tem-poral, lateral parietal, and inferior frontal cortices, including tracts mportant for language processing. Network analysis demon trates a particularly high contribution of these connections to global network integration in the human brain. Taken together our comparative connectome findings suggest an evolutionary shift n the human brain toward investment of neural resources in multimodal connectivity facilitating neural integration, combined with guage-related connectivity supporting functional

nnectome | evolution | chimpanzee | multimodal | comparative

A key step toward understanding human behavior is to un-derstand how the human brain supports advanced cognitive functions such as social cognition, language, and theory of mind abilities that are highly developed in humans (1-3). Comparative studies have pointed to several brain adaptations that may have facilitated the emergence of complex cognition during hu-man evolution. The modern human brain is approximately three times larger in volume than that of early hominins, vastly exceeding the predicted brain size for a primate species of the same body size (4-6). Cellular examinations have indicated more ronounced dendritic branching of pyramidal cells in the human brain compared with other primates, suggesting a greater po-tential for neural integration of information in humans (7-9). Indeed, the human brain allocates relatively more cortex to asciation areas than to primary sensory and motor areas (4, 10-12), along with proportionally more white matter compared with other primates (13-15). These observed differences suggest that the evolution of advanced cognitive features in humans was accompanied by widespread modifications to the complex archiecture of the human brain and its connectivity. The topologica organization of these brain connectivity adaptations and their

www.pnas.org/cgi/doi/10.1073/pnas.1818512116

### Ardesch, et al., National Acad Sciences, 2019

### Article

### Comparative cellular analysis of motor cortex in human, marmoset and mouse

https://doi.org/10.1038/s41586-021-03465-8	A list of aut
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Published online: 6 October 2021	transcript
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Single-cell transcriptomic and epigenomic metl	nods have bee

the mouse and human neocortex, diverse neuronal and no cell types can be defined<sup>2,3,5,7</sup> by their distinct transcriptio and regions of accessible chromatin or of DNA methyla and can be aligned between species<sup>3,9-11</sup> on the basis of the tudies such as these have shown the feasibility of quanti ing the evolution of cell types, but have limitations; diffe regions have been profiled in humans and mice; different scripts have been captured with single-cell and single-nuc and transcriptomic and epigenomic studies have mostly l out independently

The primary motor cortex (M1, also known as MOp in r ideal region with which to address questions about cellular rodents and primates. M1 is essential for fine-motor control tionally conserved across mammals<sup>1</sup>. The layer 5 (L5) region and primate M1 contains specialized 'giganto-cellular' neurons (Betz cells in primates<sup>12-16</sup>) with distinctive action properties that support a high conduction velocity  $^{\rm 17-19}$ vnapse directly onto spinal motor neurons, unlike roden nal neurons, which synapse indirectly via spinal interne observations suggest that Betz cells possess species-adapt mechanisms to support rapid communication that should b in their molecular signatures. To explore the evolution tion and divergence of M1 cell types and their underlyin

Bakken, et al., Nature, 2021

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Comparative transcriptomics reveals human-specific cortical features

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### Abstract:

Humans have unique cognitive abilities among primates, including language, but their molecular, cellular, and circuit substrates are poorly understood. We used comparative single nucleus transcriptomics in adult humans, chimpanzees, gorillas, rhesus macagues, and common marmosets from the middle temporal gyrus (MTG) to understand human-specific features of cellular and molecular organization. Human, chimpanzee, and gorilla MTG showed highly similar cell type composition and laminar organization, and a large shift in proportions of deep layer intratelencephalic-projecting neurons ared to macaque and marmoset. Species differences in gene expression a evolutionary distance and were seen in all cell types, although chimpanzees were more similar to

Jorstad, et al., Science, 2023

### Motor control: specialized brain region



Image Ref.: <u>https://www.flintrehab.com/primary-motor-cortex-damage/</u>



### Contributions

- Domain Abstraction
- Develop Cytosplore EvoViewer
- Expert evaluation



### Domain abstraction setup

- Participatory design approach
- Bi-weekly online meeting with experts
- Iterative development



- How do cell type abundances vary across species?
- do they vary between species?
- To what extent are marker genes related to subtrees of the phylogenetic tree or other prior evolutionary knowledge?



### Which genes are potential marker genes for a cell type and how

- How do cell type abundances vary across species?
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### Which genes are potential marker genes for a cell type and how



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# Task: Lookup cell types

**Lookup** cell types at different levels of the taxonomy

		Glutamatergic	
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# Task: Lookup cell types

**Lookup** cell types at different levels of the taxonomy

Class			Glutamatergic	
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More low-level cell type categorization

### Task: Compare cell abundance

**Compare** cell abundance of a cell type between species



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### Task: Compare cell abundance

**Compare** cell abundance of a cell type between species



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**Compare** cell abundance of a cell type between species



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# Task: Identify marker genes

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**Identify** genes with high differential expression for a specific cell type (marker genes) in one or more species



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### Task: Explore markers across species

for marker genes, explore the relevance of these genes for the same cell type in other species



All cells of selected species are shown colored by expression of selected gene

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DEF8	3	🖚 pig				
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### Task: Compare prior knowledge

**Compare** species according to prior knowledge, such as traits or phylogeny according to differences in marker gene properties



### Mean expression for RORB in selected cells



### Task: Compare prior knowledge

**Compare** species according to prior knowledge, such as traits or phylogeny according to differences in marker gene properties



### Mean expression for RORB in selected cells



### Task: Compare prior knowledge

**Compare** species according to prior knowledge, such as traits or phylogeny according to differences in marker gene properties







### User study

- Exercises based on research questions
- Likert scale usability responses
- Open ended feedback



# User study setup

- 3 expert participants
- Participants not familiar with the software and design
- Online one hour sessions



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**Patterns in abundance** 

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	Easy selection	Easy identification	Confident findings	Easy confirmation

**Open Feedback**:

"Side-by-side absolute and relative abundances enable unbiased crossspecies comparisons."

**Open Feedback**: "Embedding view provides clear insights. P-values and fold changes can be added for deeper analysis."





### **Phylogenetic relationships**

Helpful tree	HelpfulEasyConfidtreecomparisonfindin	

**Open Feedback**: "Phylogenetic tree offers valuable information. Differential expression can be added for more comprehensive analysis."

### Conclusion

- Compare multi-species single-cell data
- Find conserved cell types & genes
- Developed with expert collaboration



# Conclusion

- Compare multi-species single-cell data
- Find conserved cell types & genes
- Developed with expert collaboration
- Future:

**Reverse confirmation workflow** 



Current: Cell types  $\rightarrow$  Genes  $\rightarrow$  Species

Future: Species  $\rightarrow$  Genes  $\rightarrow$  Cell types

Cytosplore EvoViewer

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Delft University of Technology







Installer:







