IMAG Interagency Modeling And Analysis Group

A modeling framework for Biomedical Digital Twins

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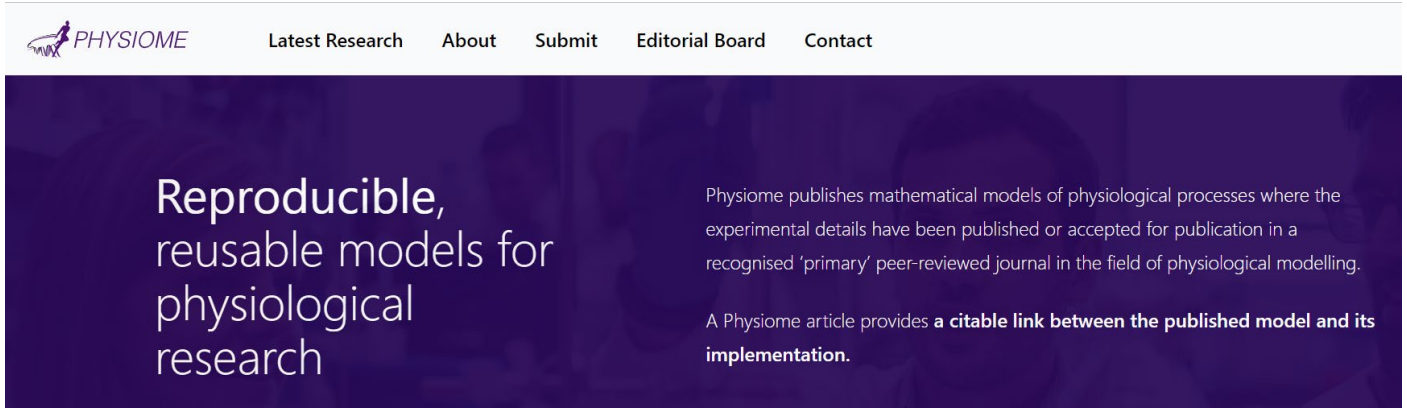
Community resources

CellML homepage https://www.cellml.org/

OpenCOR software https://opencor.ws/ (Download, documentation, tutorial)



https://journal.physiomeproject.org/

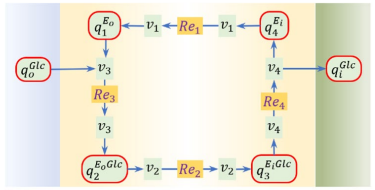
Mapping tools https://docs.sparc.science/docs/map-core-scaffold-mapping-tools

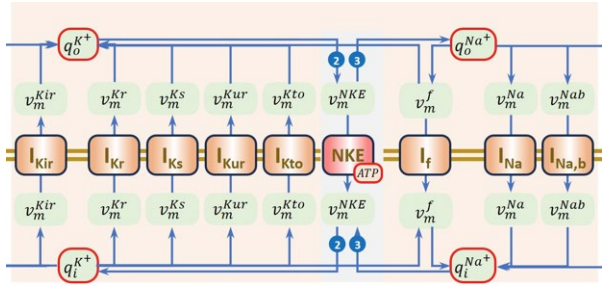
Multiscale modelling with bond graphs

1. BG protein templates

(full) (reduced)

- Metabolic enzymes
- SLC transporters
- ATPase pumps
- ABC transporters
- Ion channels
- Contractile proteins
- Receptors: GPCR, TRK
- Signal transduction
- Immune cytokines
- Cell cycle
- Gene transcription & translation



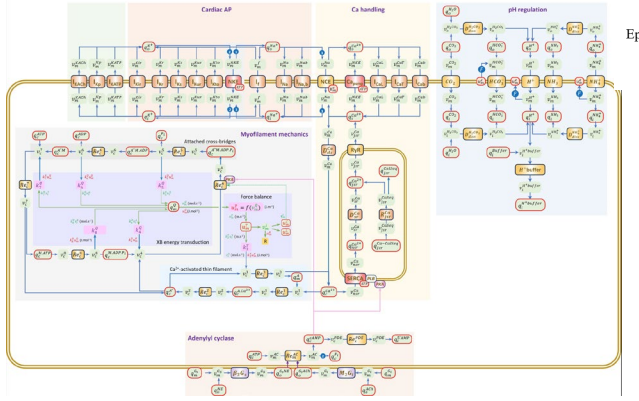


2. FCUs

- Metabolism
- Action potentials
- Calcium handling
- pH regulation
- Myofilament mechs
- Receptors & signaling
- Glucose transport
- Na/K regulation
- Cell cycle
- Cell adhesion
- Gene regulation
- …

