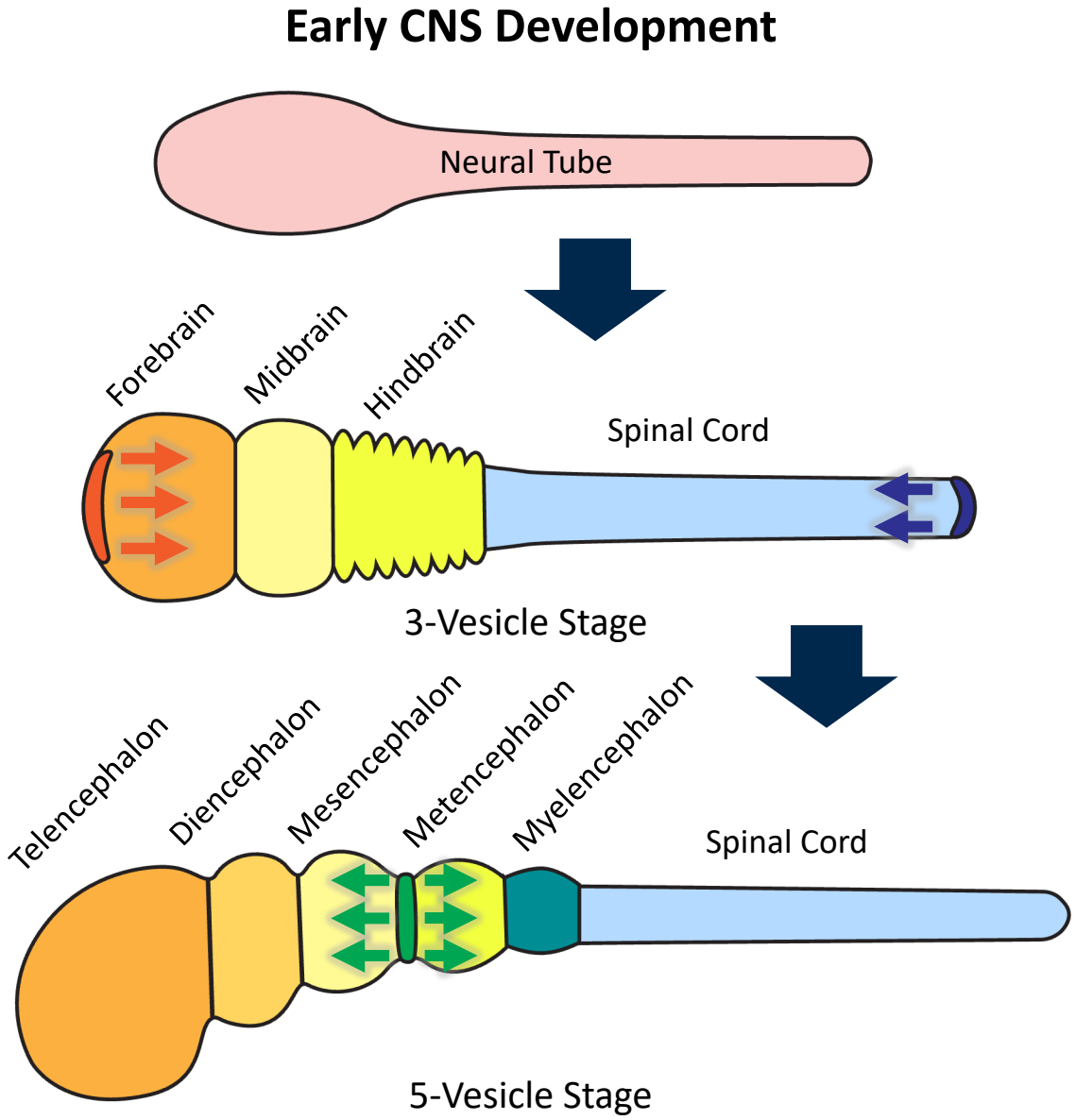
Background

Patterning in Biology

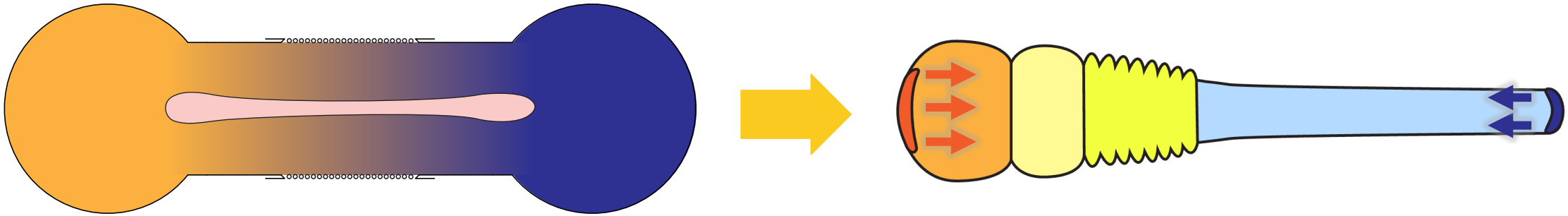
Generation of complex organizations through cell fate decisions

