11PM

4AM in London (GMT), 1PM in Tokyo (GMT+9)

Multiscale Visualizations

Moderator: Andreas Bueckle, *Indiana University*

Presenters:

- Tobias Isenberg, *National Institute for Research in Digital Science and Technology (Inria)*
- Ludovic Autin, *Scripps Research Institute*
- Griffin Weber, *Harvard Medical School*

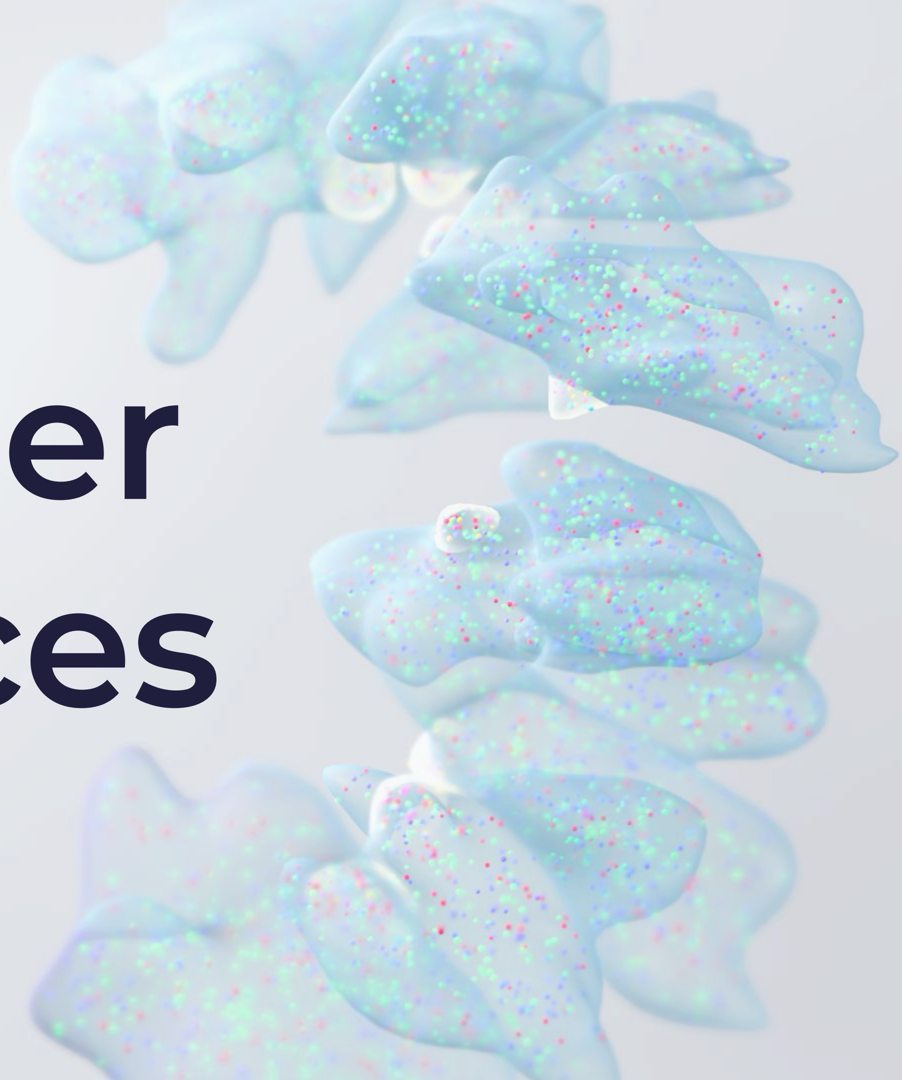
Setting the Stage: Building and Exploring the Human Reference Atlas with Virtual Reality

Andreas "Andi" Bueckle, Ph.D.
Research Lead

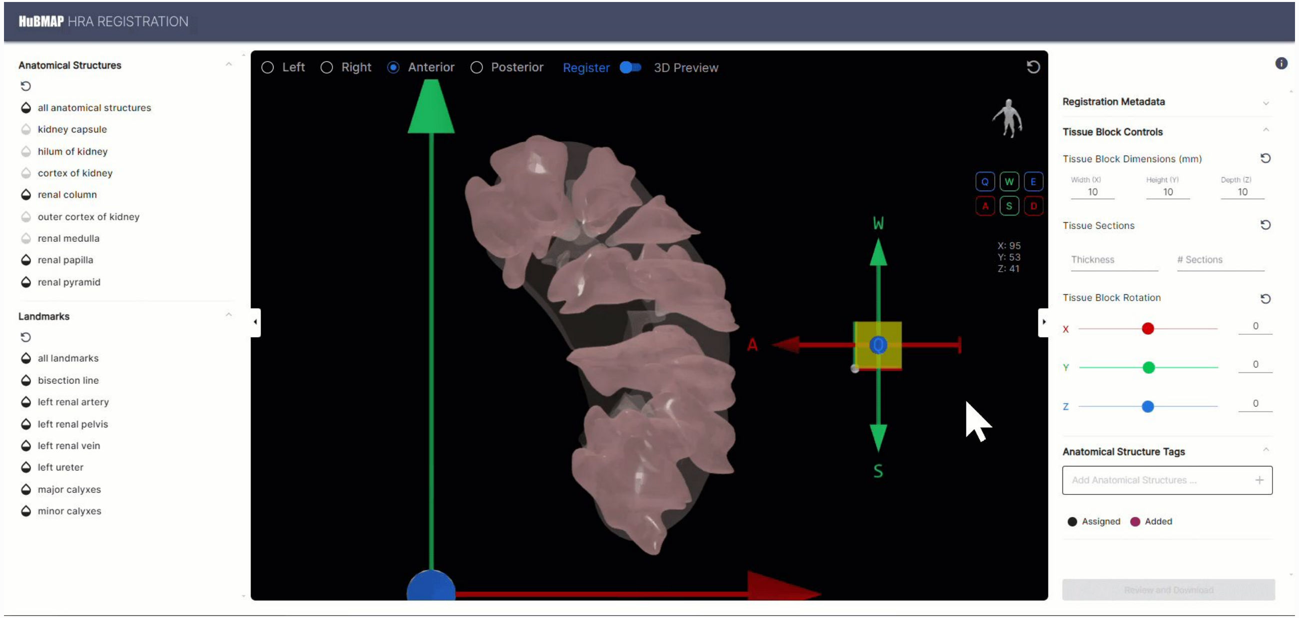
Cyberinfrastructure for Network Science Center
Department of Intelligent Systems Engineering
Luddy School of Informatics, Computing, and Engineering
Indiana University, Bloomington, IN, USA

24h Multiscale Human Event | Virtual | December 14, 2024

HRA User Interfaces

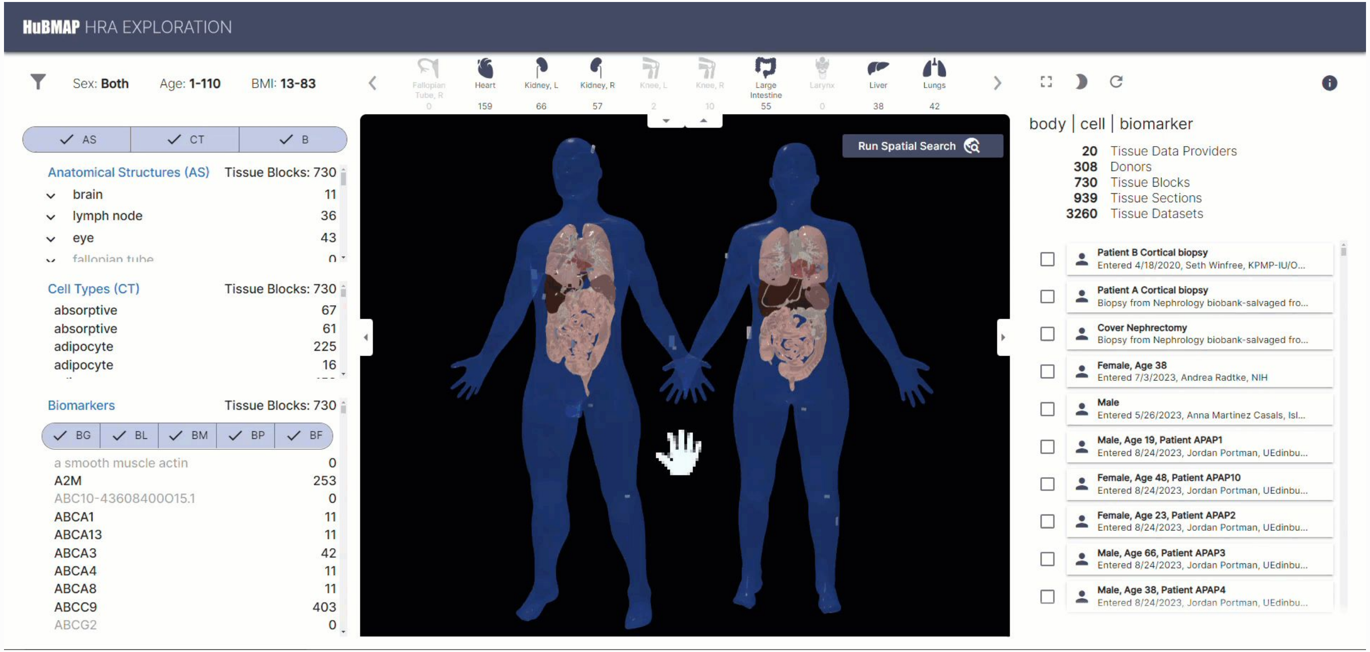


Registration User Interface (RUI)



https://apps.humanatlas.io/rui/

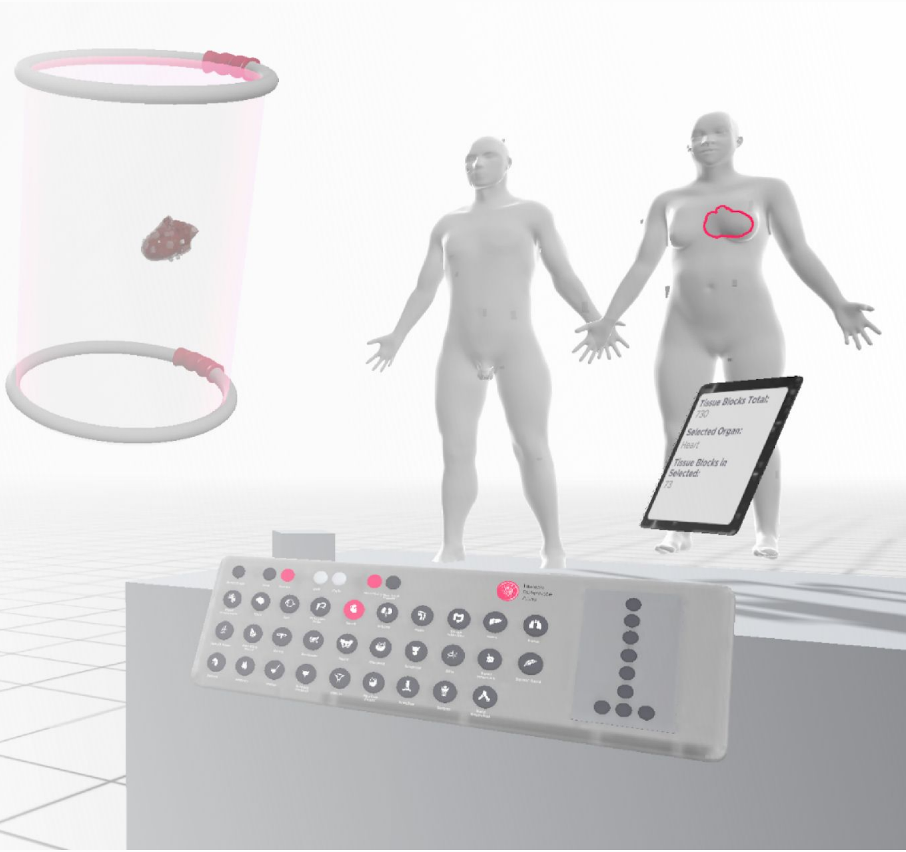
Exploration User Interface (EUI)



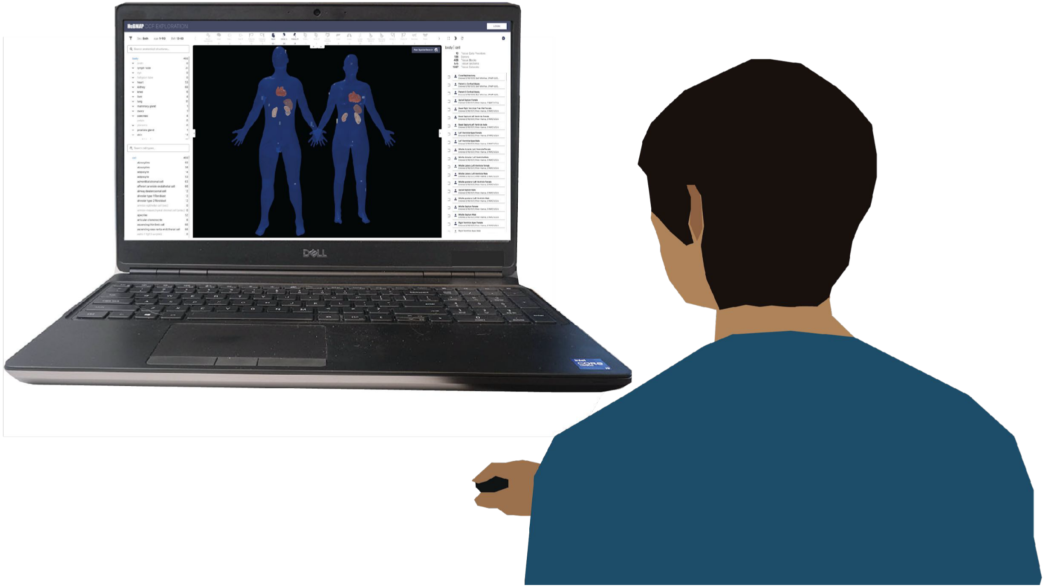
https://apps.humanatlas.io/eui/

HRA Organ Gallery in VR

What if...?


Tissue Blocks Total:
730
Selected Organ:
Heart
Tissue Blocks in Selected:
73

What if?



HRA Exploration User Interface: https://apps.humanatlas.io/eui/

HRA Organ Gallery in VR

APP

Scan to download

Meta

Identified **3 major use cases**:

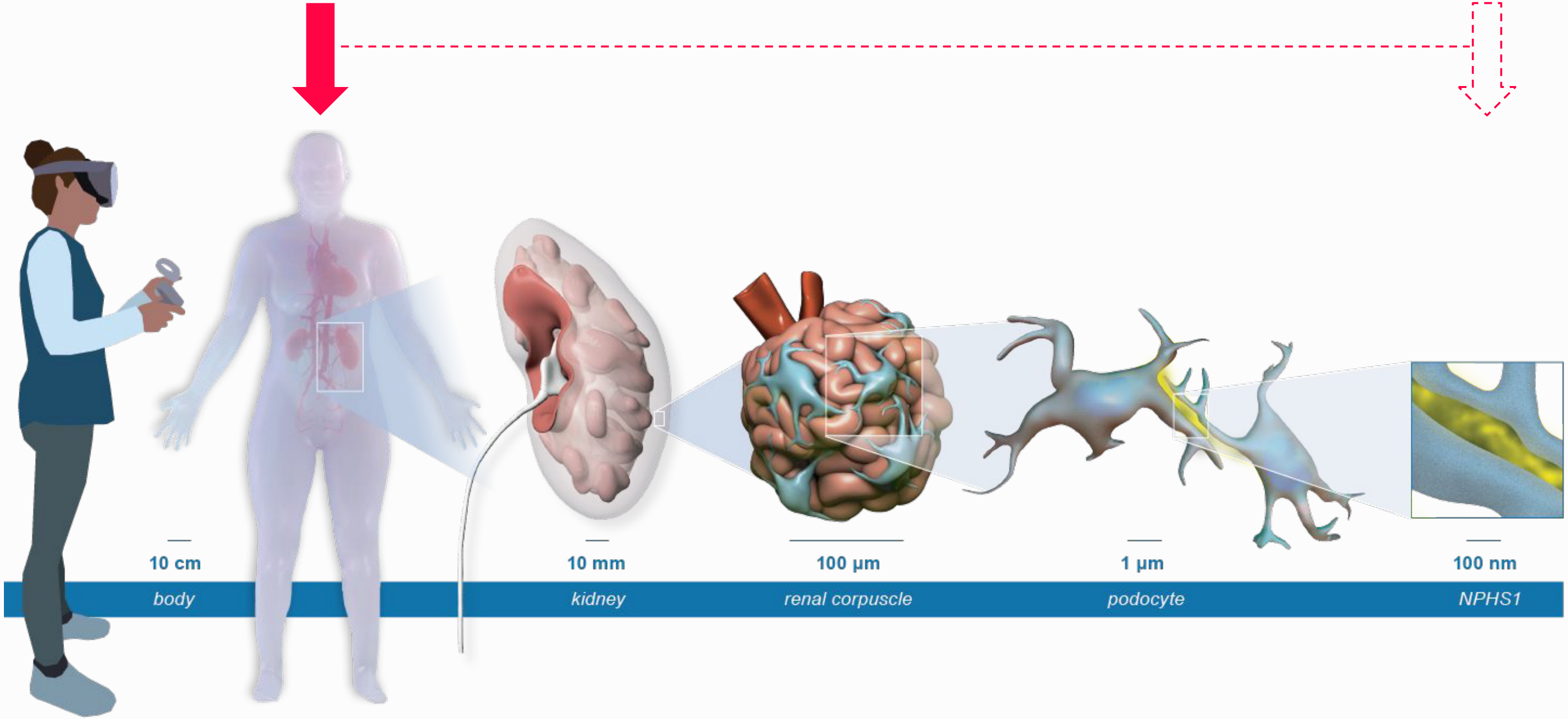
- Quality Assurance/Quality Control for registered tissue blocks
- Onboarding to the HRA
- Telling Embodied Data Stories