3. Cells

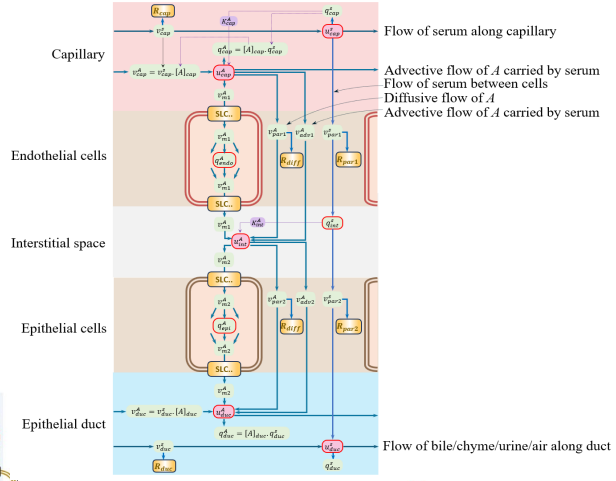
- Endothelial cell
- Epithelial cell
- Cardiomyocyte
- Muscle fiber
- Fibroblast
- Smooth muscle cell
- Osteocyte
- Enterochromaffin cell
- Hepatocyte
- Goblet cell
- Red blood cell
- …



4. FTUs

(including 3D structure)

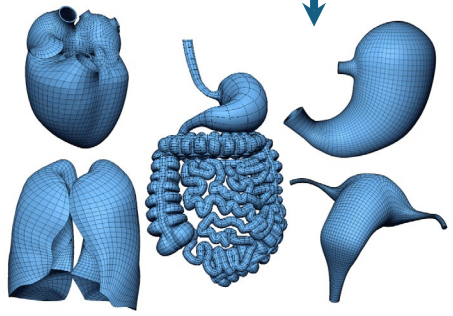
- Glomerulus, … → nephron
- Lung alveoli → acinus
- Myocardial sheet → block
- Liver lobule → lobules
- Bone osteon → osteon
- Fibre, etc → fascicle
- … → …



5. Organs

=surrogate

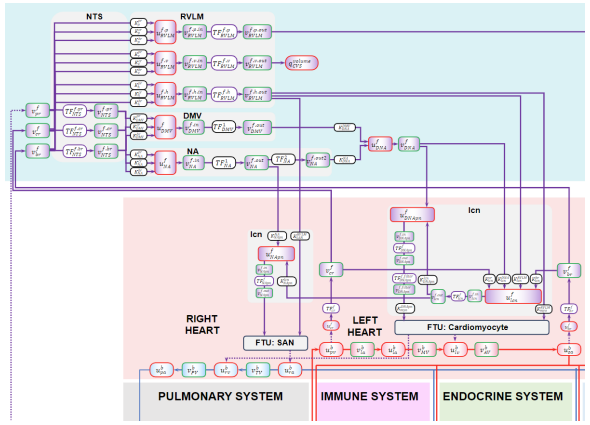
- Kidney
- Lung
- Heart
- Liver
- Bone
- Muscle
- …



6. FPUs

(3D anatomical model of the body)

- Regulation of fluid volume
- Regulation of arterial blood pressure
- Regulation of pH
- Regulation of electrolyte balance
- Regulation of glucose
- Regulation of O_2 and CO_2
- Regulation of calcium
- Regulation of phosphate
- Regulation of body temperature
- …