Rostrocaudal (RC) Patterning
of neural tube



Background

Recapitulate CNS patterning using engineering tools



Achieve patterning

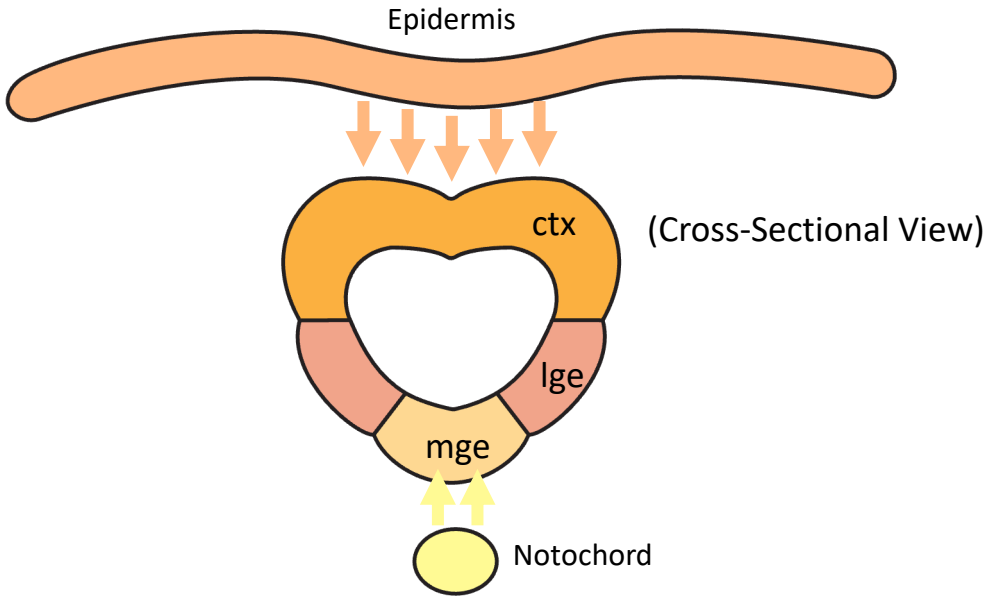
Patterning achieved

?