Paper:
https://doi.org/10.3389/fbinf.2023.1162723

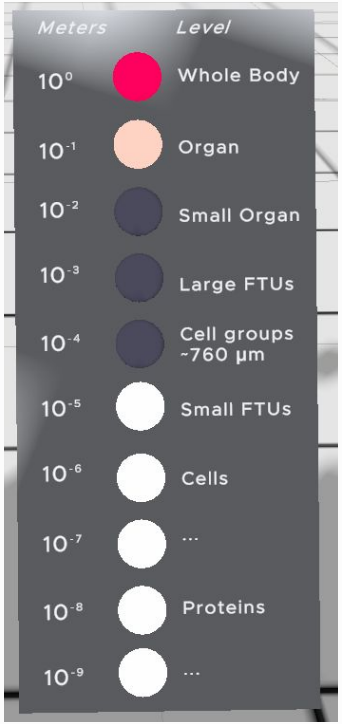
HRA Organ Gallery in VR:
https://www.meta.com/experiences/5696814507101529

Exploring Spatial Data in VR

Common Coordinate Framework (CCF)

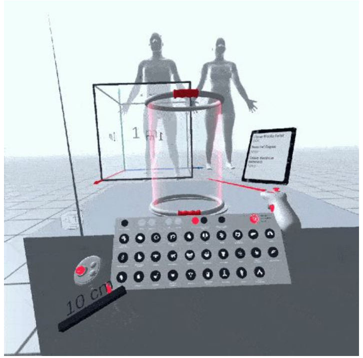


Common Coordinate Framework (CCF)

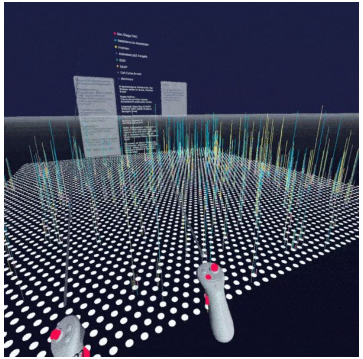


- Start at highest floor
- Take an elevator across levels, from Whole Body to Proteins
- Currently open for business:
  - Whole Body
  - Small Organ
  - Large FTUs
  - Cell Groups (~760 µm)

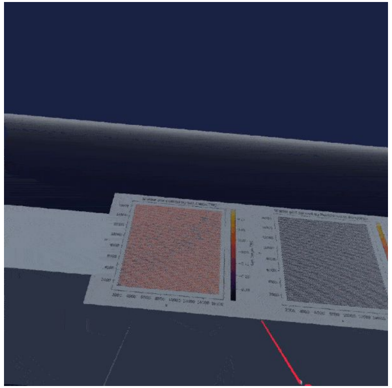
HRA Organ Gallery in VR



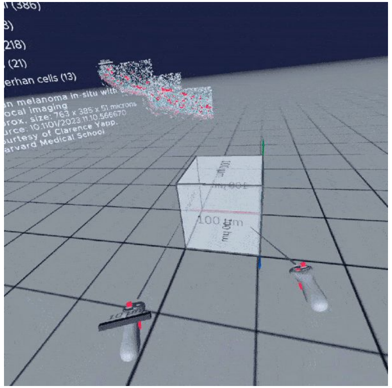
Level 0: Whole Body



Level -3: 3D stepped relief map for senescence hallmarks in Visium slide



Also Level -3: auxiliary 2D scatter graphs



Level -4: Cell groups ~760 microns

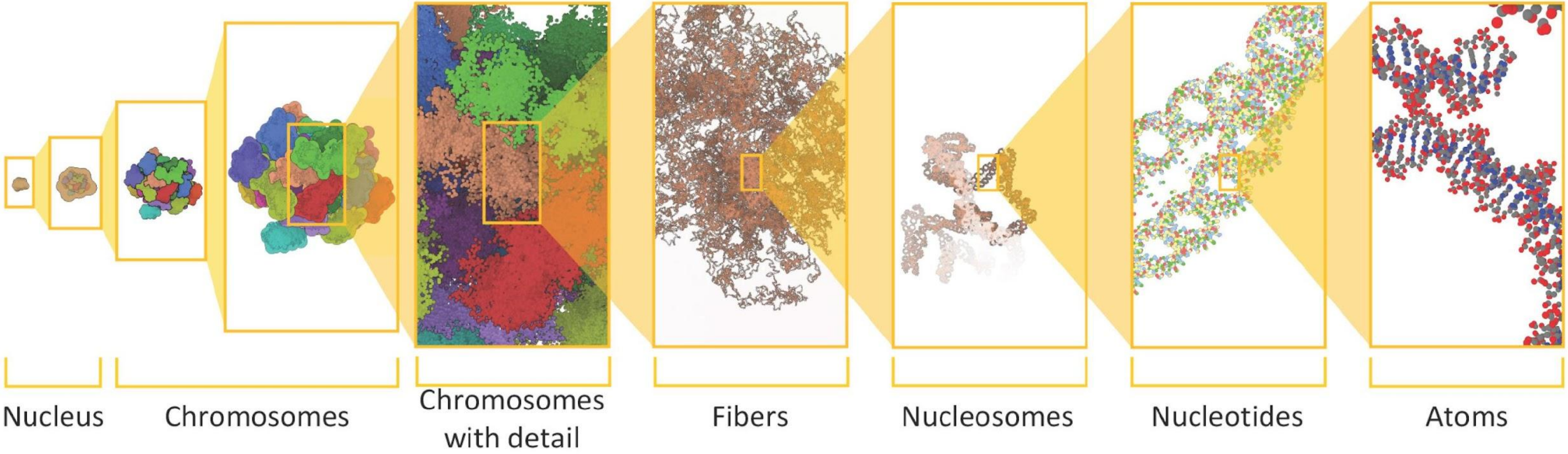
Multiscale exploration of the HRA

- **Level 0: Whole Body**
- **Level -2: Small Organ**
- **Level -3: Large FTUs**
- **Level -4: Cell Groups ~760 Microns**

Talk to Andreas "Andi" Bueckle if you would like a demo. Video: https://www.youtube.com/watch?v=Wy0BCOFWClk

Tobias Isenberg

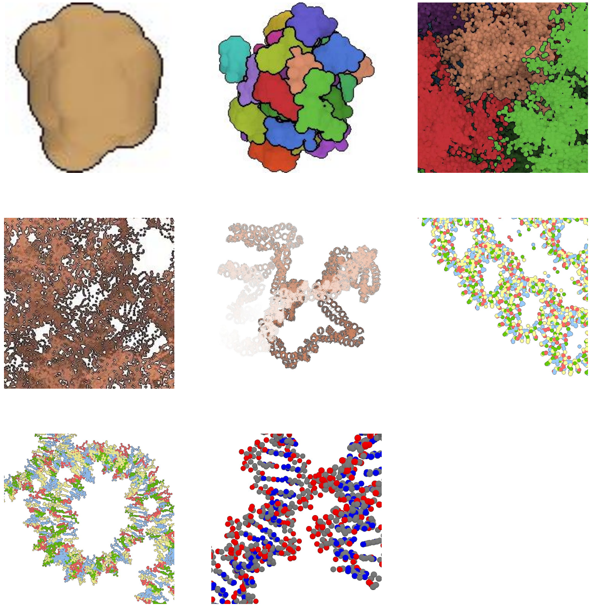
ScaleTrotter



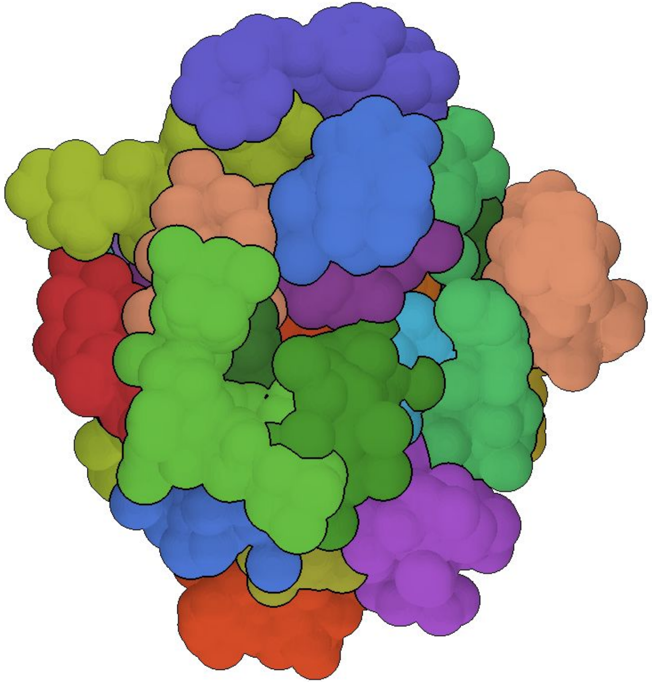
“Simple,” straightforward transitions

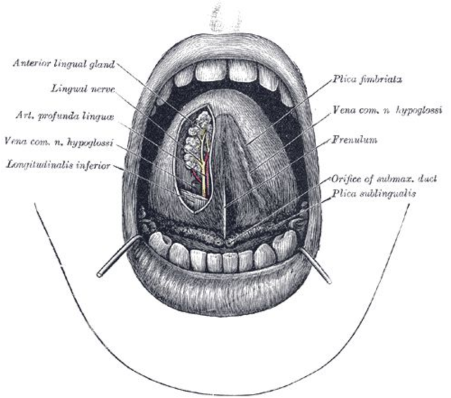
[van der Zwan et al., 2011]

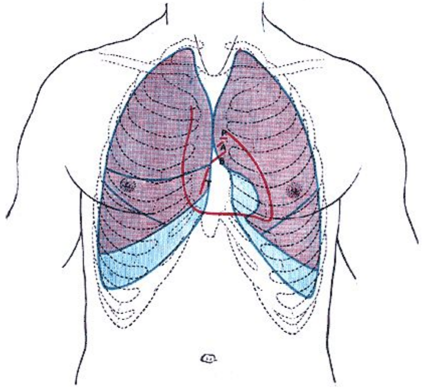
↯



Visual embedding transition

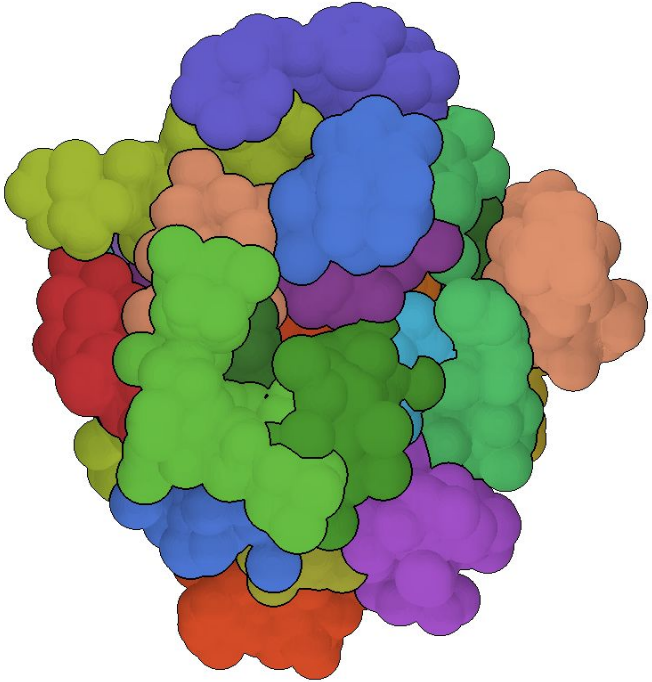






[Gray’s Anatomy, 1918]

Visual embedding transition



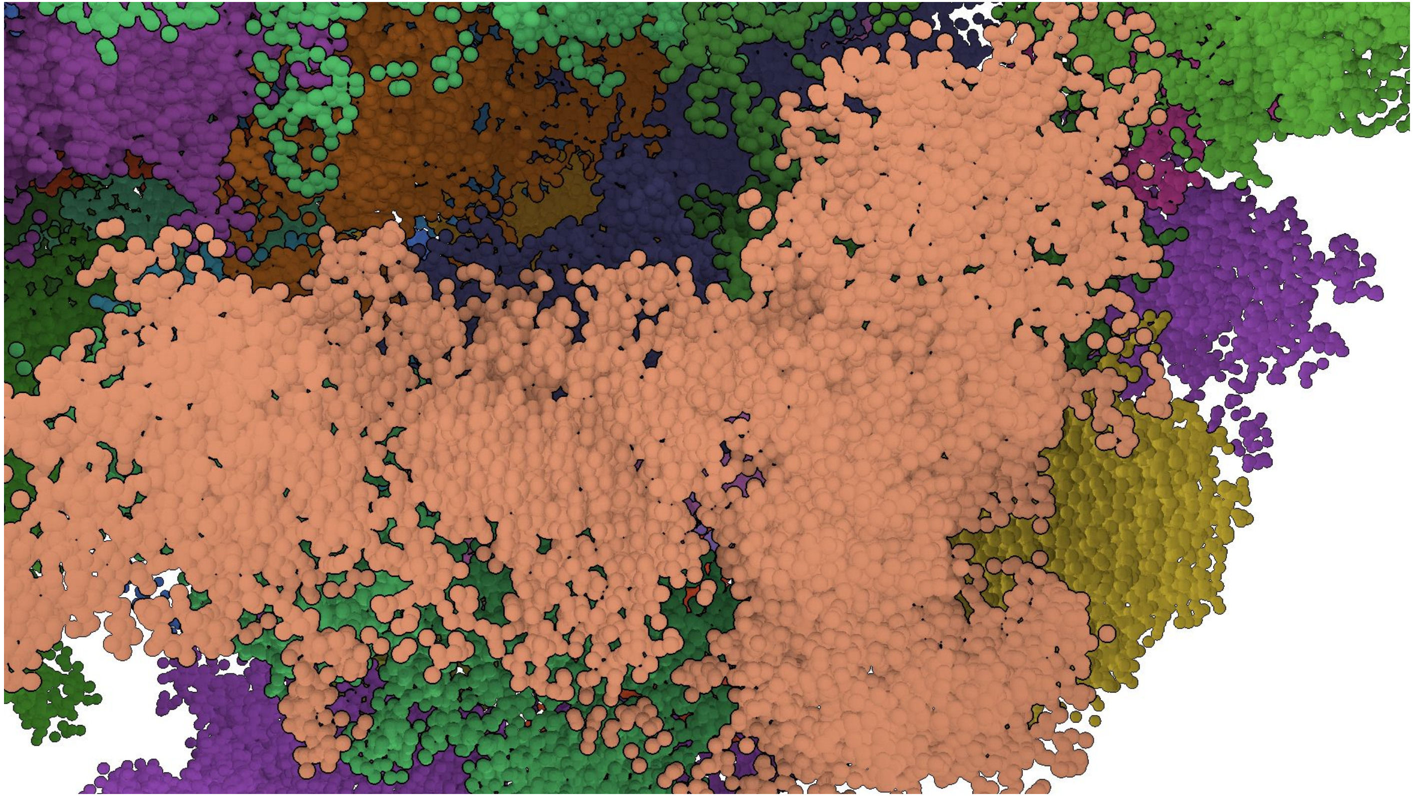
coarse scale in 3D

coarse scale flattened to canvas

detailed scale in 3D on top of canvas

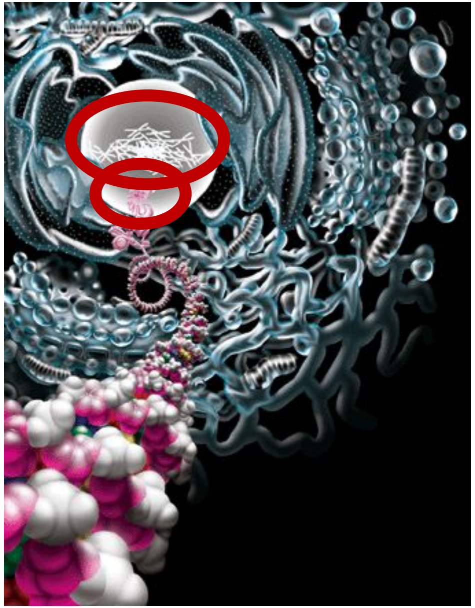
canvas disappears

Visual embedding transition

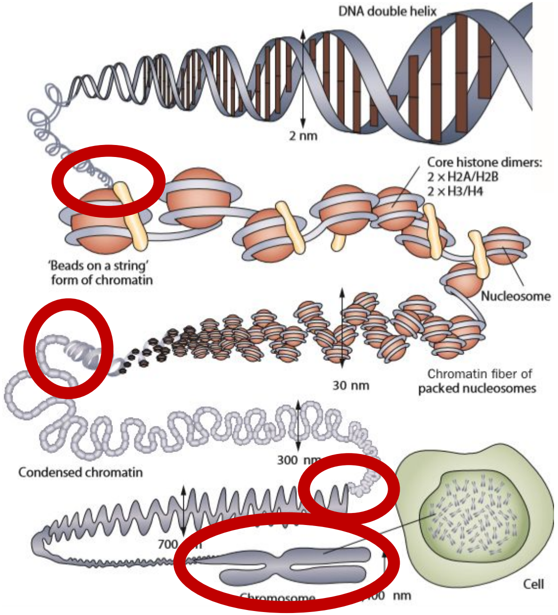


Interactive exploration

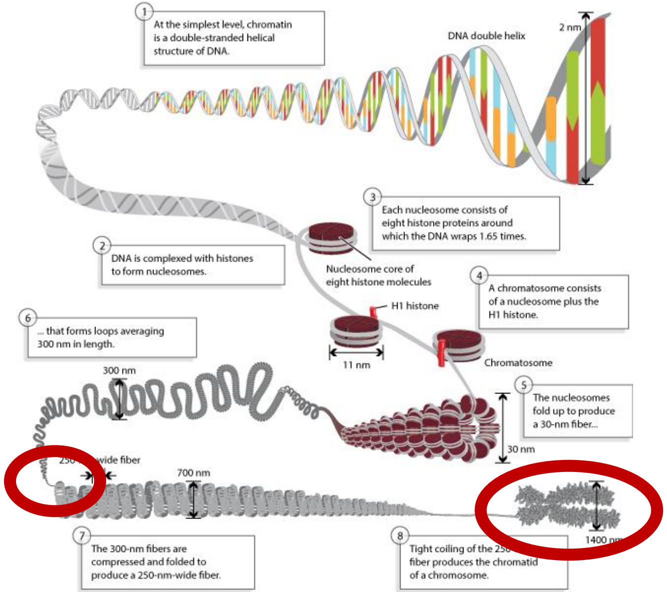
Further Inspiration: Multiscale DNA illustration