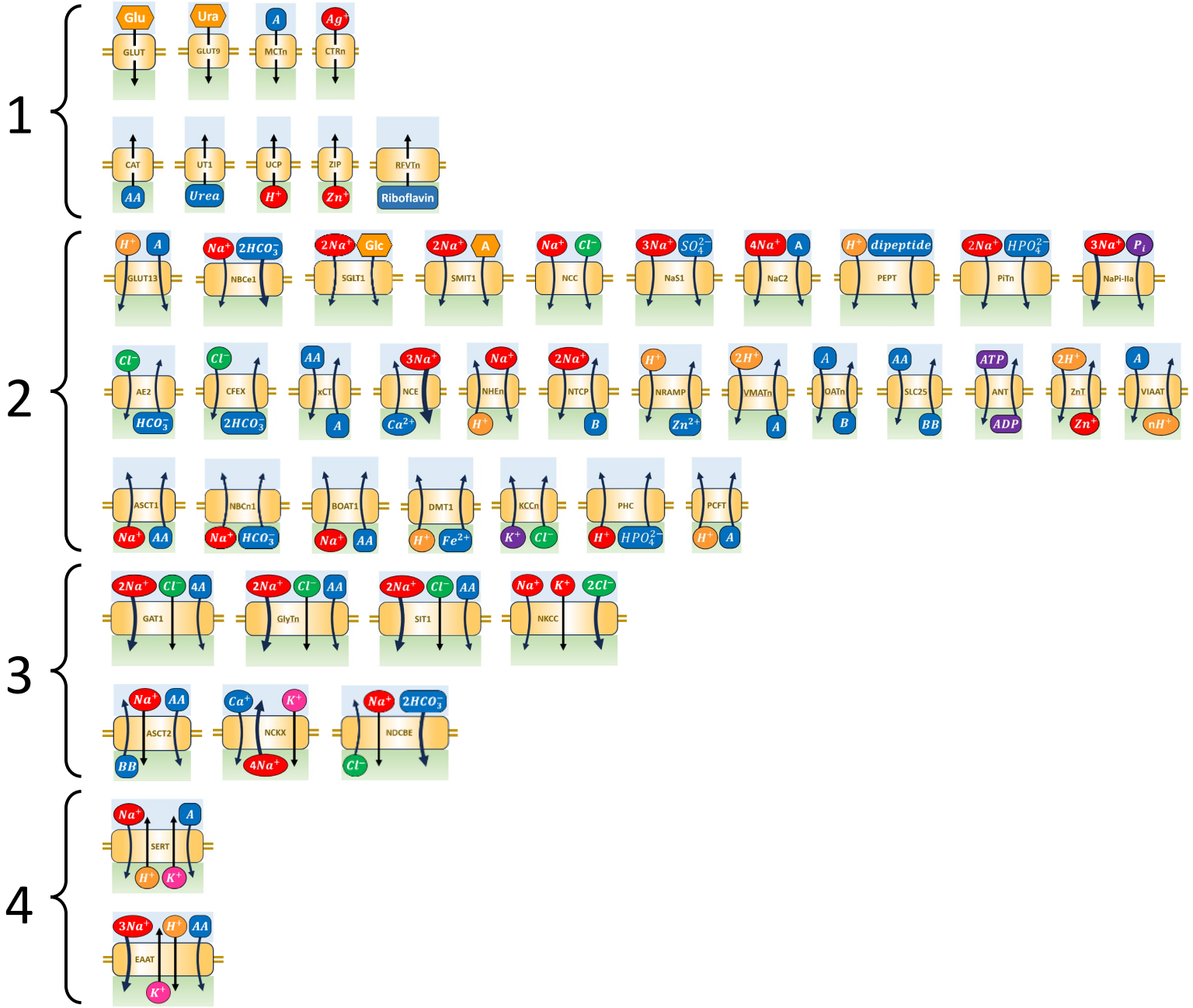
Finite element models that are subsequently reduced (with AI methods) to surrogate models.