Microfluidics generate chemical gradient

Differential secretion of soluble factors

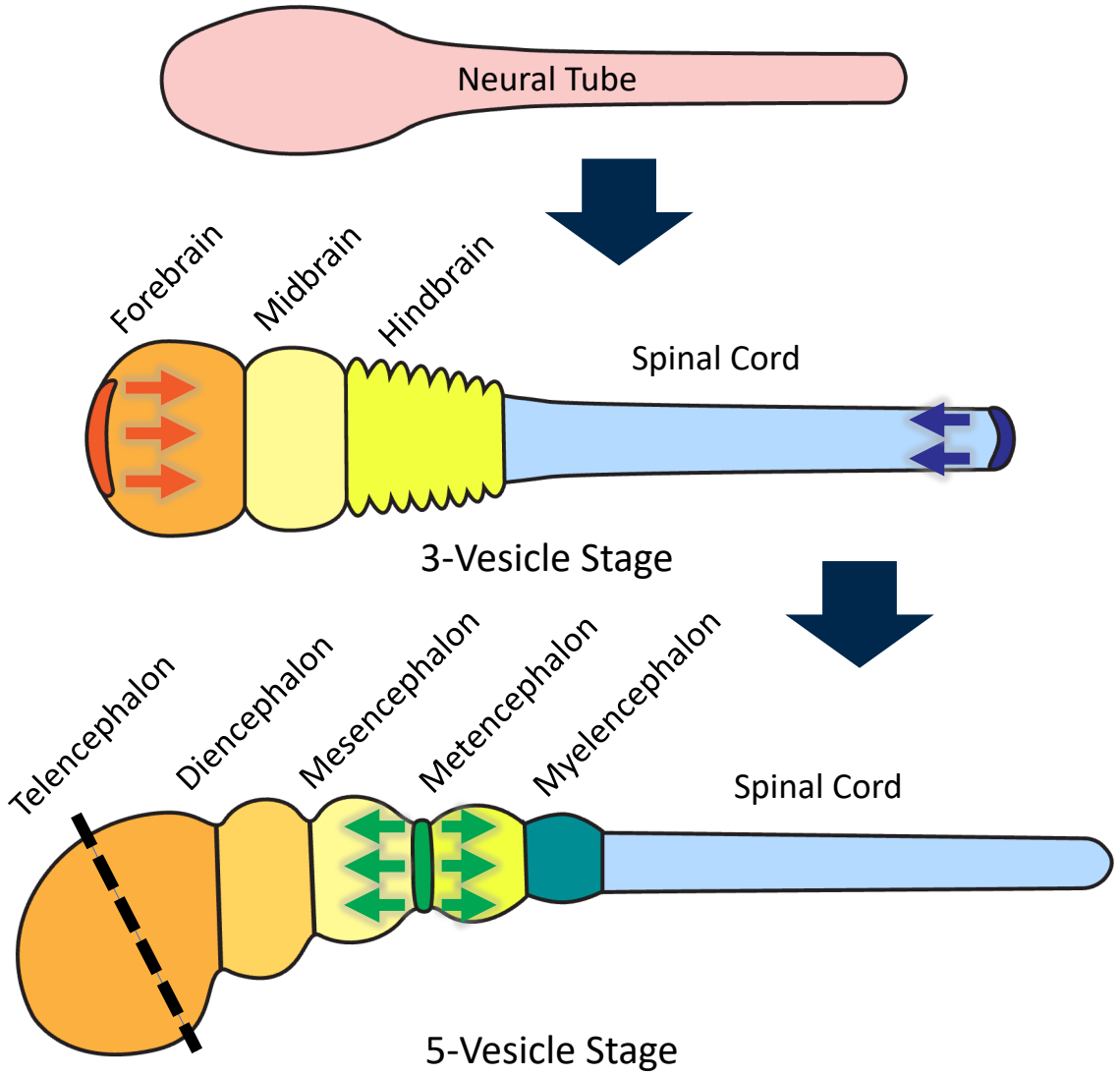
Brain Organoid



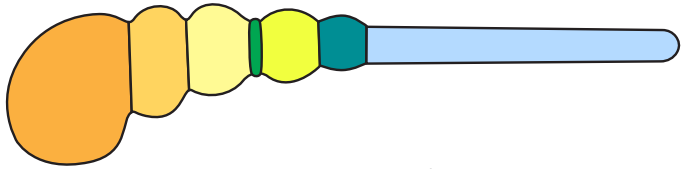
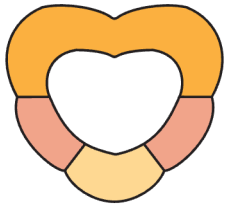
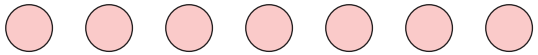
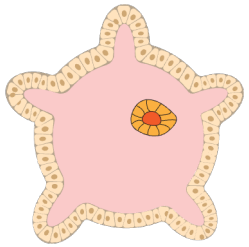
(Cross-Sectional View)