[Pennisi, 2001]

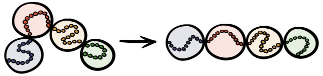


[Tonna et al., 2010]

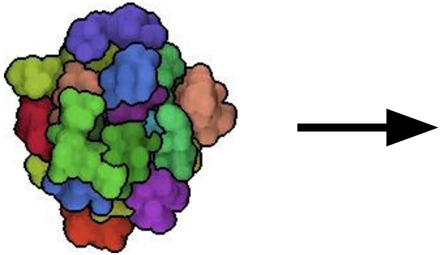


[Nature Education, 2013]

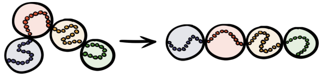
Spatial straightening



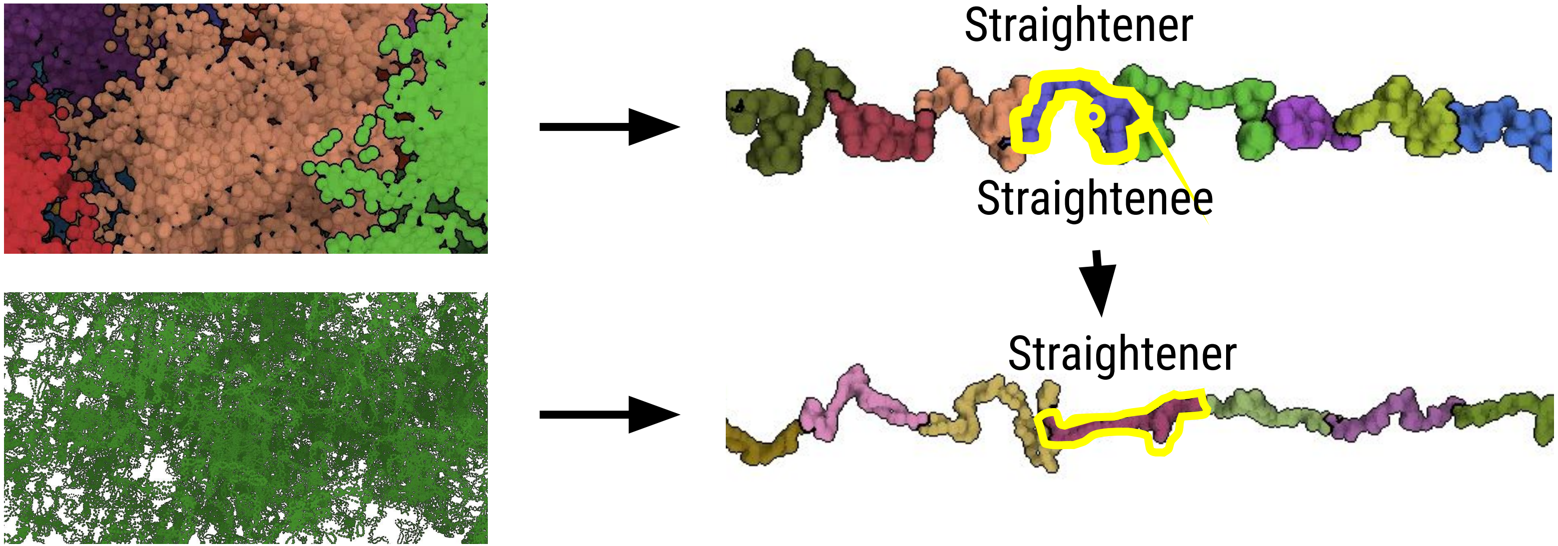
Chromosome scale



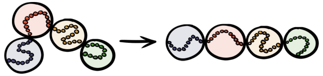
Spatial straightening



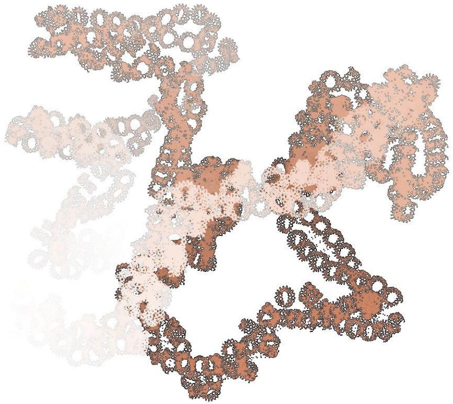
Loci and fiber scales



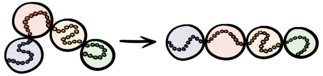
Spatial straightening



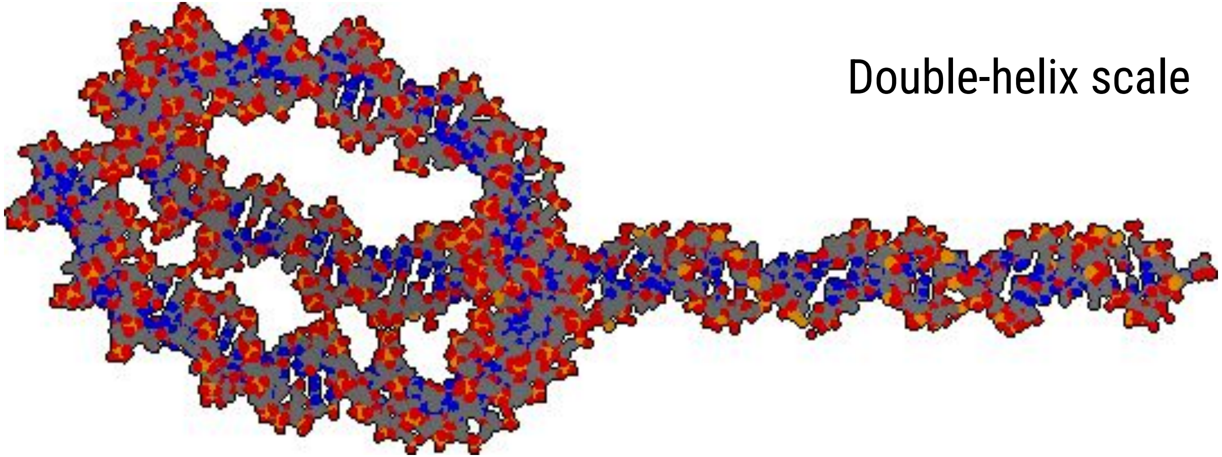
Nucleosome scale



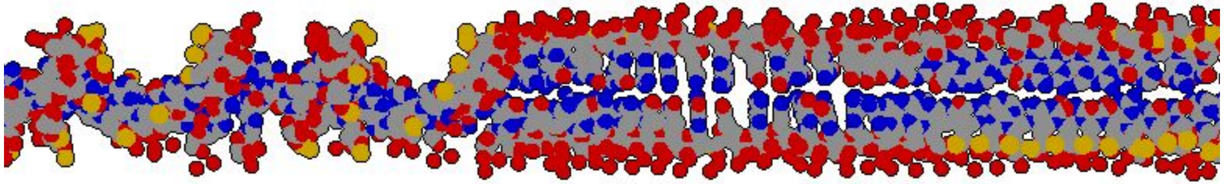
Spatial straightening



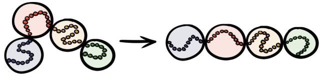
Double-helix scale



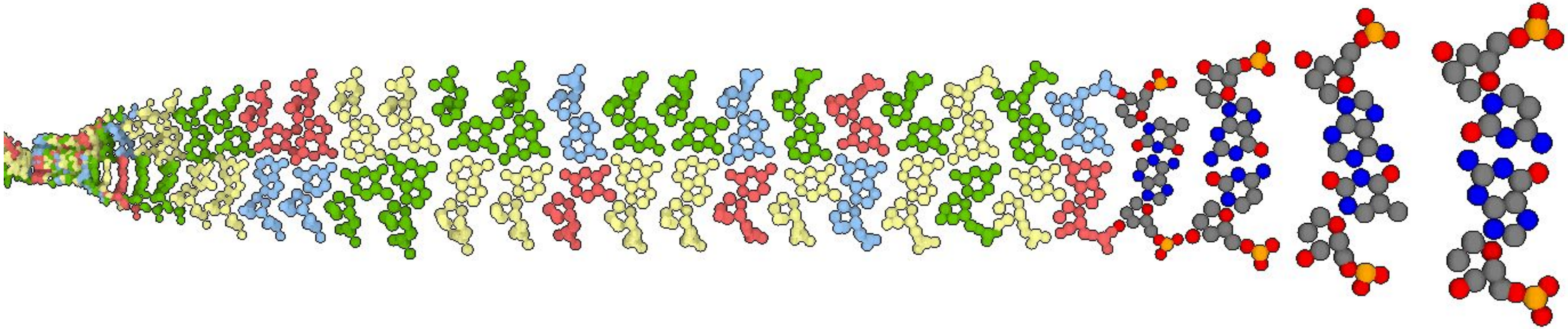
Bases scale



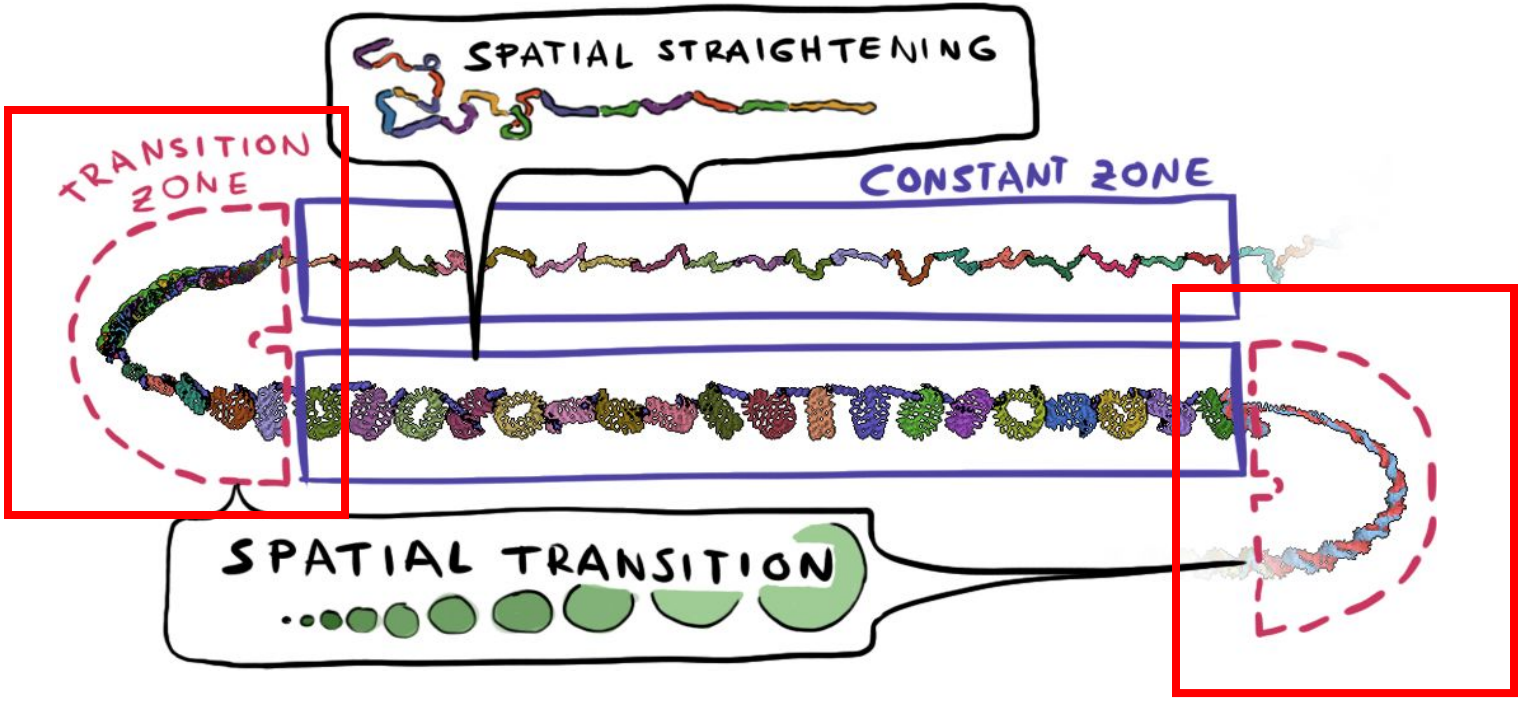
Spatial straightening



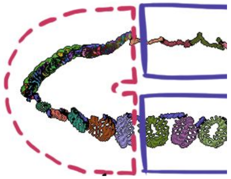
Bases scale



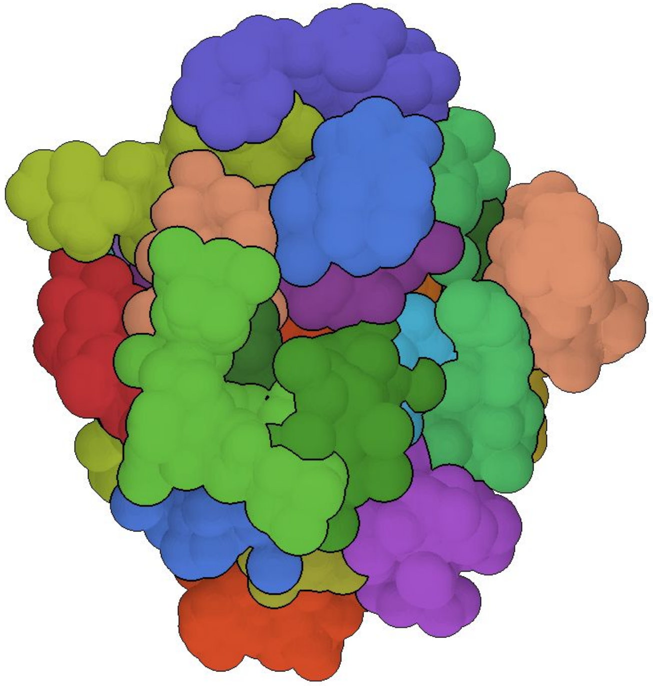
Conceptual arrangement

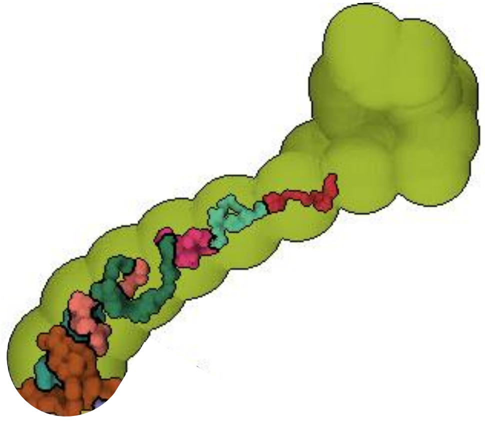


Spatial transitions

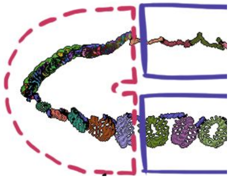


Chromosomes-to-loci

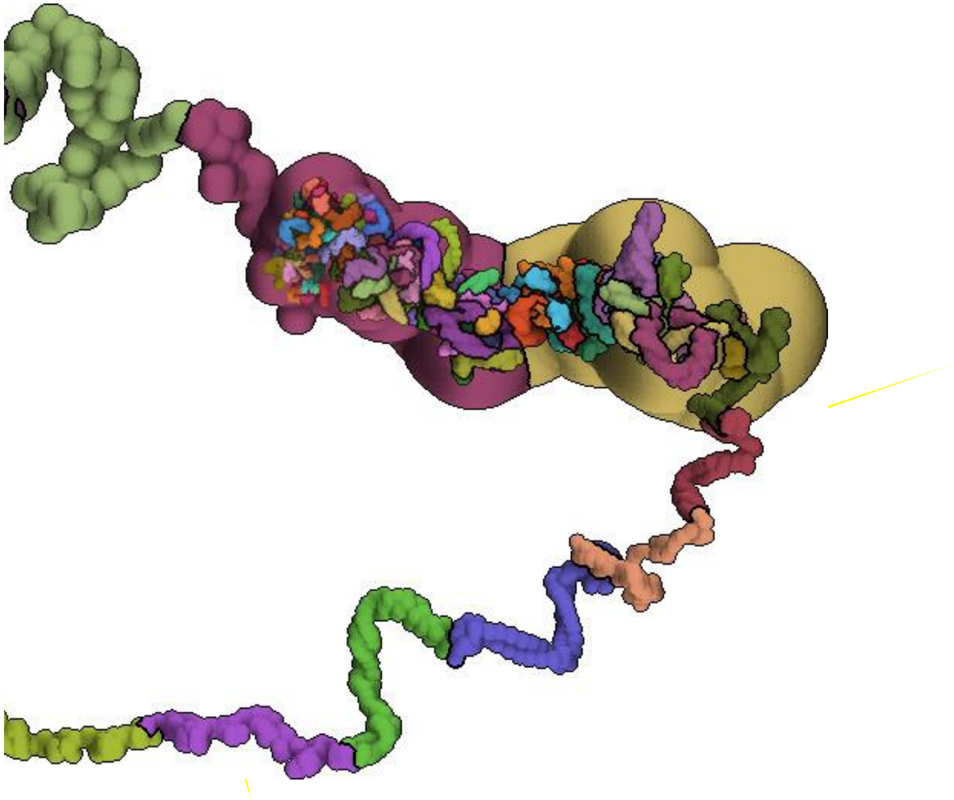




Spatial transitions



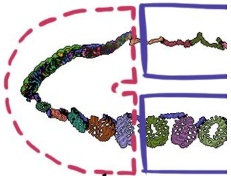
Loci-to-fibers



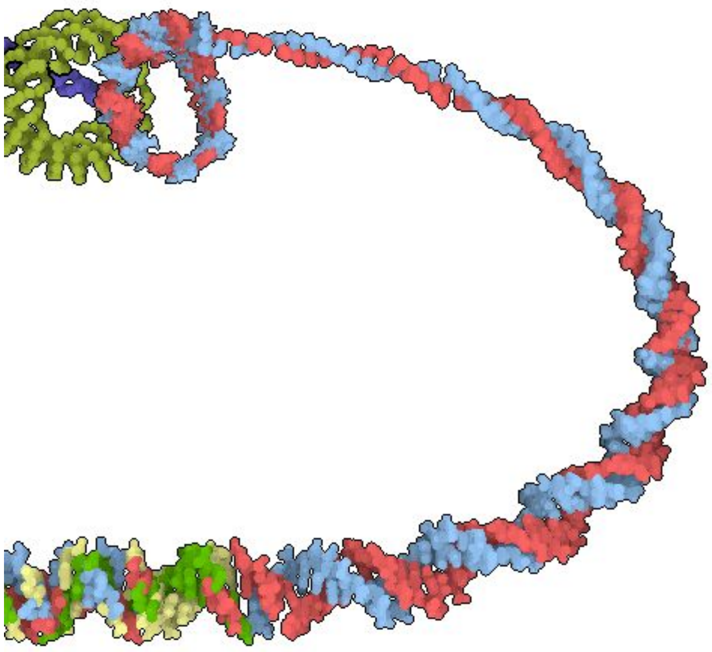
Spatial transitions

Fibers-to-nucleosomes

Spatial transitions

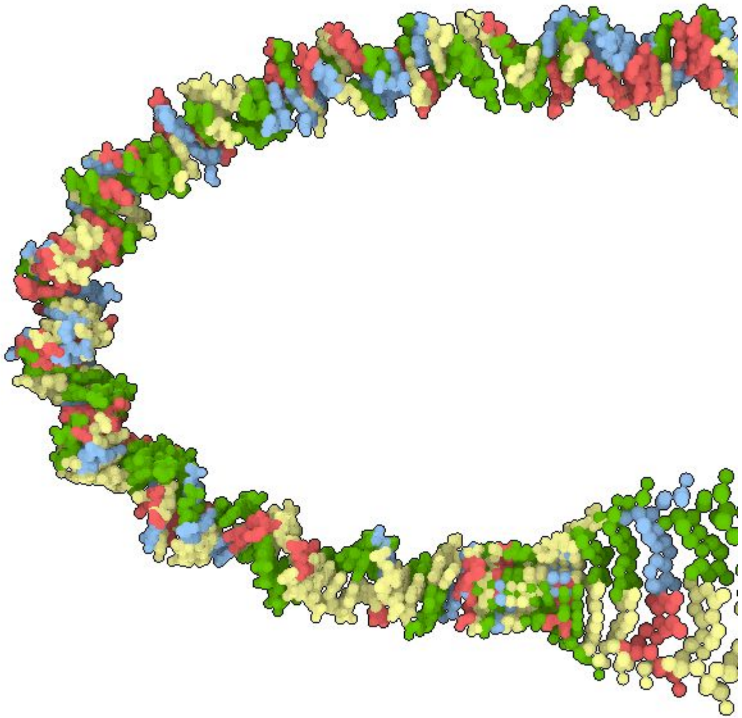