Example: SLC transporters

458 genes

66 gene families

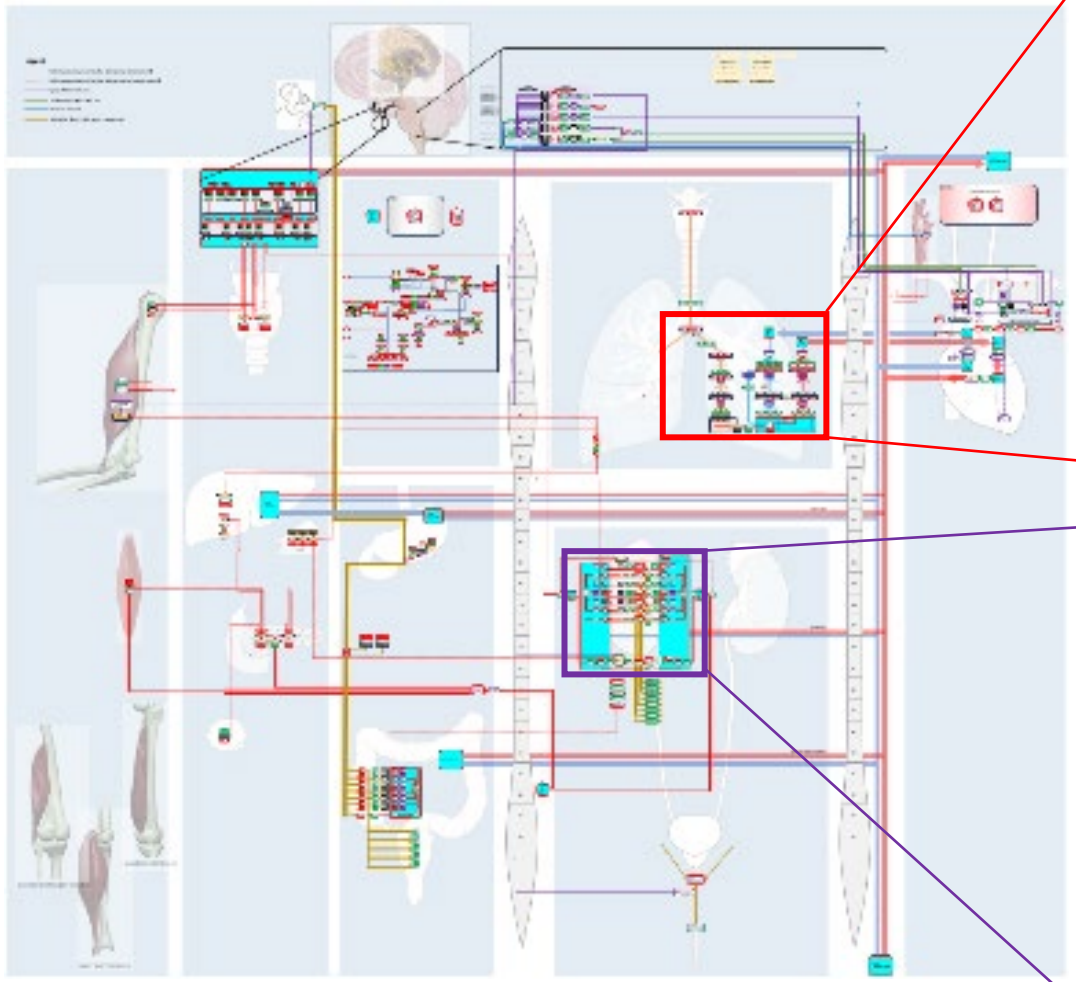
bond graph templates

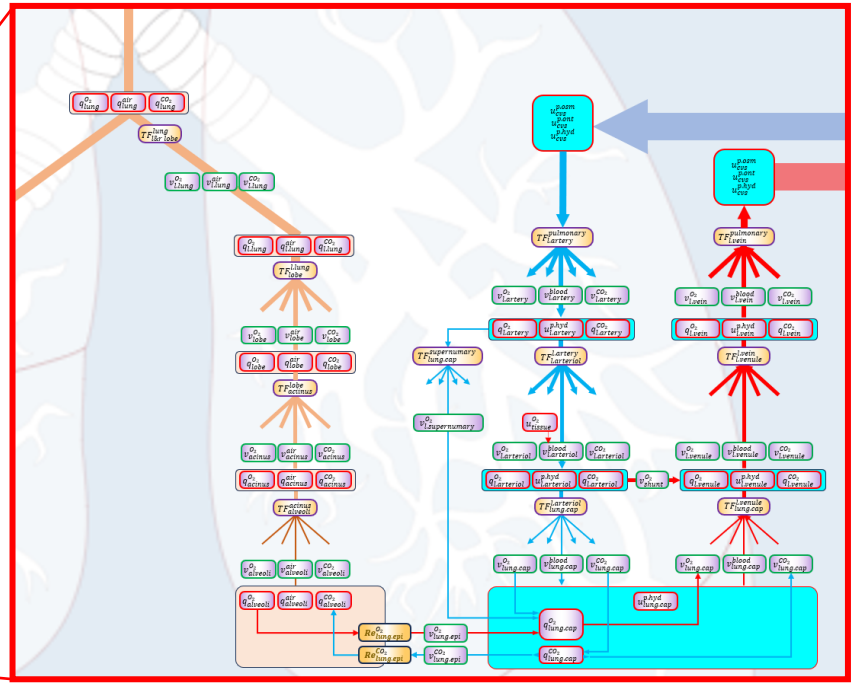


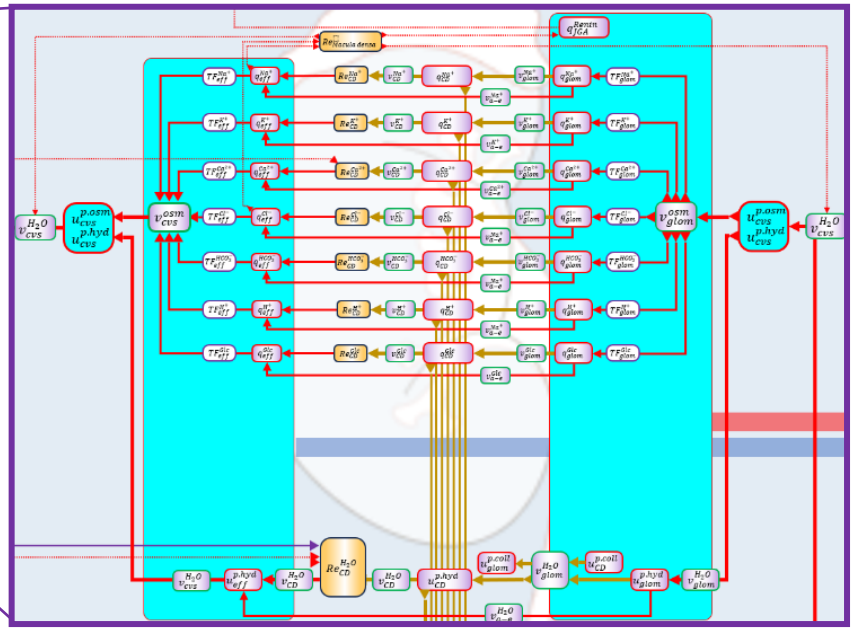
Examples:
SLC1: (EAAT) Glutamate transport
SLC2: (GLUT) Facilitated glucose transport
SLC4: (AE, NBC) Bicarbonate cotransporters
SLC5: (SGLT) Na-glucose cotransport
SLC8: (NCE) Na-Ca exchange
SLC9: (NHE) Na-H exchange

Linking systems physiology with molecular mechanism

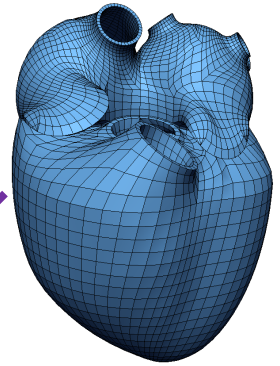
Food intake and glucose control
Control of BP: Baroreceptors and the Renin-Angiotensin-Aldosterone System (RAAS)
Control of blood volume
Control of metabolism
Calcium homeostasis
Circadian rhythms
Growth regulation
…