Dorsoventral (DV) Patterning
of neural tube

Early CNS Development

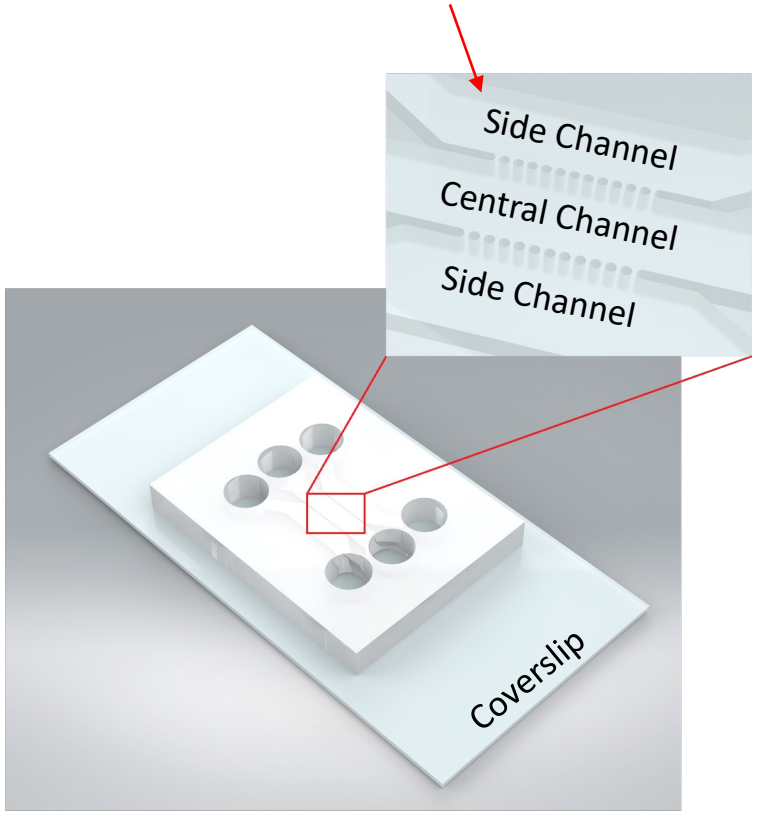


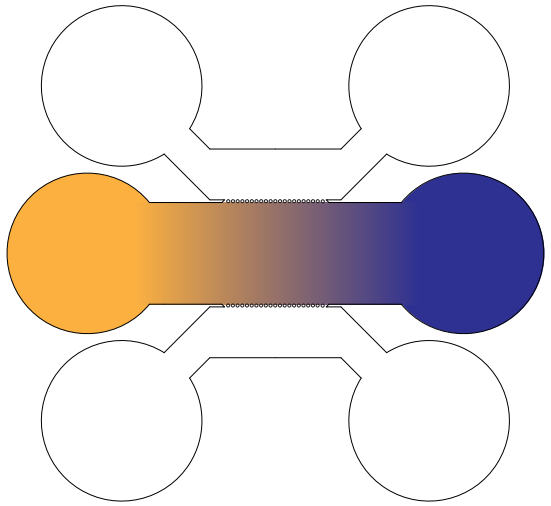
Brain Organoid

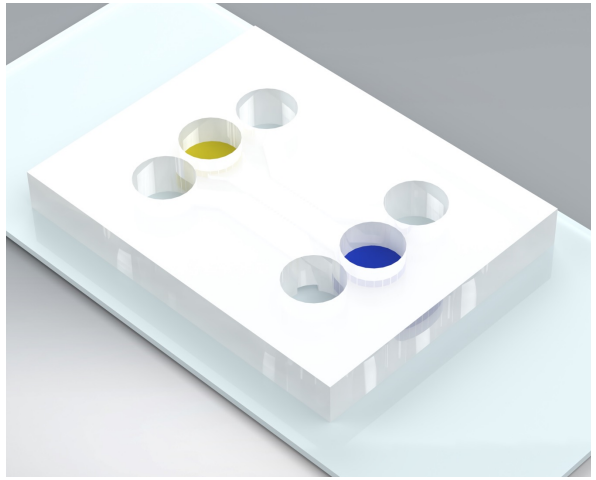
	 RC Patterning	 DV Patterning
Continuous Model (tissue interactions and dynamics)	 Neural Tube	? DV Patterned Brain Organoid
Discrete Model (modularity and in-depth study)	 Neural Cyst	 Dorsal/Ventral Brain Organoid

Brain Organoid

Supply additional medium for larger tissue

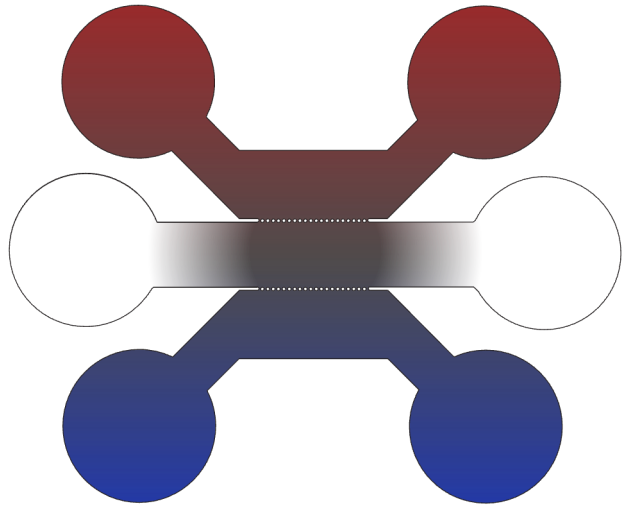


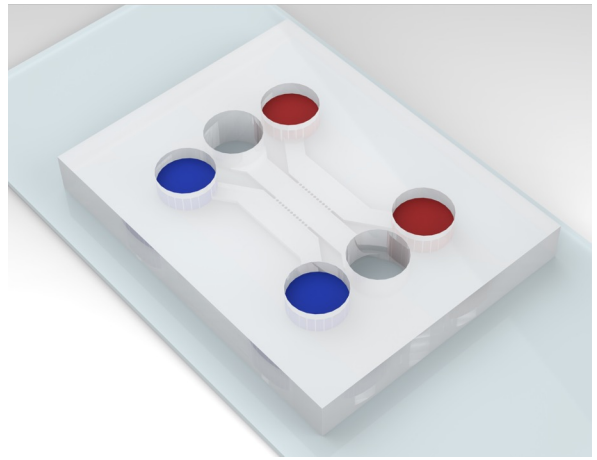




Achieve DV patterning with similar principle

?