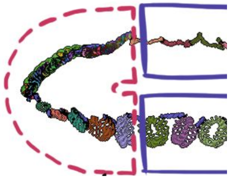
Nucleosomes-to-double-helix



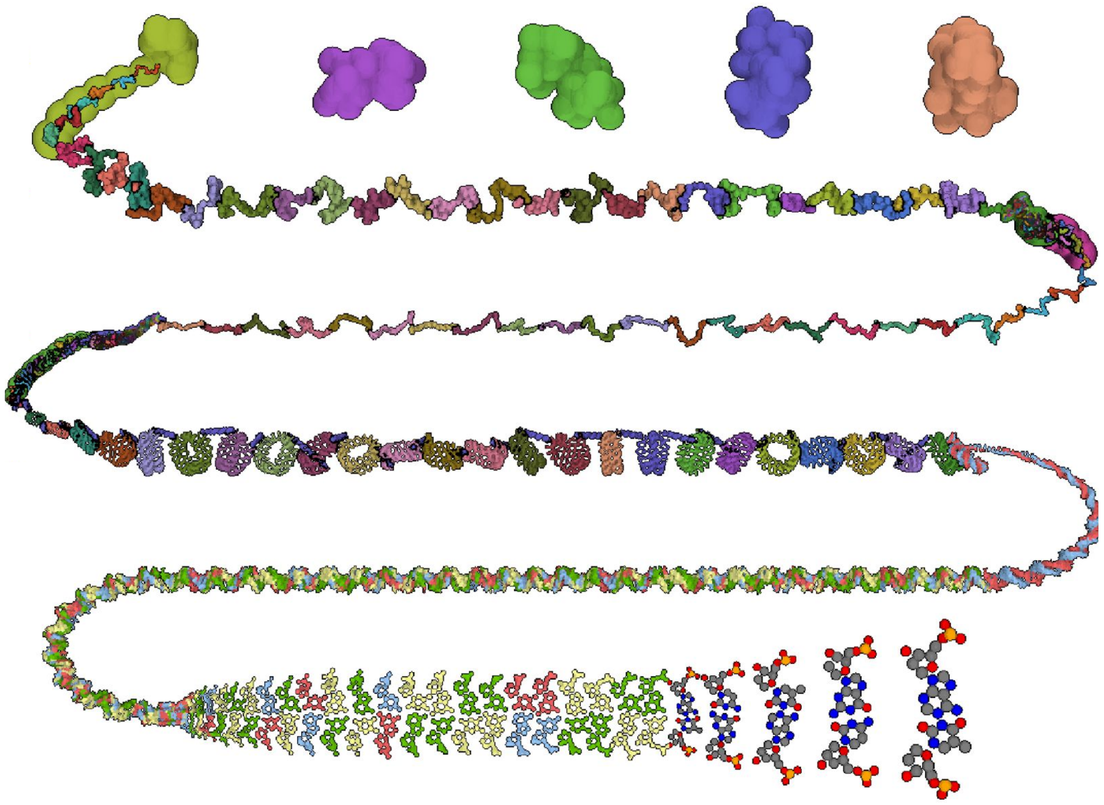
Spatial transitions

Double-helix-to-bases

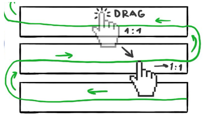


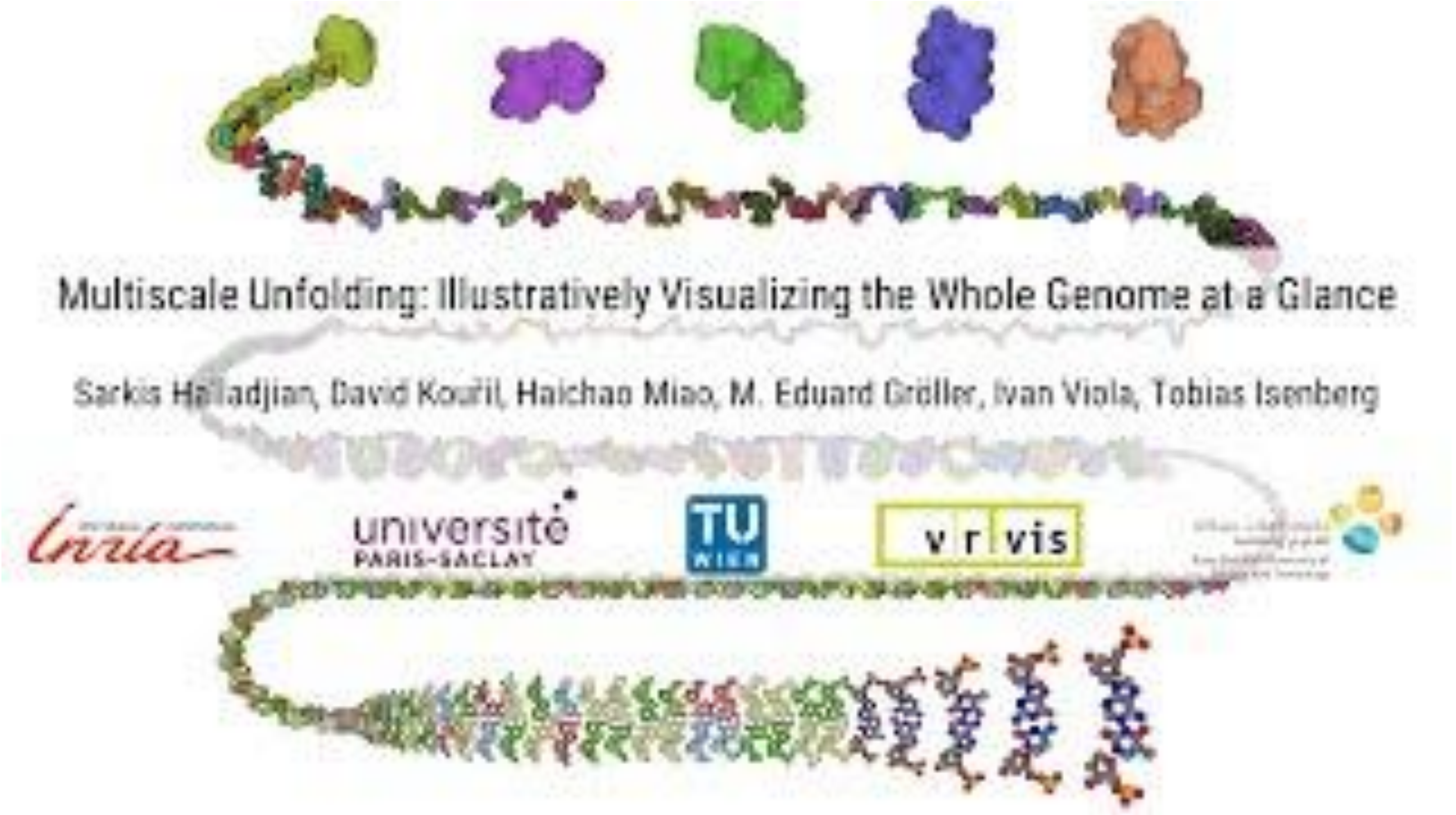


Multiscale Unfolding



Panning the scales



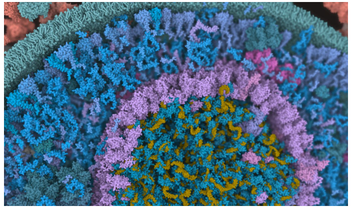


Collaborators

TECHNISCHE UNIVERSITÄT WIEN
Vienna University of Technology

جامعة الملك عبدالله
للعلوم والتقنية
King Abdullah University of Science and Technology

nanographics



Sarkis Halladjian

David Kouřil

Haichao Miao

Eduard Gröller

Ivan Viola

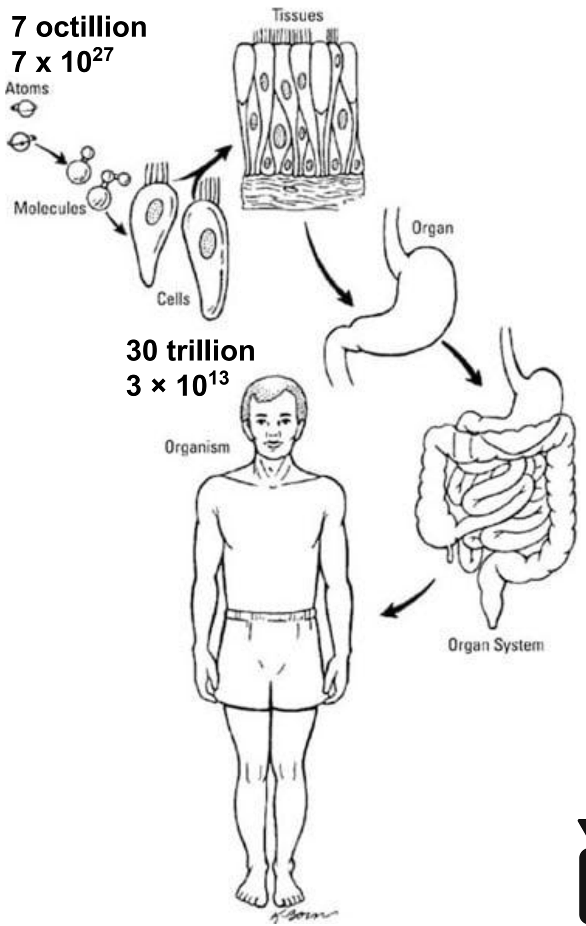
tinyurl.com/scaletrotter

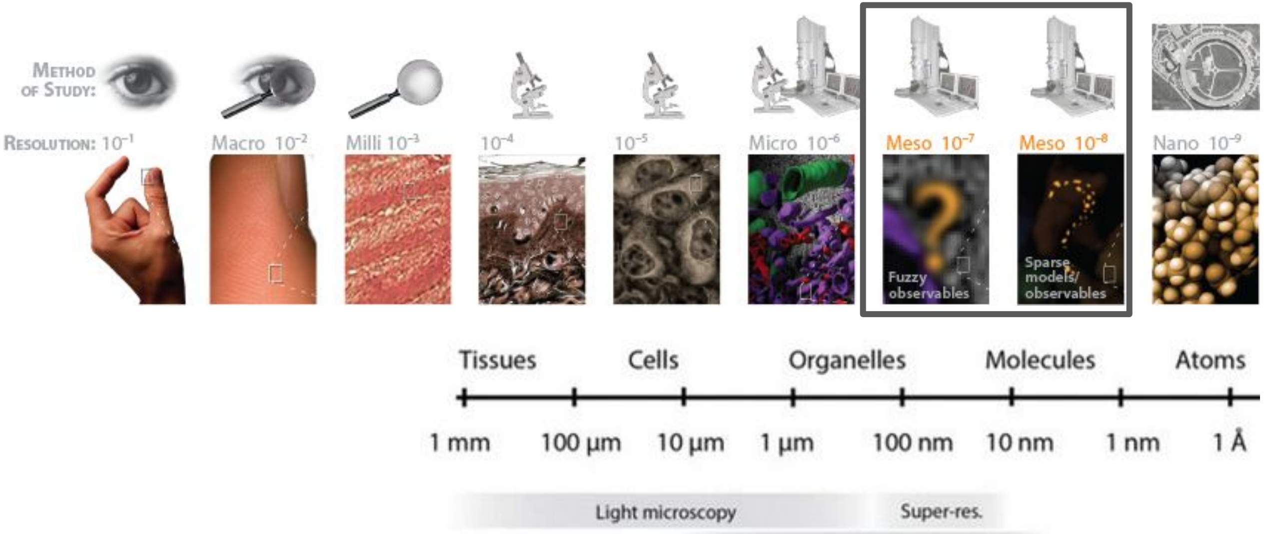
tinyurl.com/multiscale-unfolding

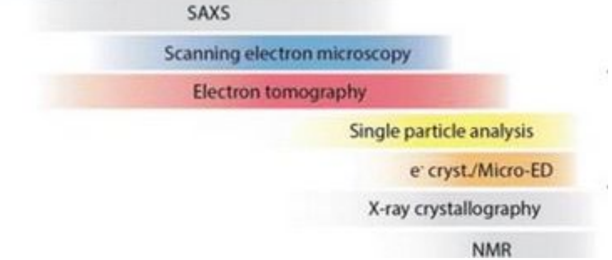
Ludovic Autin

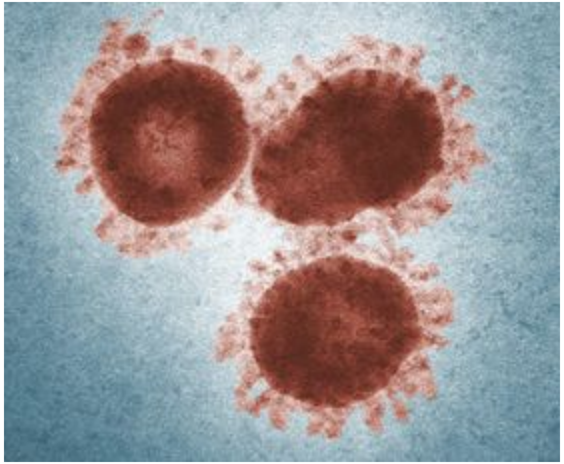
The Mesoscale Challenge

National Institutes of Health
Turning Discovery Into Health

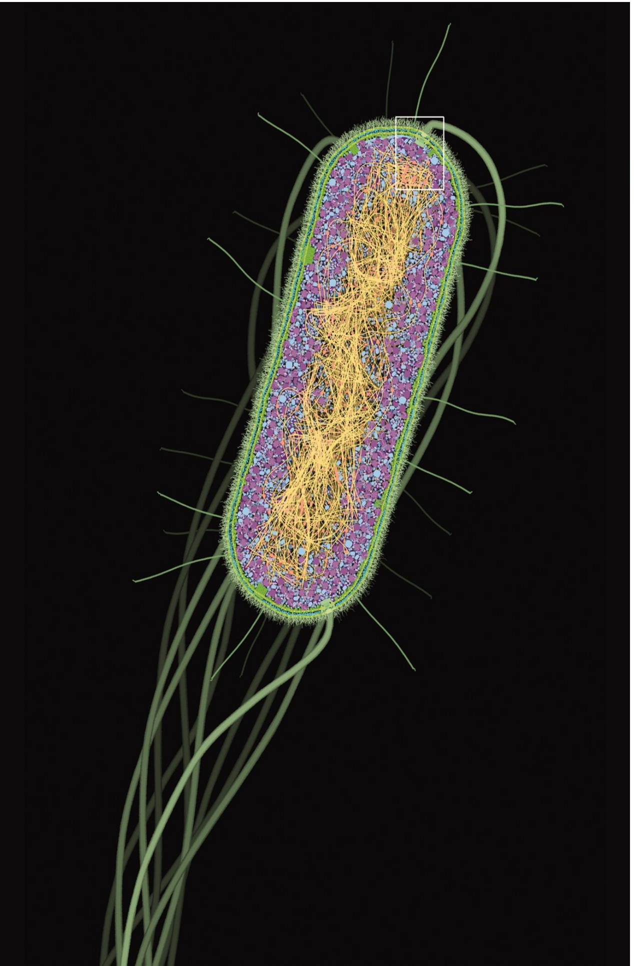

7 octillion
7×10^{27}
Atoms
Molecules
Cells
Tissues
Organ
Organ System
30 trillion
3×10^{13}
Organism


Method of Study:
Resolution: 10^{-1}
Macro 10^{-2}
Milli 10^{-3}
10^{-4}
10^{-5}
Micro 10^{-6}
Meso 10^{-7}
Meso 10^{-8}
Nano 10^{-9}
Fuzzy observables
Sparse models/ observables
Tissues
Cells
Organelles
Molecules
Atoms
1 mm
100 µm
10 µm
1 µm
100 nm
10 nm
1 nm
1 Å
Light microscopy
Super-res.