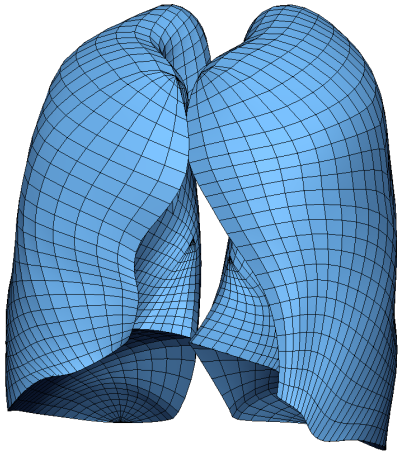


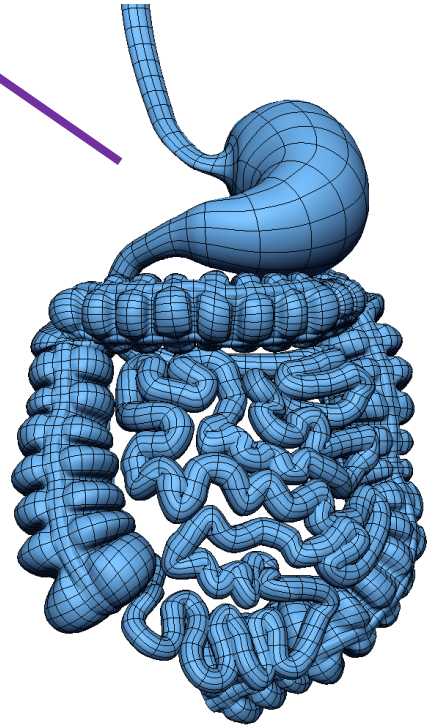


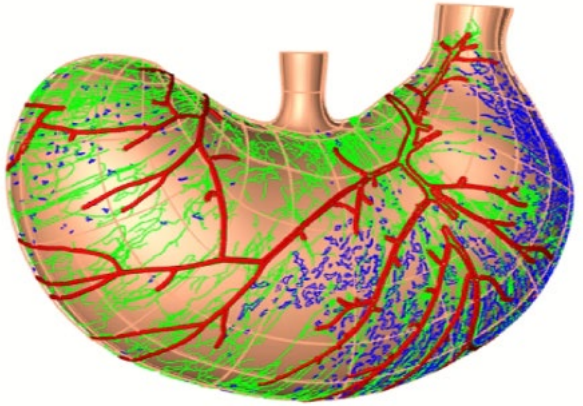


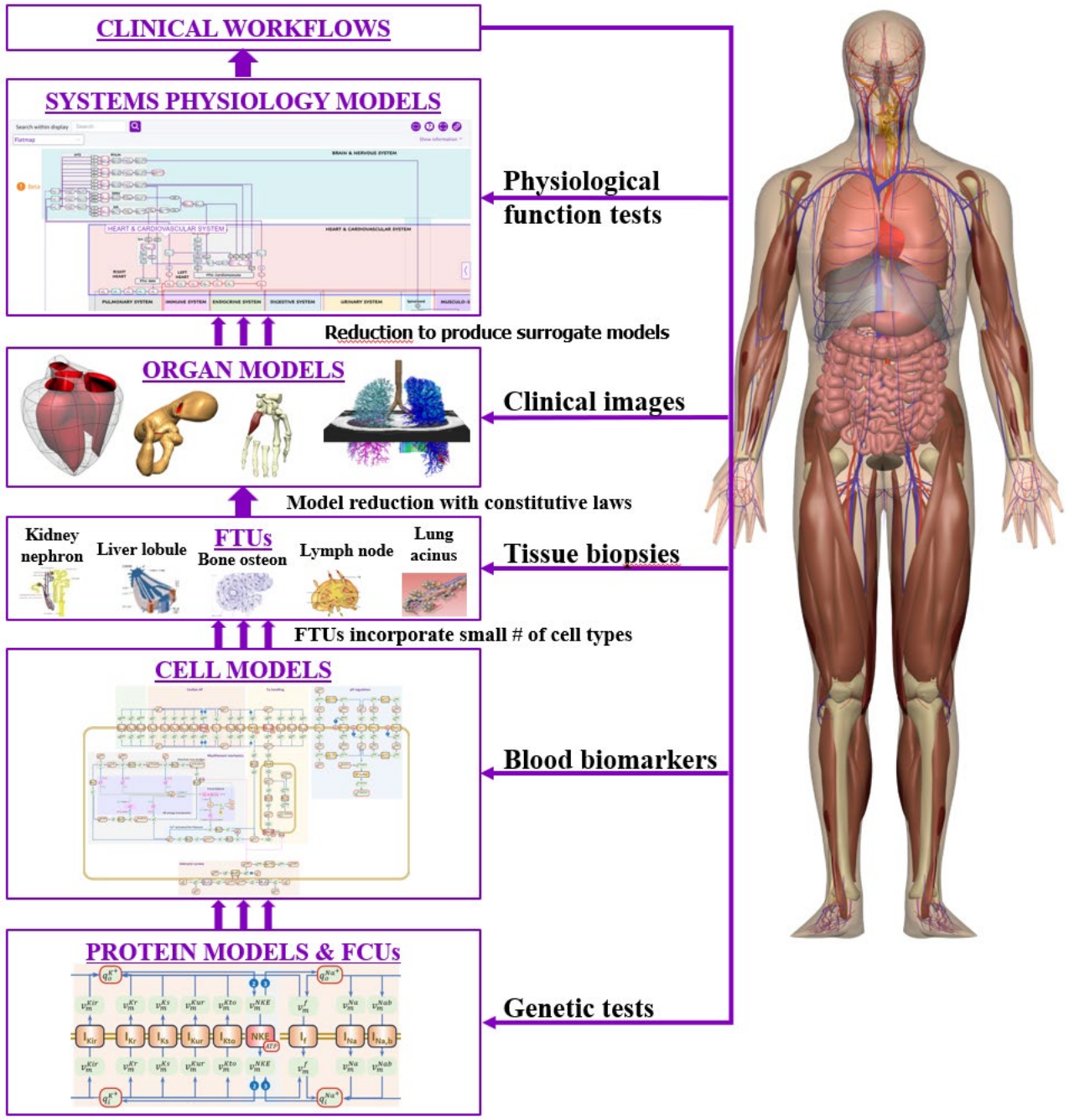
Scaffolds for spatial mapping











Constrained by observed behaviour

Model parameters

Constrained by physics and genetics

Thank you!