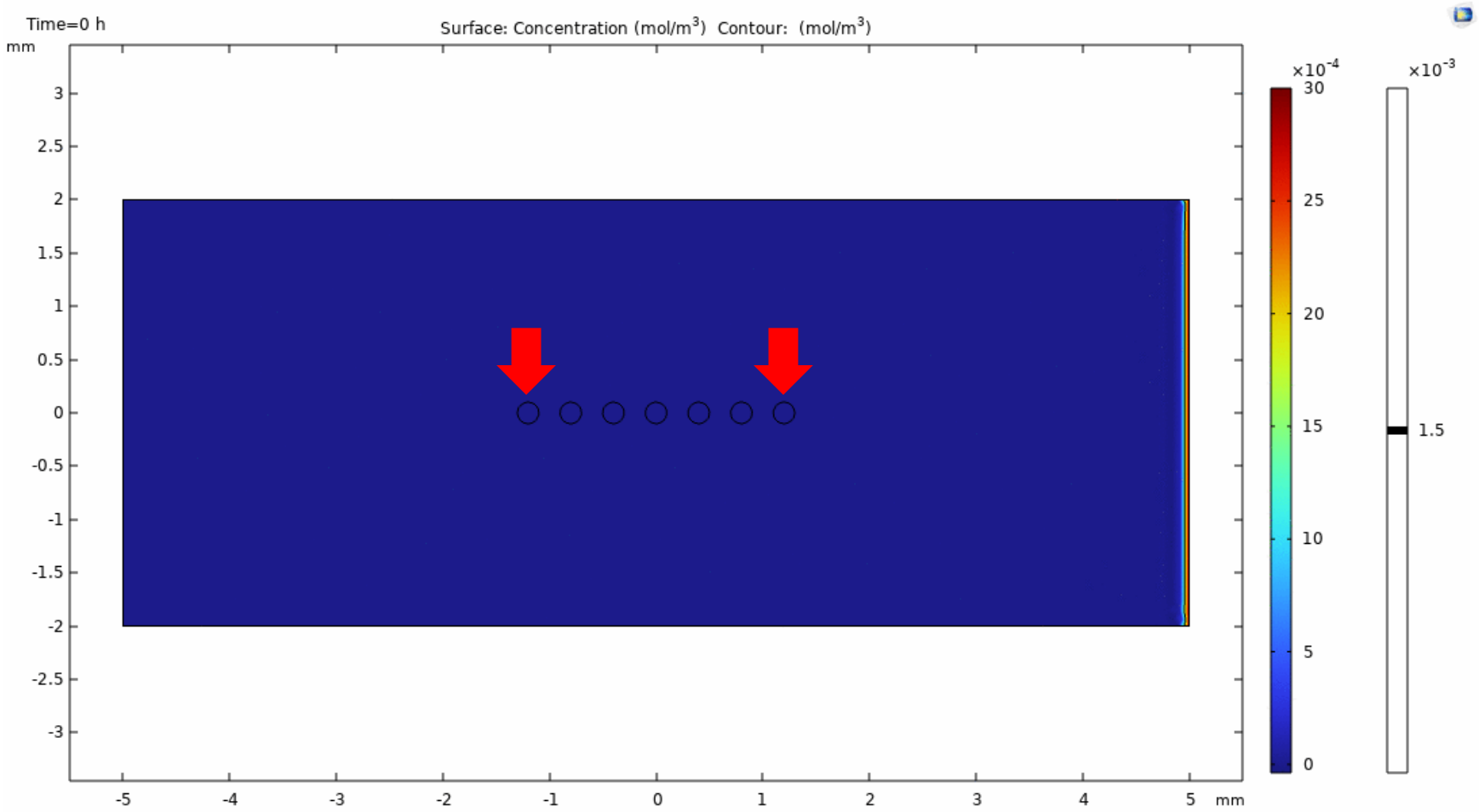




Brain Organoid

Caudal cysts subject to ~**2µM** of inductive chemicals at steady state (compared to **rostral** ones at ~**1µM**, a two-fold change)