SAXS
Scanning electron microscopy
Electron tomography
Single particle analysis
e⁻ cryst./Micro-ED
X-ray crystallography
NMR



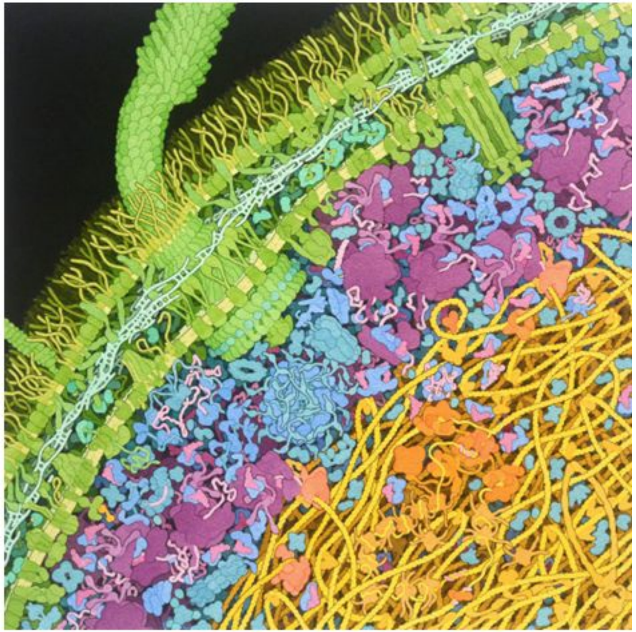
Theodor Escherich 1886
Escherichia coli

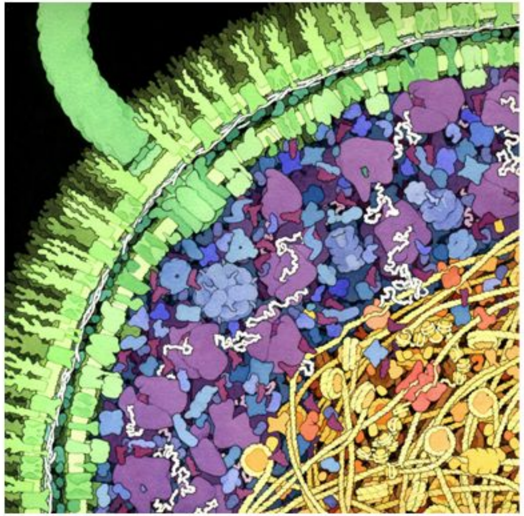


David Goodsell

1991

Largely invisible to experiment
Integrates the *current* state of knowledge

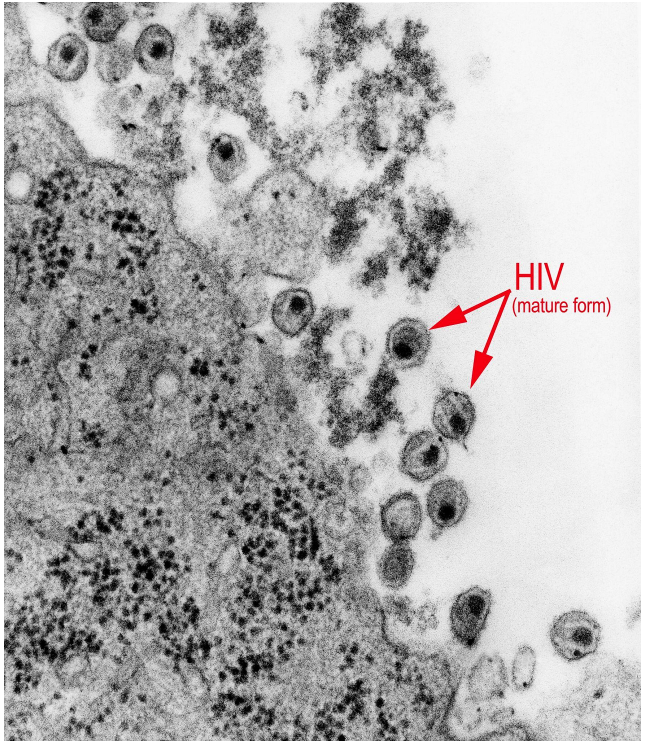


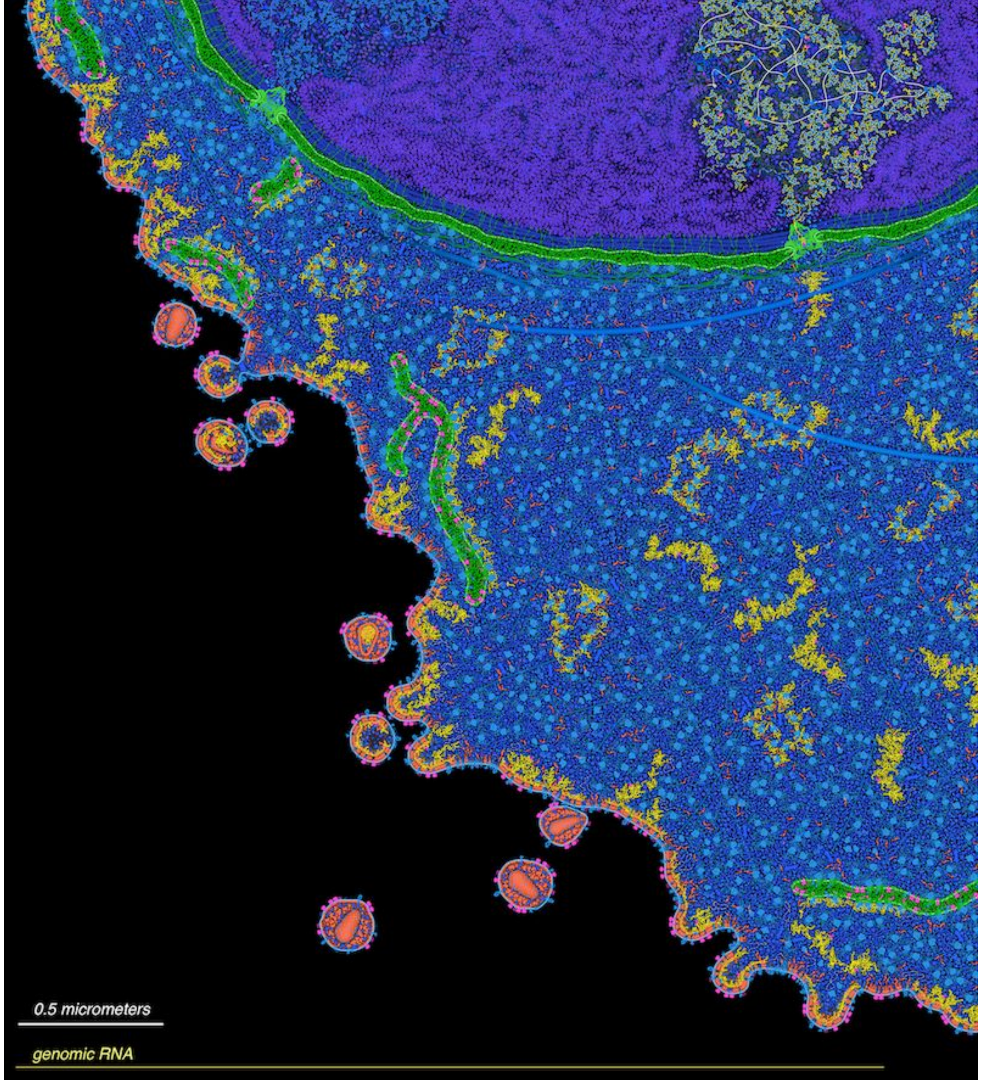


1999

2021

David Goodsell





David Goodsell

Illustrating Cellular Environments

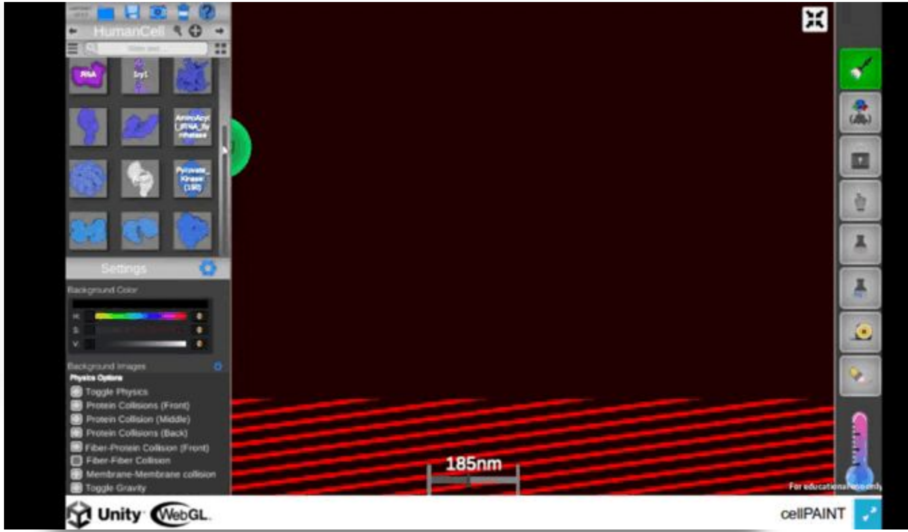
Adam Gardner

User-Friendly Interactive Tools ...CellPAINT

Goodsell Watercolor

- Consistent scale
- Simplified iconic shapes
- Cross-sectional view
- Limited depth (3 layers)
- Informative colors

"Goodsell-like" cellPAINT

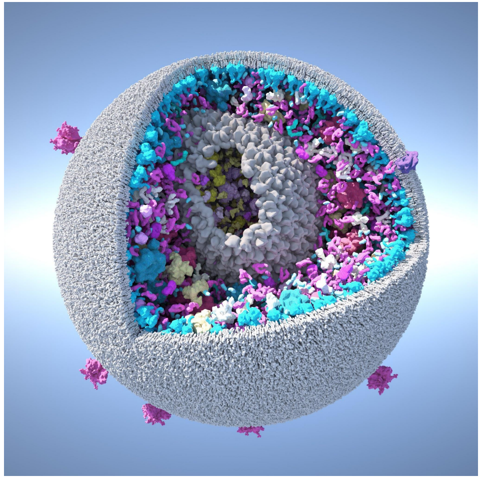


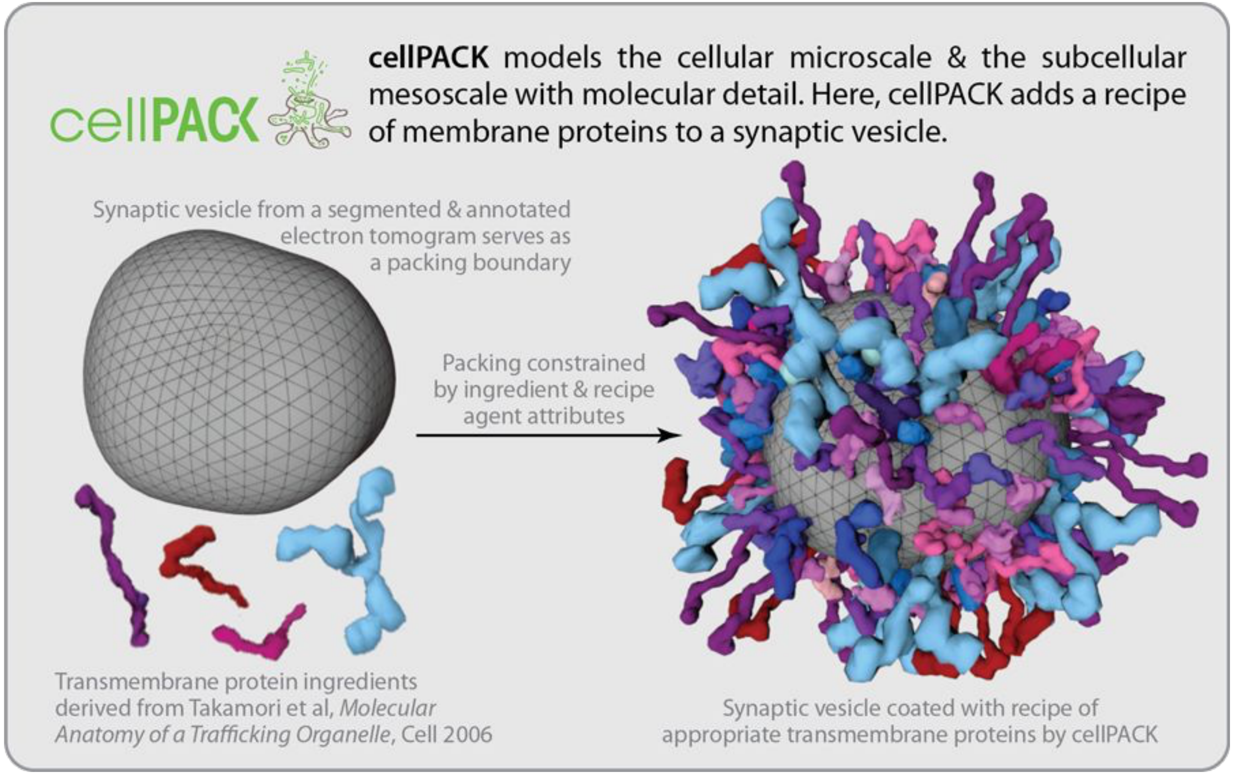
http://cellpaint.scripps.edu

cellPACK: a virtual mesoscope to model and visualize structural systems biology

Graham Johnson

2014

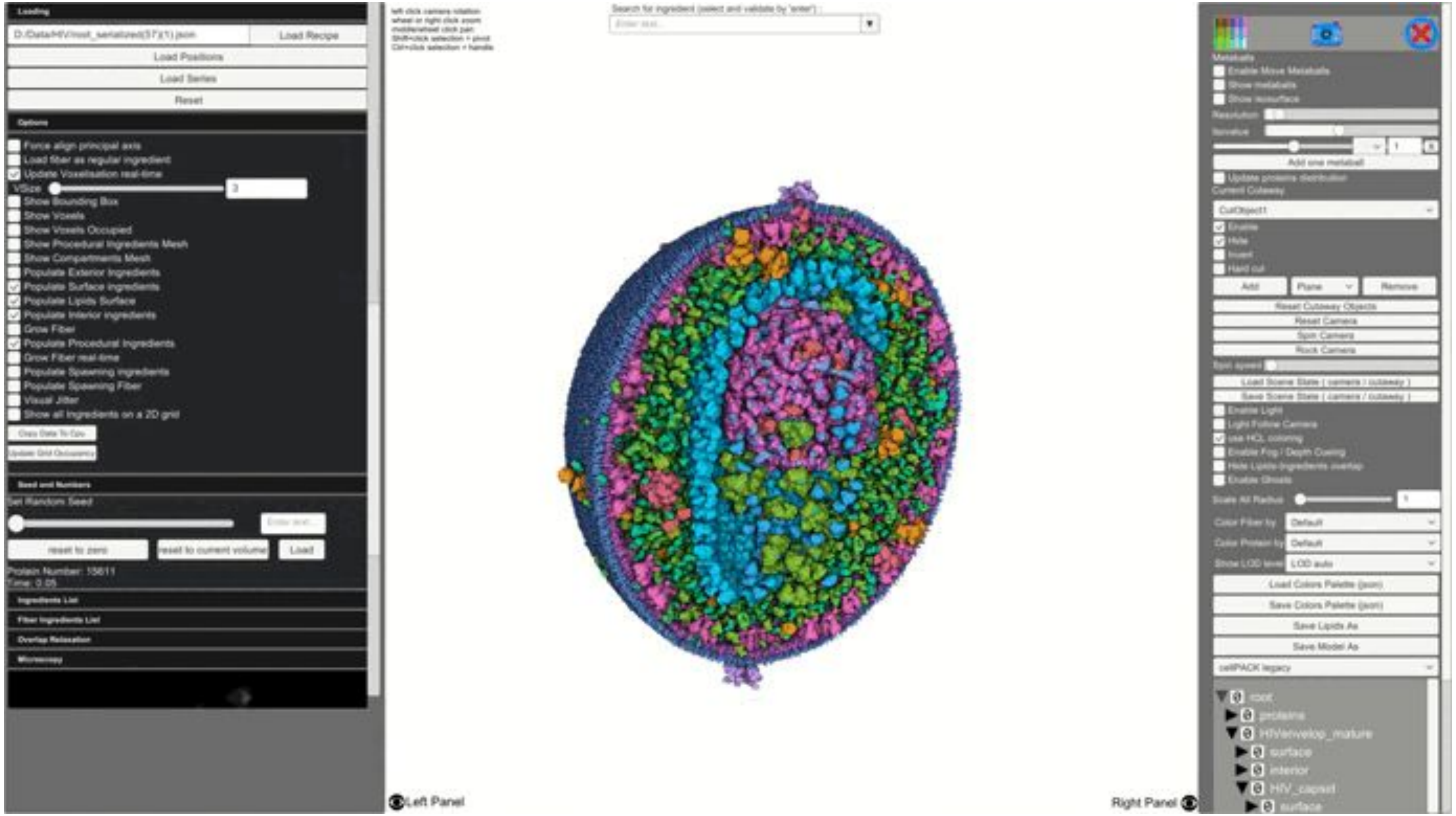




Instant Construction and Visualization of Crowded Biological Environments - cellpack on the gpu

2017

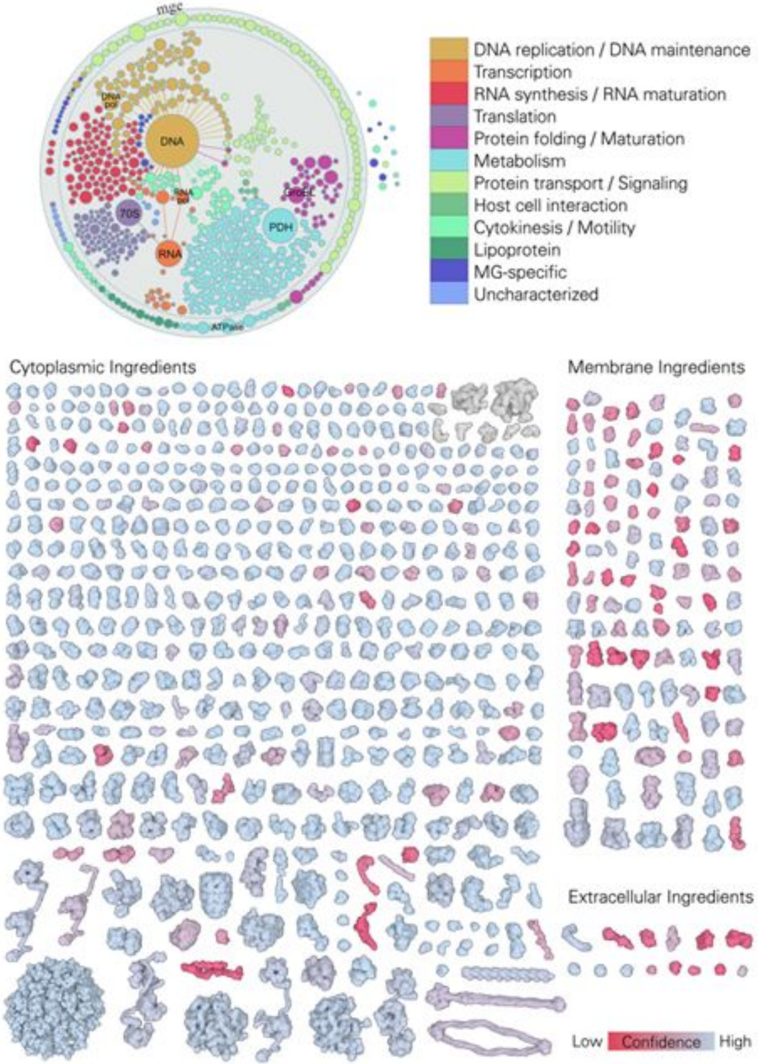
2018



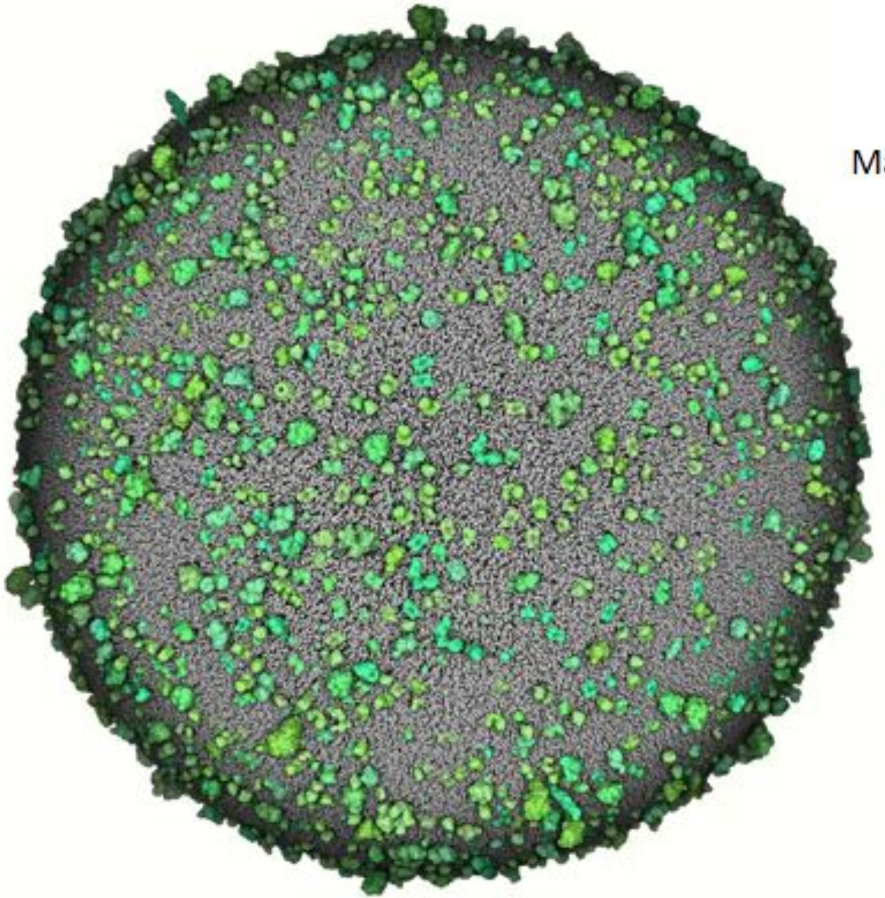
Mathieu Le Muzic

Tobias Klein

Ivan Viola



Mycoplasma genitalium, 2022



Martina Maritan

David Sehnal

Alexander Rose

Mol*

Mesoscale Explorer[BETA]

https://molstar.org/me/

A Mol* app for exploring mesoscale models

The advent of cryo-EM and cryo-ET, coupled with computational modeling, has enabled the creation of integrative 3D models of viruses, bacteria, and cellular organelles. Based on these models, the **Mesoscale Explorer** provides unprecedented access and insight into the molecular fabric of life, enhancing perception, streamlining exploration, and simplifying visualization of diverse data types, showcasing the intricate details with unparalleled clarity.

Read about Mesoscale Explorer in Protein Science

When using Mesoscale Explorer, please cite:

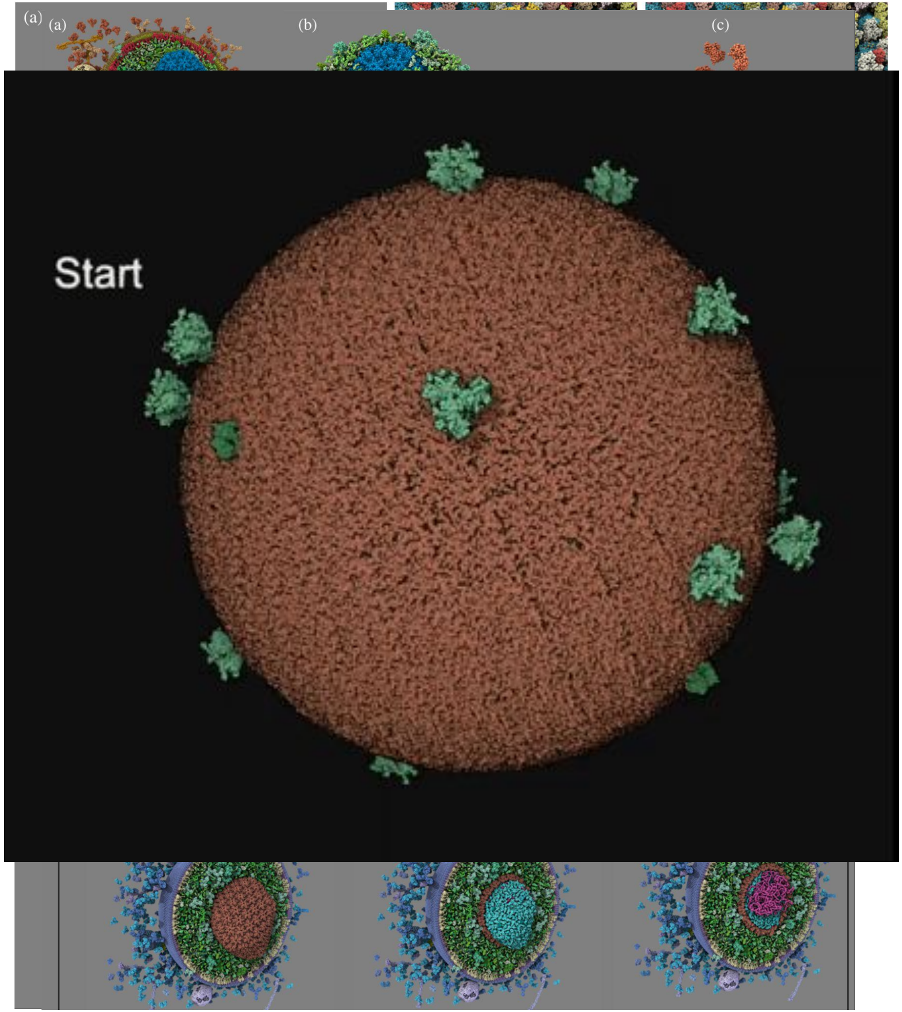
Alexander Rose, David Sehnal, David S. Goodsell, Ludovic Autin: Mesoscale explorer: Visual exploration of large-scale molecular models, *Protein Science*, 2024; 10.1002/pro.5177.

PDBe Protein Data Bank in Europe

RCSB PDB PROTEIN DATA BANK

Clipping

Level of Detail

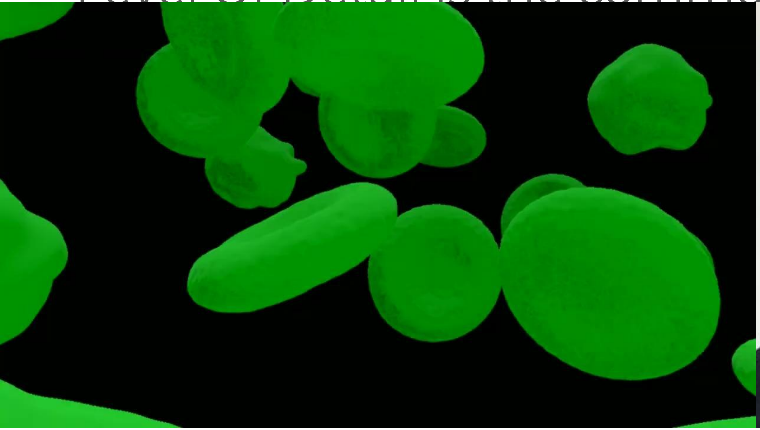


Collaboration is Key

How far are we to visualize a full human cell with molecular details in real-time ?

Data gathering is a bottleneck

Level Of Detail is the common approach for multiscale visualization



Pr. Arthur Olson

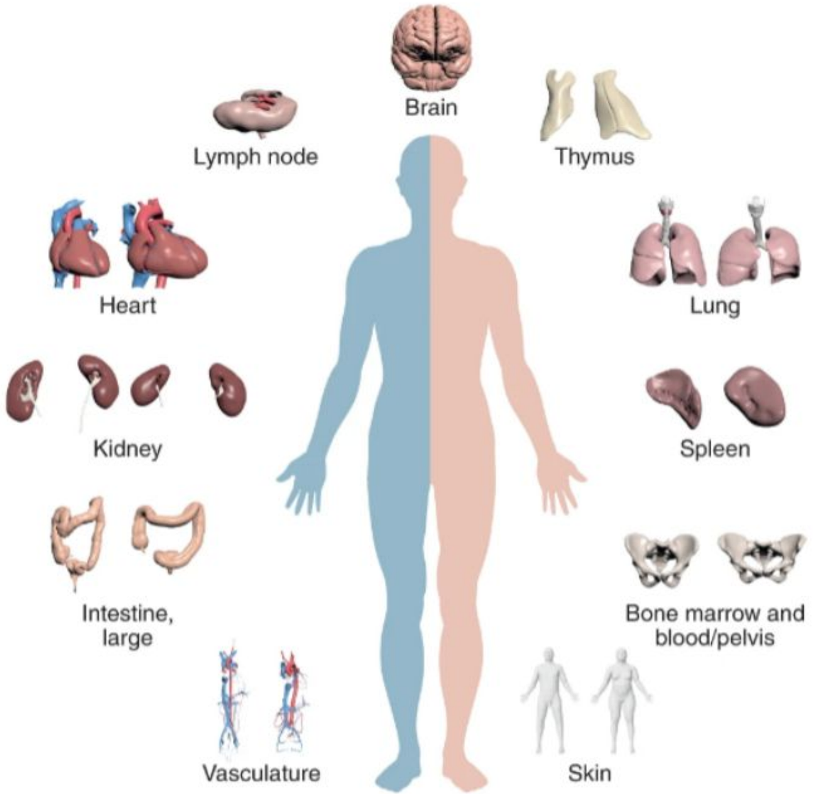
NIH National Institutes of Health
Turning Discovery Into Health

100 YEARS
A Century of Science Changing Life
SCRIPPS RESEARCH

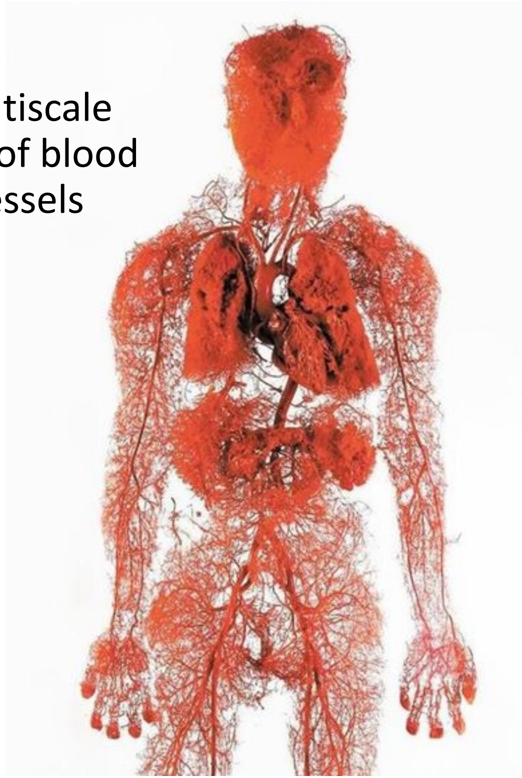
Griffin Weber

Human Reference Atlas (HRA)

https://humanatlas.io/



Multiscale map of blood vessels



https://bodyworlds.com/

Katherine S Gustilo

Avinash Boppana

Sujin Lee

Rajeev Malhotra

Marc Halushka

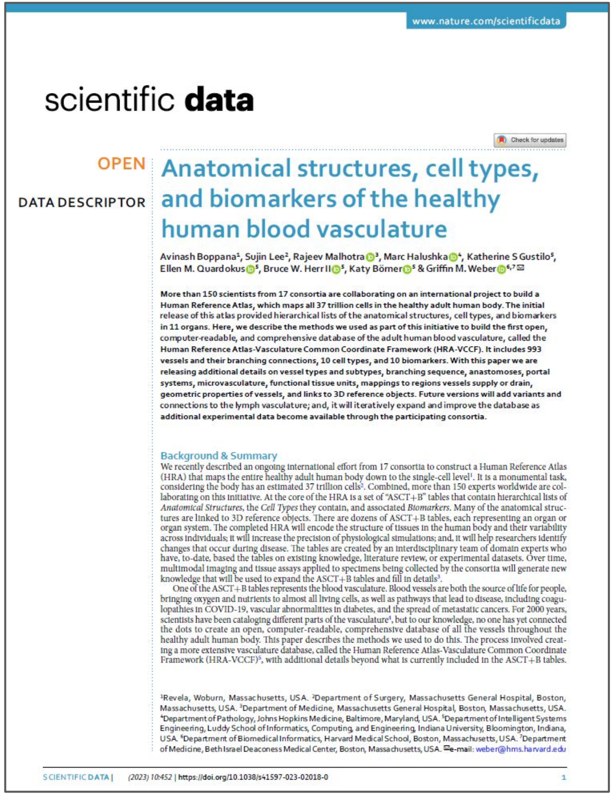
Ellen M Quardokus

Bruce W Herr II

Ushma Patel

Zorina Galis

Katy Börner



www.nature.com/scientificdata

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DATA DESCRIPTOR

Anatomical structures, cell types, and biomarkers of the healthy human blood vasculature

Avinash Boppana[1], Sujin Lee[2], Rajeev Malhotra[3], Marc Halushka[4], Katherine S Gustilo[5], Ellen M. Quardokus[5], Bruce W. Herr II[5], Katy Börner[5] & Griffin M. Weber[6,7]✉

More than 150 scientists from 17 consortia are collaborating on an international project to build a Human Reference Atlas, which maps all 37 trillion cells in the healthy adult human body. The initial release of this atlas provided hierarchical lists of the anatomical structures, cell types, and biomarkers in 11 organs. Here, we describe the methods we used as part of this initiative to build the first open, computer-readable, and comprehensive database of the adult human blood vasculature, called the Human Reference Atlas-Vasculature Common Coordinate Framework (HRA-VCCF). It includes 993 vessels and their branching connections, 10 cell types, and 10 biomarkers. With this paper we are releasing additional details on vessel types and subtypes, branching sequence, anastomoses, portal systems, microvasculature, functional tissue units, mappings to regions vessels supply or drain, geometric properties of vessels, and links to 3D reference objects. Future versions will add variants and connections to the lymph vasculature; and, it will iteratively expand and improve the database as additional experimental data become available through the participating consortia.

Background & Summary

We recently described an ongoing international effort from 17 consortia to construct a Human Reference Atlas (HRA) that maps the entire healthy adult human body down to the single-cell level[1]. It is a monumental task, considering the body has an estimated 37 trillion cells[2]. Combined, more than 150 experts worldwide are collaborating on this initiative. At the core of the HRA is a set of "ASCT+B" tables that contain hierarchical lists of *Anatomical Structures*, the *Cell Types* they contain, and associated *Biomarkers*. Many of the anatomical structures are linked to 3D reference objects. There are dozens of ASCT+B tables, each representing an organ or organ system. The completed HRA will encode the structure of tissues in the human body and their variability across individuals; it will increase the precision of physiological simulations; and, it will help researchers identify changes that occur during disease. The tables are created by an interdisciplinary team of domain experts who have, to-date, based the tables on existing knowledge, literature review, or experimental datasets. Over time, multimodal imaging and tissue assays applied to specimens being collected by the consortia will generate new knowledge that will be used to expand the ASCT+B tables and fill in details[3].