RC patterning relies on concentration difference over distance

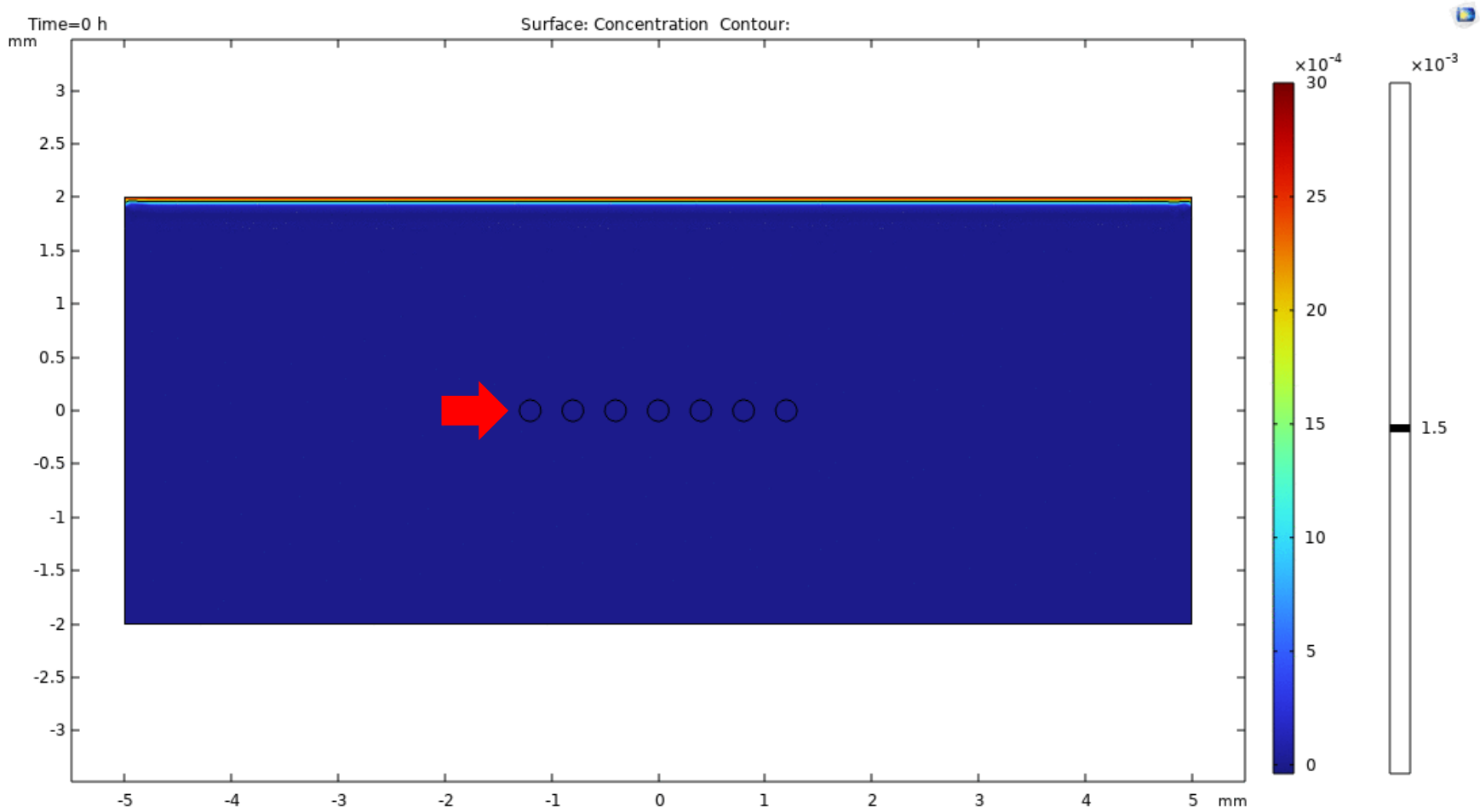


Dorsal
Rostral Caudal
Ventral

Brain Organoid

Because of their small size, each cyst is not subject to sufficiently different microenvironment.