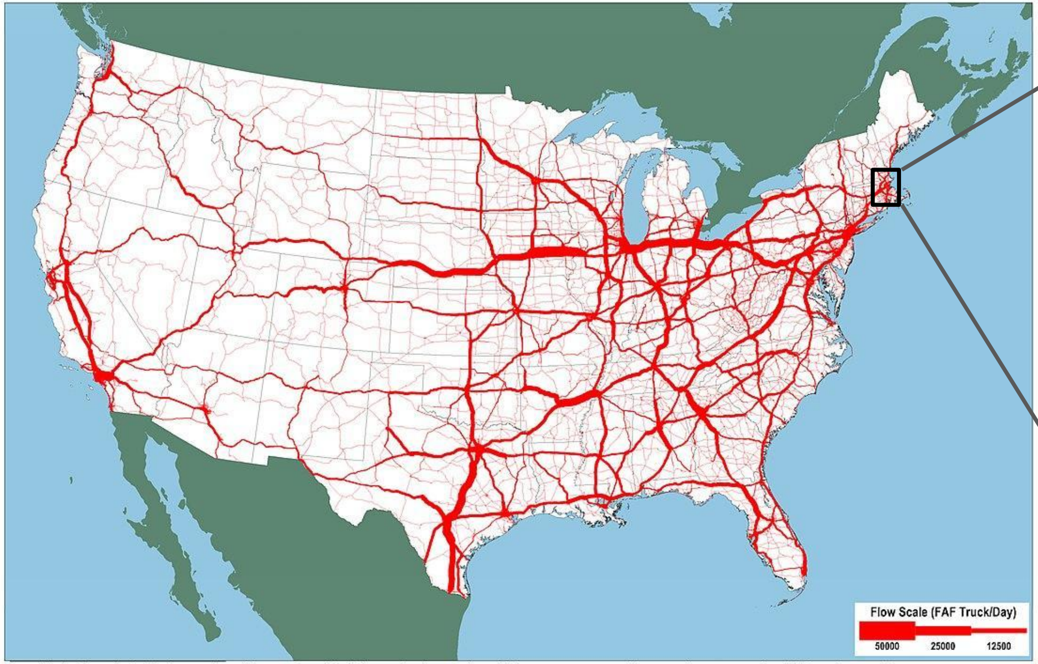
One of the ASCT+B tables represents the blood vasculature. Blood vessels are both the source of life for people, bringing oxygen and nutrients to almost all living cells, as well as pathways that lead to disease, including coagulopathies in COVID-19, vascular abnormalities in diabetes, and the spread of metastatic cancers. For 2000 years, scientists have been cataloging different parts of the vasculature[4], but to our knowledge, no one has yet connected the dots to create an open, computer-readable, comprehensive database of all the vessels throughout the healthy adult human body. This paper describes the methods we used to do this. The process involved creating a more extensive vasculature database, called the Human Reference Atlas-Vasculature Common Coordinate Framework (HRA-VCCF)[5], with additional details beyond what is currently included in the ASCT+B tables.

[1]Revela, Woburn, Massachusetts, USA. [2]Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts, USA. [3]Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA. [4]Department of Pathology, Johns Hopkins Medicine, Baltimore, Maryland, USA. [5]Department of Intelligent Systems Engineering, Luddy School of Informatics, Computing, and Engineering, Indiana University, Bloomington, Indiana, USA. [6]Department of Biomedical Informatics, Harvard Medical School, Boston, Massachusetts, USA. [7]Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA. ✉e-mail: weber@hms.harvard.edu

Boppana A, et al. Anatomical structures, cell types, and biomarkers of the healthy human blood vasculature. Sci Data. 2023 Jul 19;10(1):452. doi: 10.1038/s41597-023-02018-0.

Multiscale Maps of Roads

Daily traffic, U.S. National Highway System

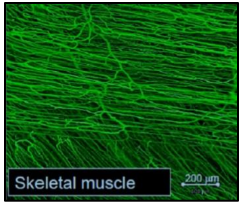


Note: Major flows include domestic and international freight moving by truck on highway segments with more than twenty five FAF trucks per day and between places typically more than fifty miles apart.
Source: U.S. Department of Transportation, Federal Highway Administration, Office of Freight Management and Operations, Freight Analysis Framework, version 4.3, 2017.

Boston "Central Artery"

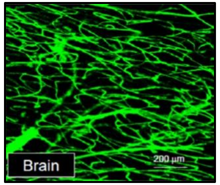
John F. Fitzgerald Expressway, By Sswonk, Public Domain, https://commons.wikimedia.org/w/index.php?curid=4538754

Back Bay

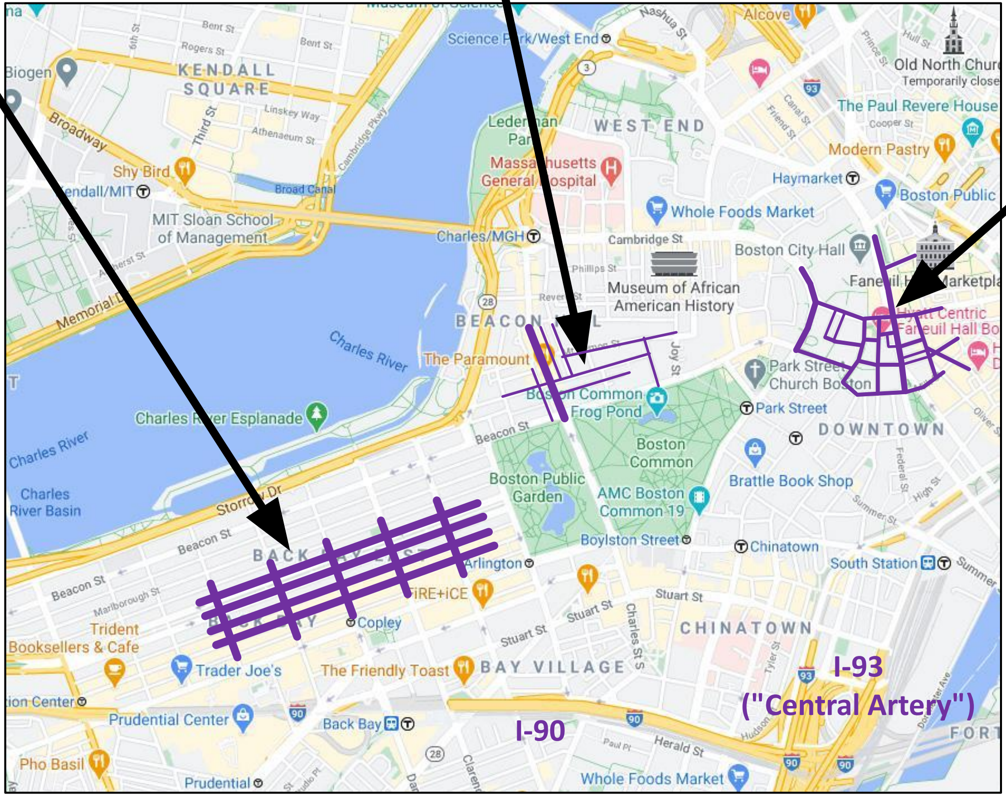


Skeletal muscle

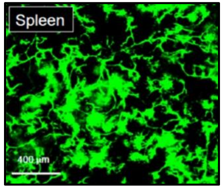
Beacon Hill



Brain



Downtown



Spleen

https://www.zumper.com/blog/best-neighborhoods-in-boston-for-newcomers/

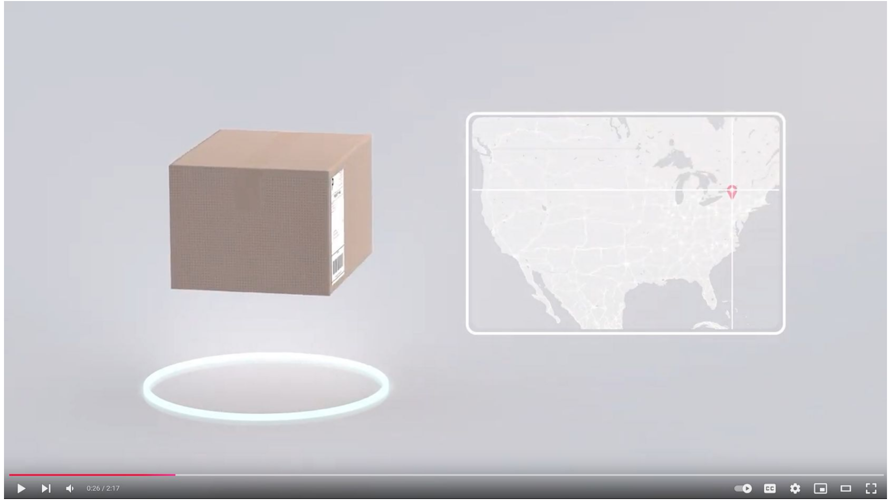
https://www.75statestreetgarage.com/nearby-destinations/financial-district/

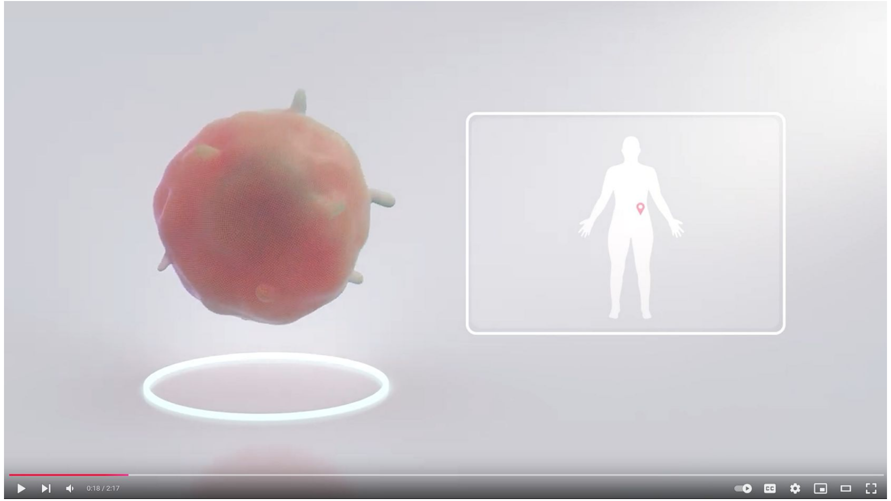
https://pubmed.ncbi.nlm.nih.gov/27815267/

Green lines show microvasculature in different tissues

Trucks follow roads to deliver a package to a house

Blood cells follow vessels to deliver oxygen to organs

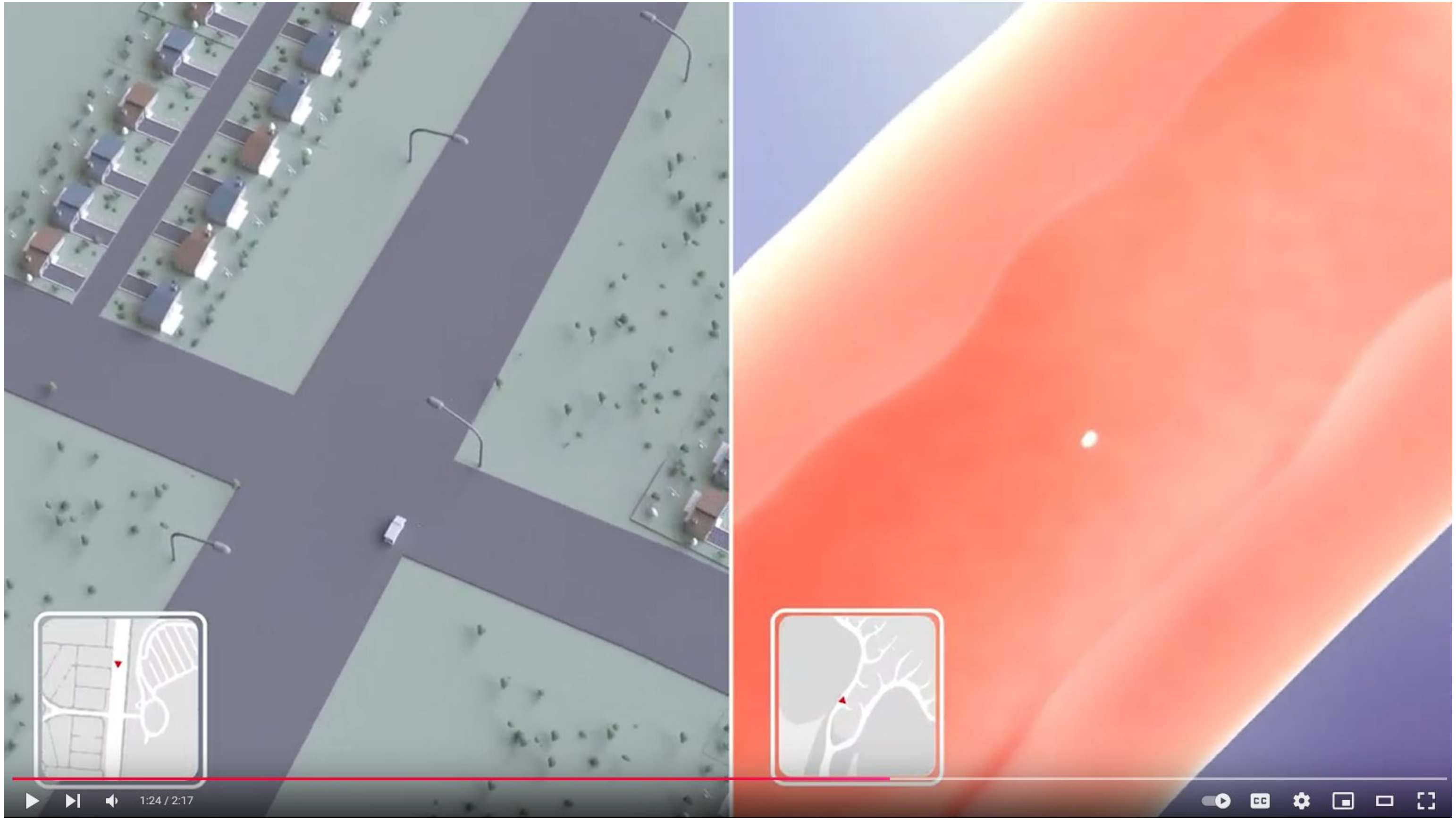




https://www.youtube.com/watch?v=zQeMgxo8n_U

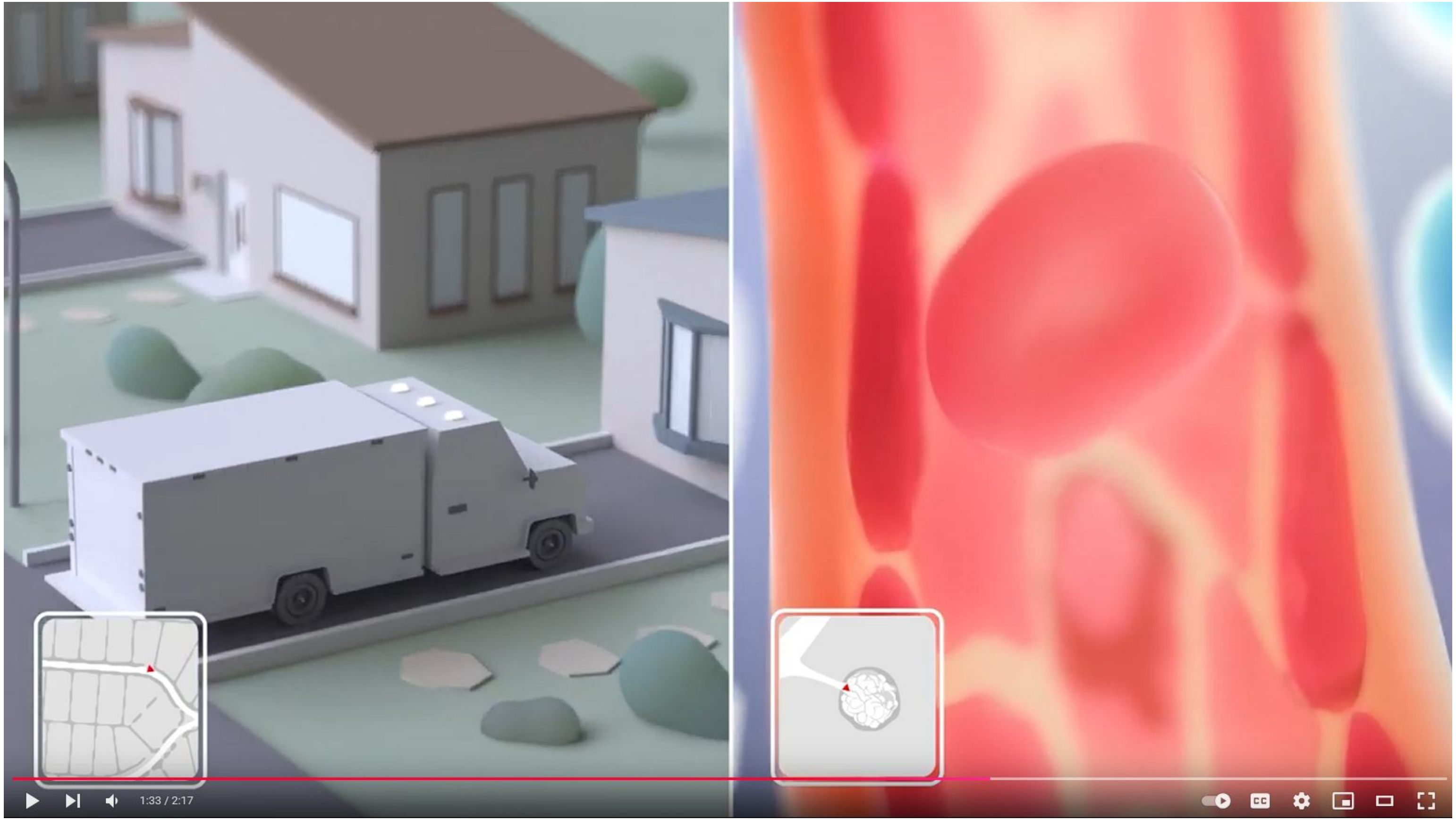
Highway (1000 km)

Artery (1 m)



https://www.youtube.com/watch?v=zQeMgxo8n_U

Street (1 km) Arteriole (0.5 cm)



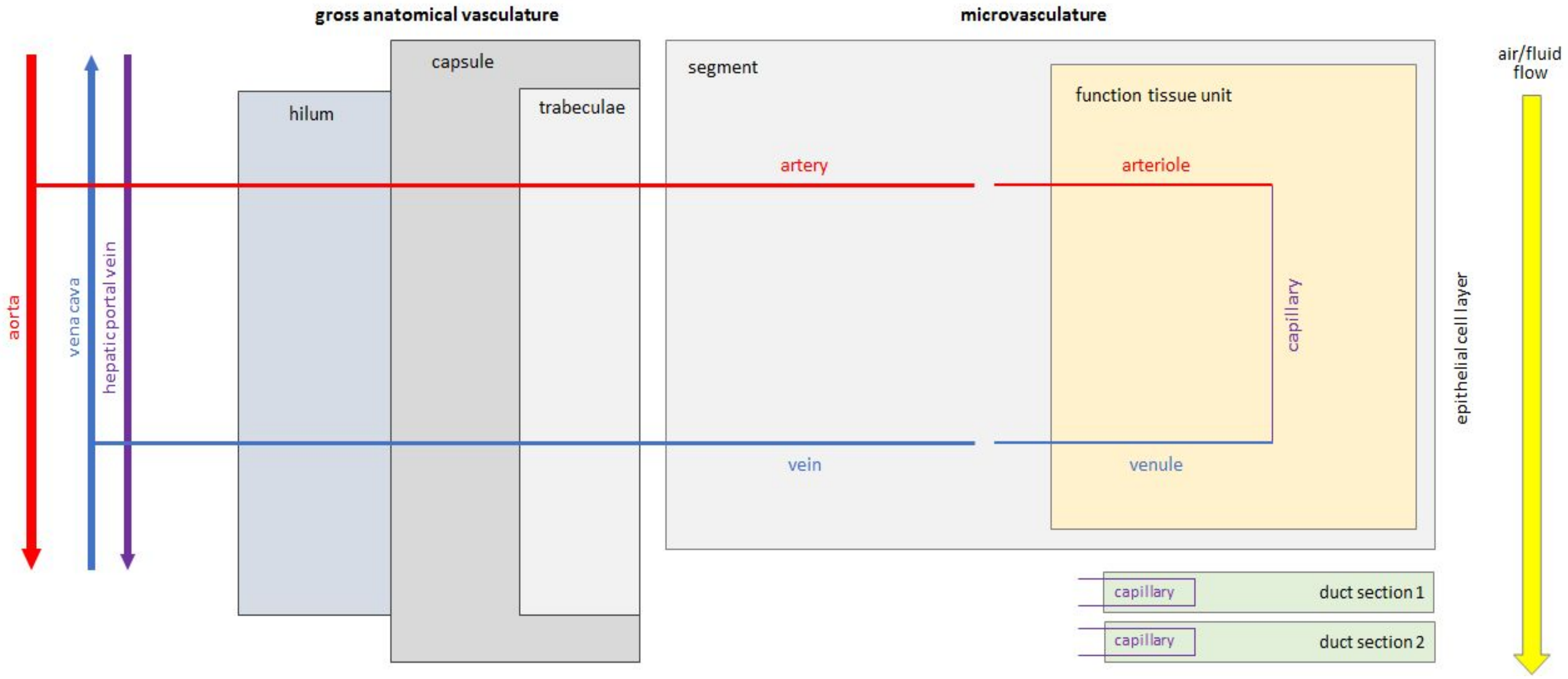
https://www.youtube.com/watch?v=zQeMgxo8n_U

Driveway (10 m) Capillary (0.5 mm x 0.01 mm)

https://www.youtube.com/watch?v=zQeMgxo8n_U

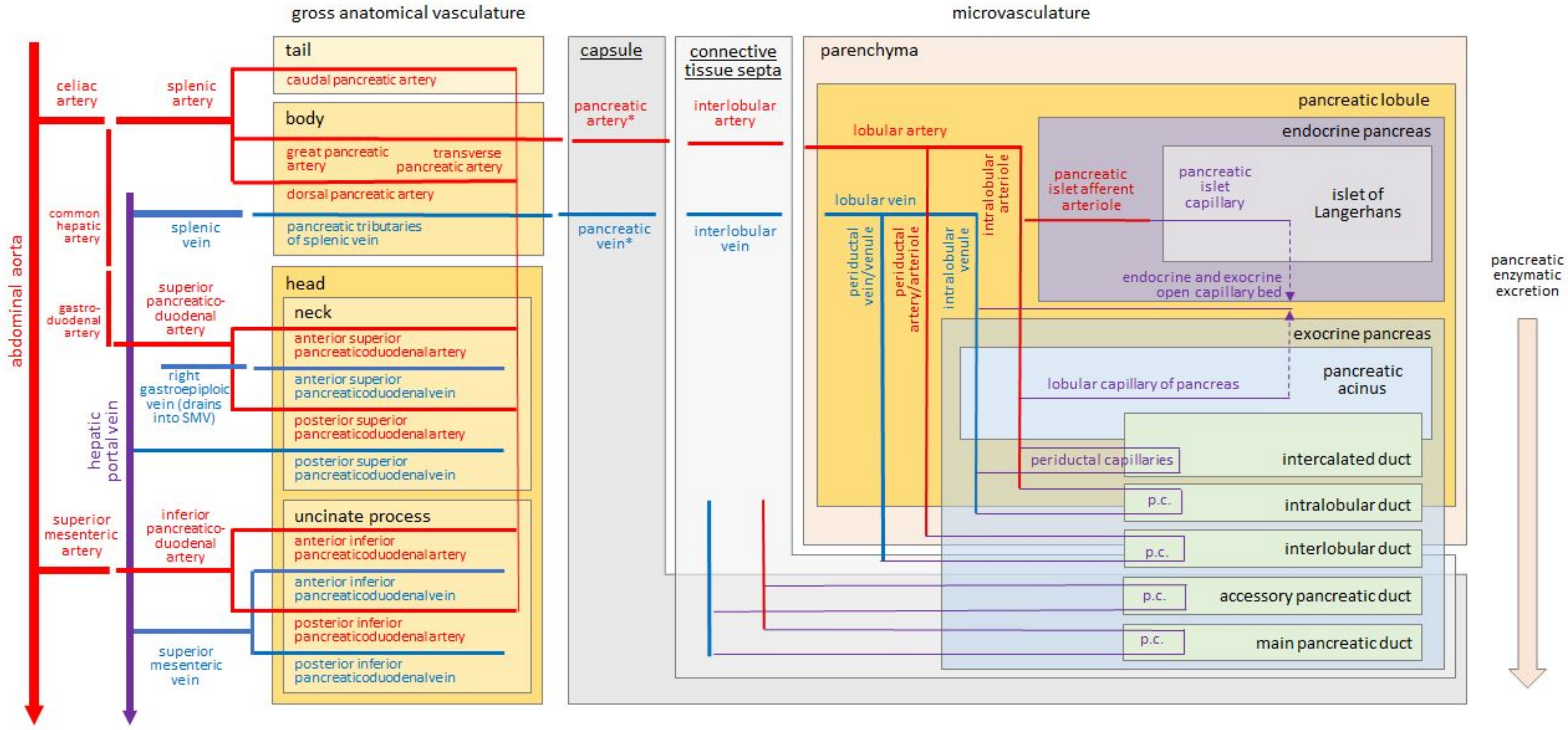
Blood Vasculature to Organ Crosswalk Diagrams

Template



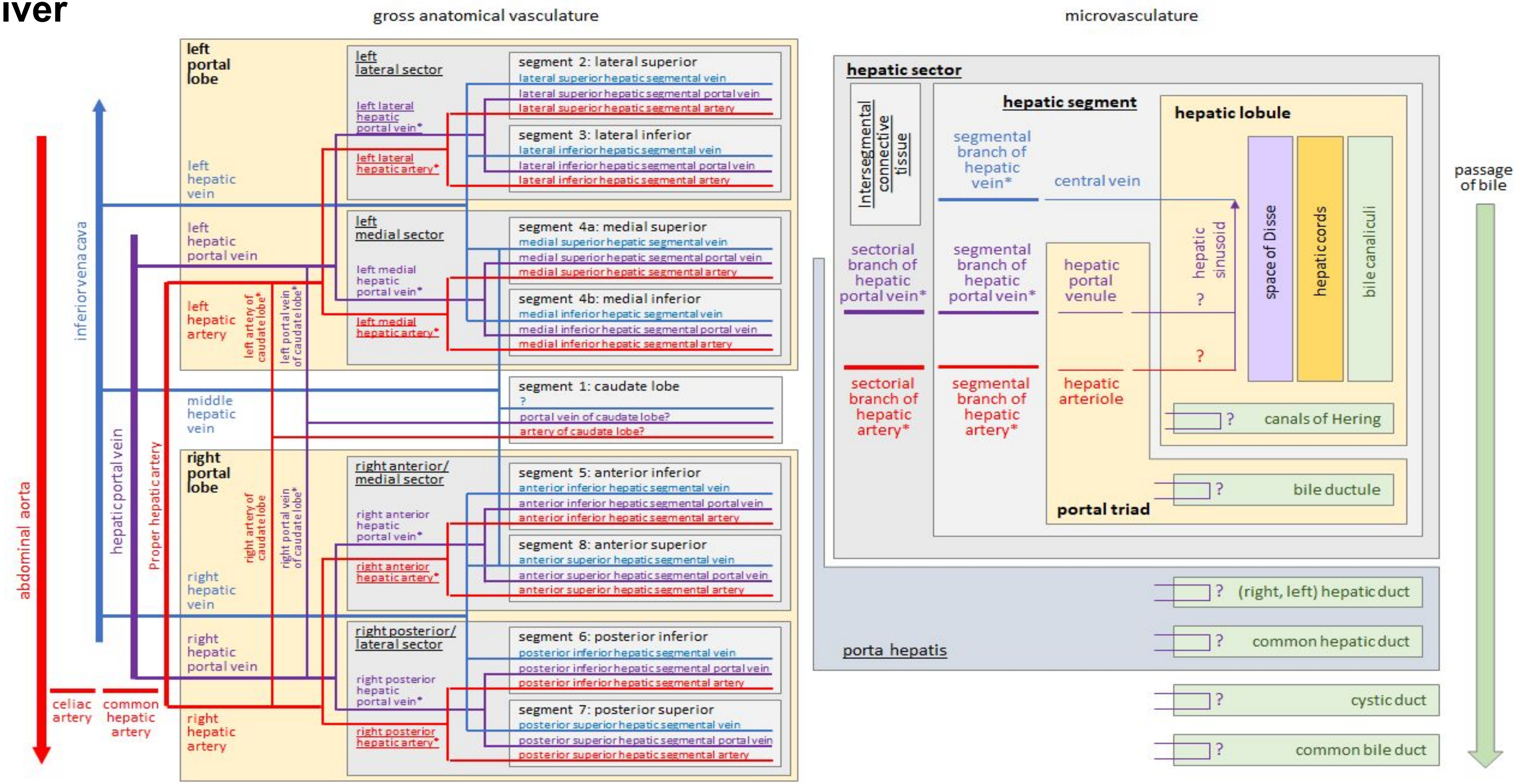
Blood Vasculature to Organ Crosswalk Diagrams

Pancreas



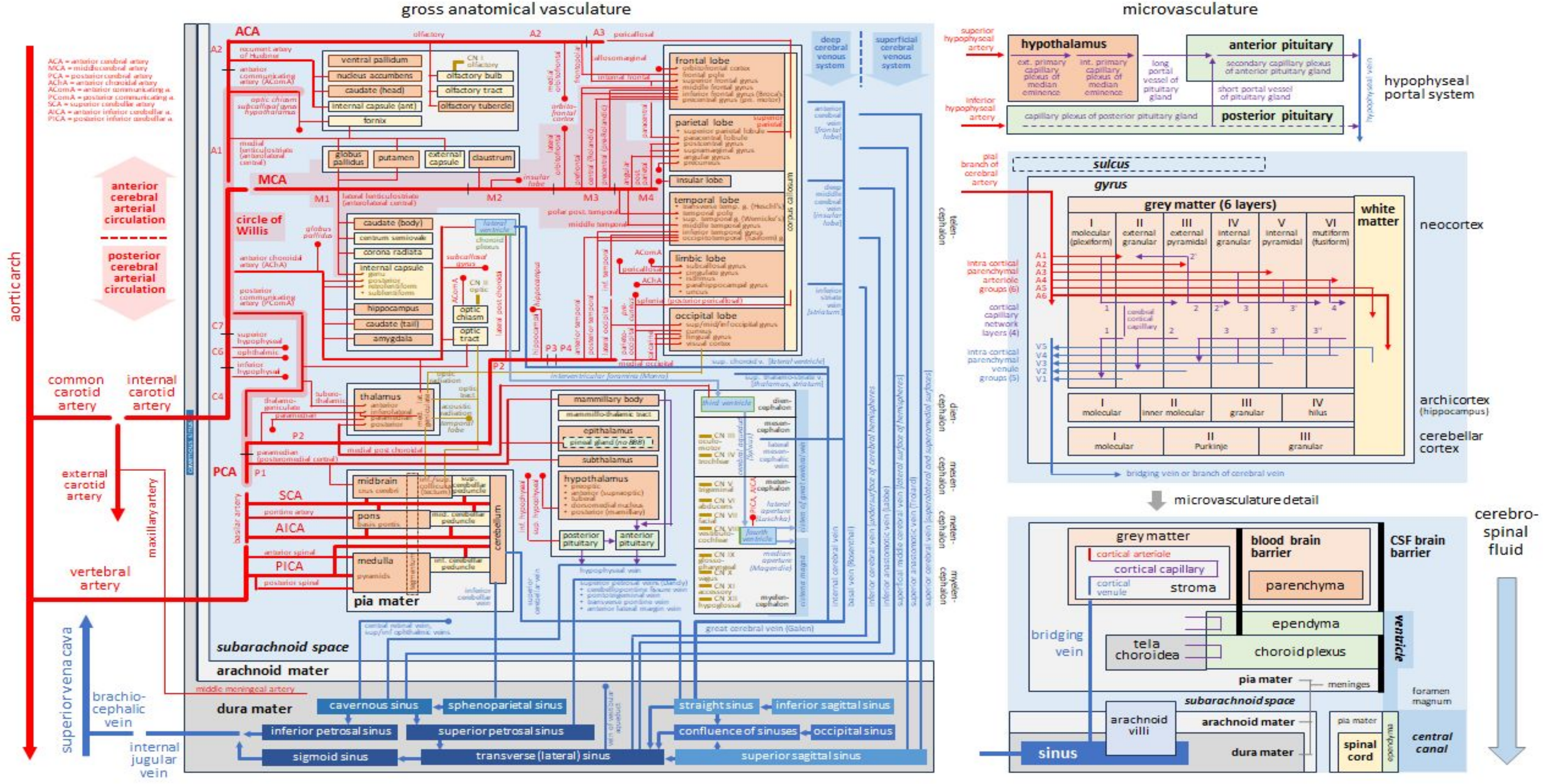
Blood Vasculature to Organ Crosswalk Diagrams

Liver

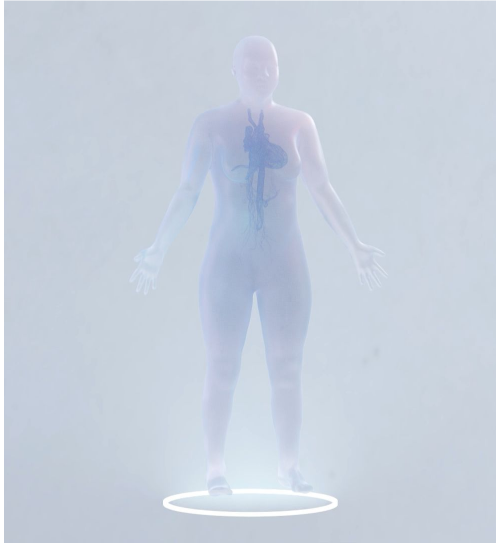


Blood Vasculature to Organ Crosswalk Diagrams

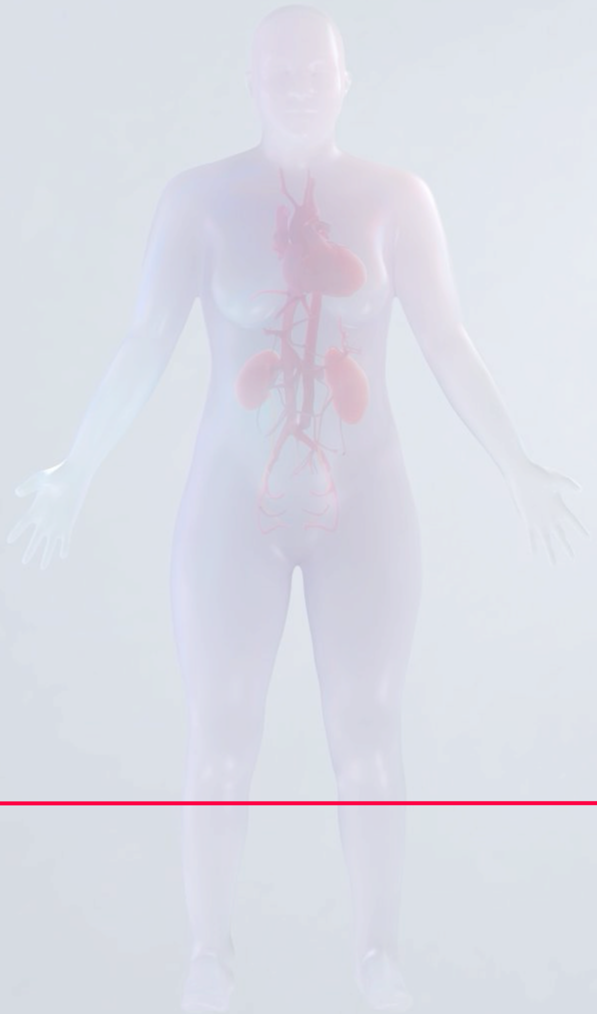
Brain



Q&A



- What is the best definition of “multiscale visualizations”?
- What application domains are best and worst served by multiscale visualizations?
- What kinds of conceptual and cognitive challenges exist for constructing and reading multiscale visualizations?
- What kinds of visual encodings make sense only in multiscale visualizations, and which ones do not make much sense?
- What kinds of interactions are needed to make multiscale visualizations usable?
- **What are the opportunities afforded and challenges posed by using extended reality (XR) technologies such as virtual, augmented, and mixed reality (VR, AR, MR) for multiscale visualizations?**
- **What is the relationship between multiscale visualizations and one-scale visualizations, such as bar graphs, scatter graphs, or line graphs? How can one be served by the other?**
- **When are stepless and stepped zooms better, respectively?**



Q&A

https://humanatlas.io/events/2024-24h

Thank you