Difficult to trigger DV patterning in current design



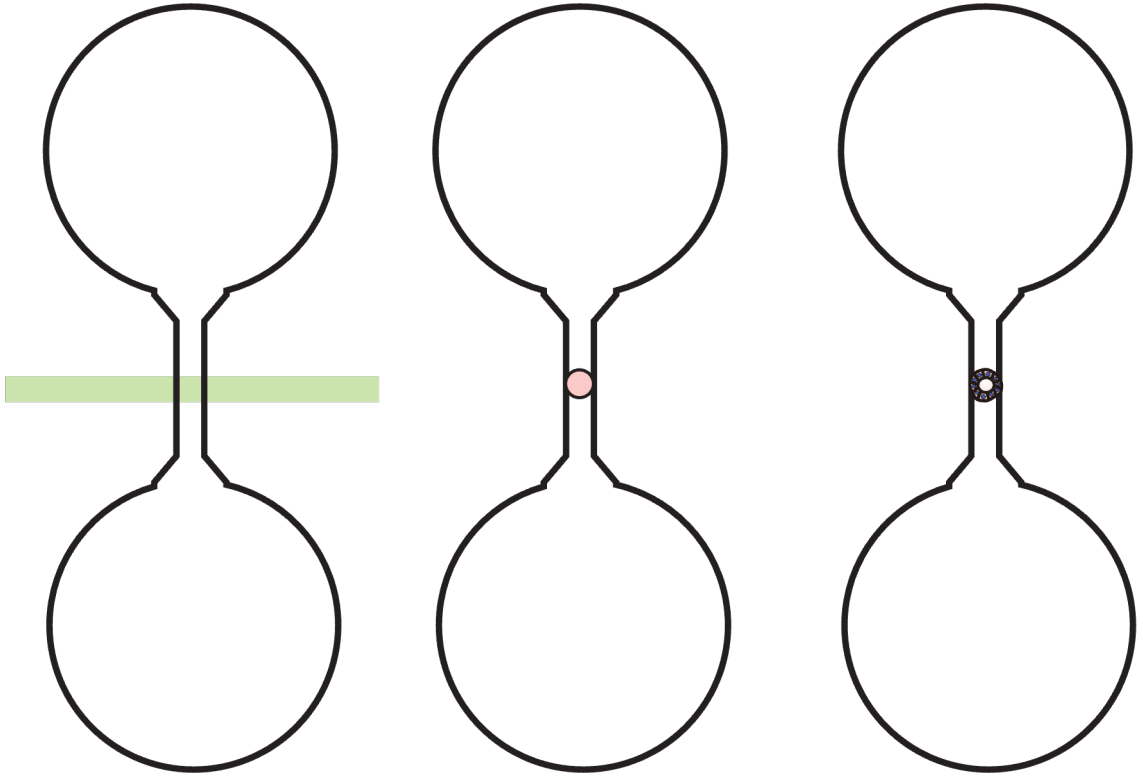
Dorsal
Rostral Caudal
Ventral

Brain Organoid

Goal:
New device design to create a sharp chemical gradient at single-cyst level

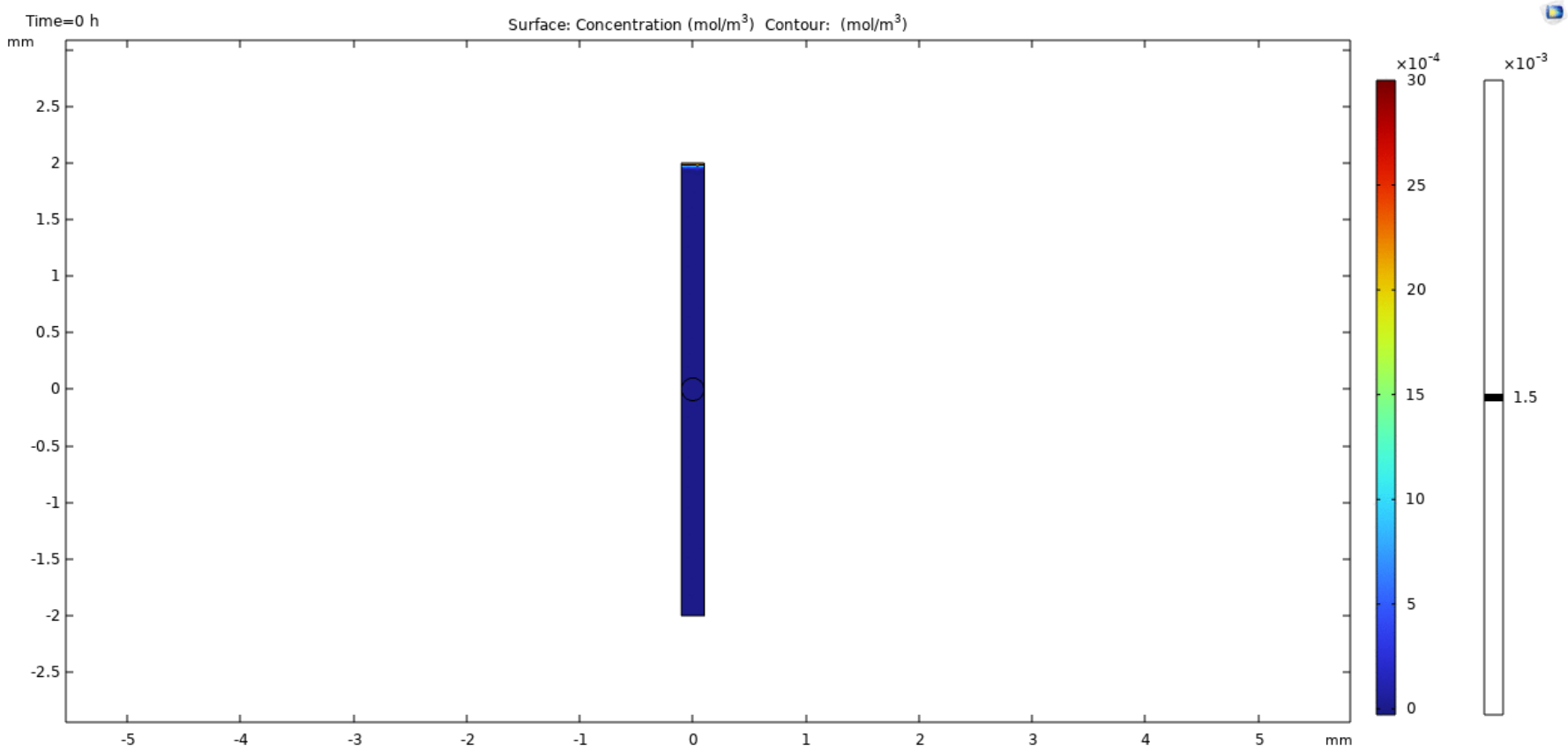
Strategy:
Use cyst tissue to block chemical diffusion

Design:



Brain Organoid

Geometric confinement helps form sharper chemical gradient



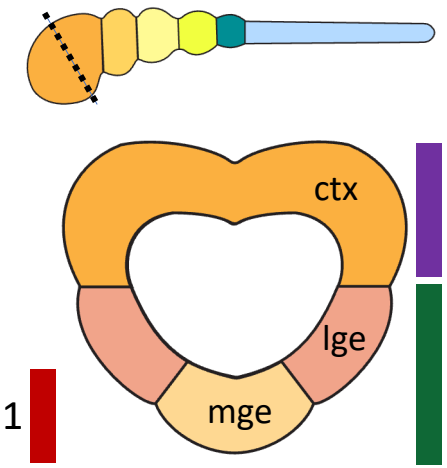
Dorsal

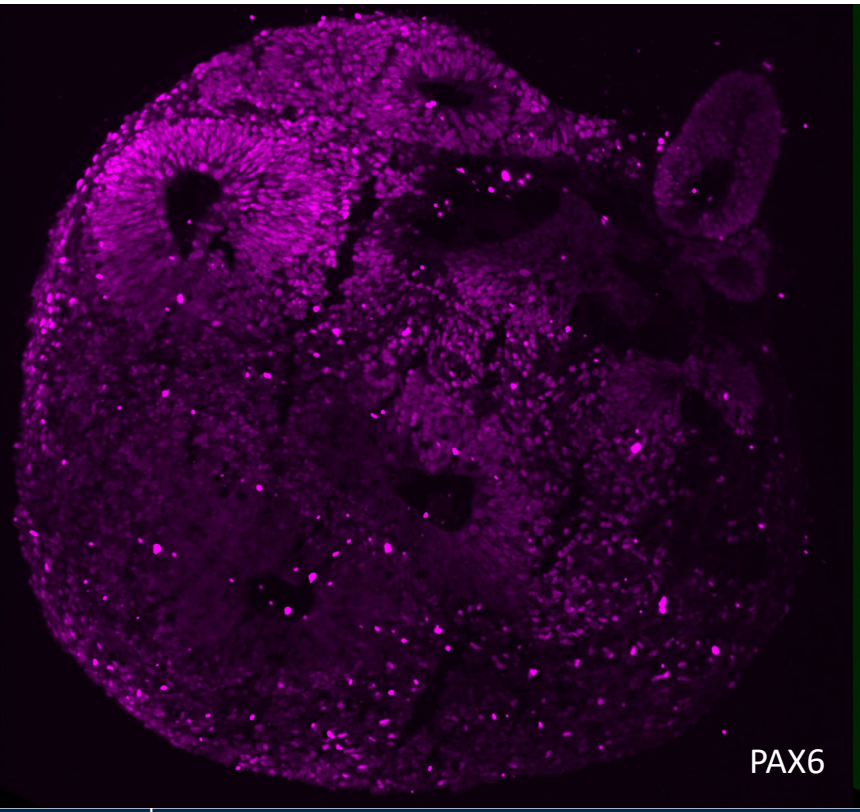
Ventral

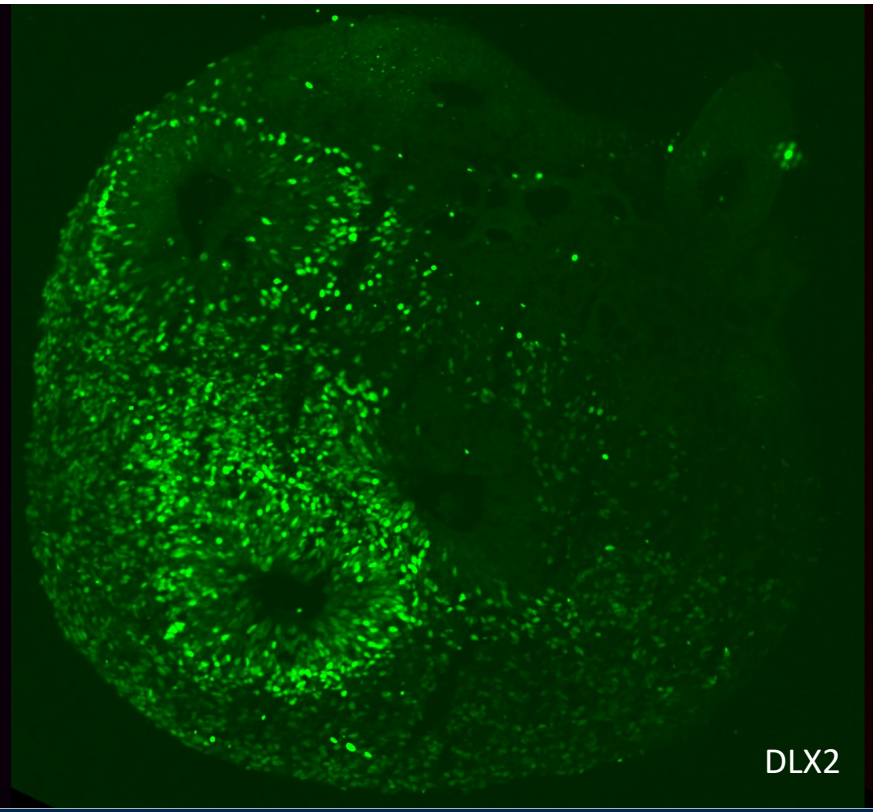
Brain Organoid

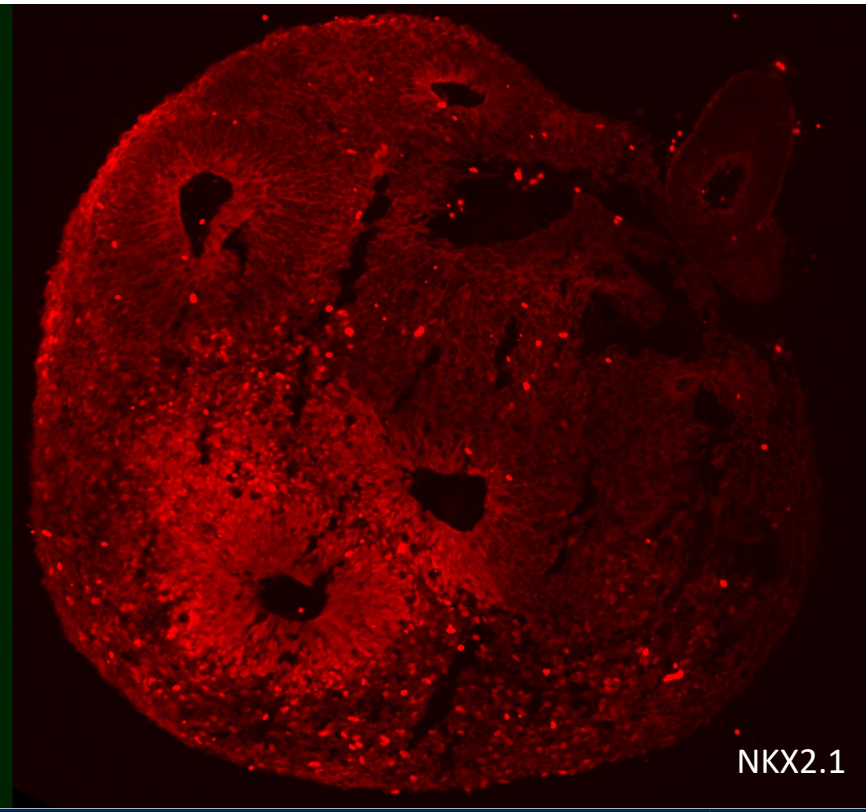
1. Single cyst
2. Correct localization of DV markers
3. Lumen present at the center of structure

New design facilitates DV patterning on a single neural cyst









Dorsal
Ventral