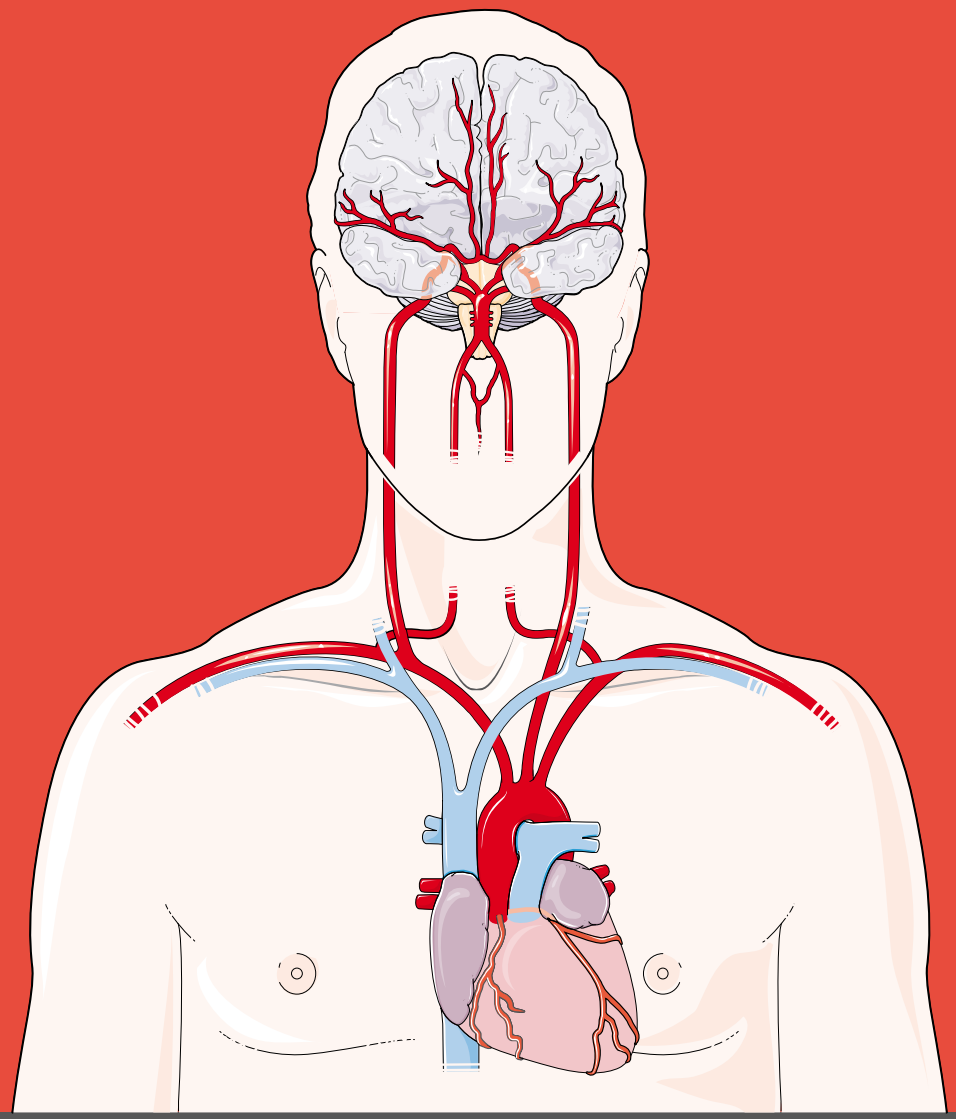
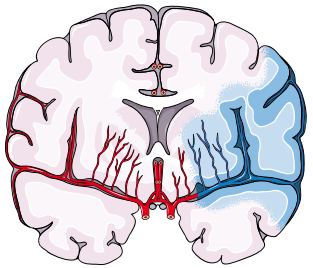


Two-Photon Microscopy Imaging of Cerebral Blood Flow after Ischemic Stroke

Speaker: Senik Matinyan

MD, PhD student



Stroke-related DALYs

All strokes[6]

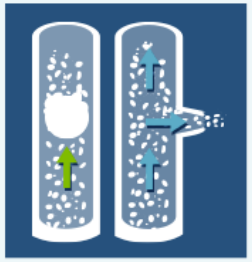
There are over 13.7 million new strokes of all types each year.

Globally, every fourth person aged over 25 years will suffer a stroke in their lifetime.

Stroke is the second leading cause of death worldwide. Five and a half-million people die of stroke annually.

Stroke is the leading cause of serious, long-term disability. Every year, over 116 million years of healthy life is lost due to stroke.

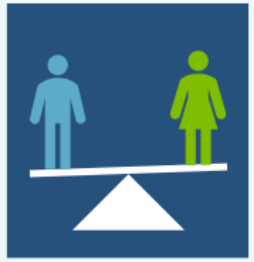
Ischaemic stroke[6]



Of all strokes, about 88% are ischaemic and 12% are haemorrhagic in nature.

In 2016, over 9.5 million new cases of ischaemic stroke occurred worldwide.

Strokes can happen at any age: Nearly 60% of all new ischaemic strokes happen in people younger than 70 years, and even 7% occur in people under 44 years.

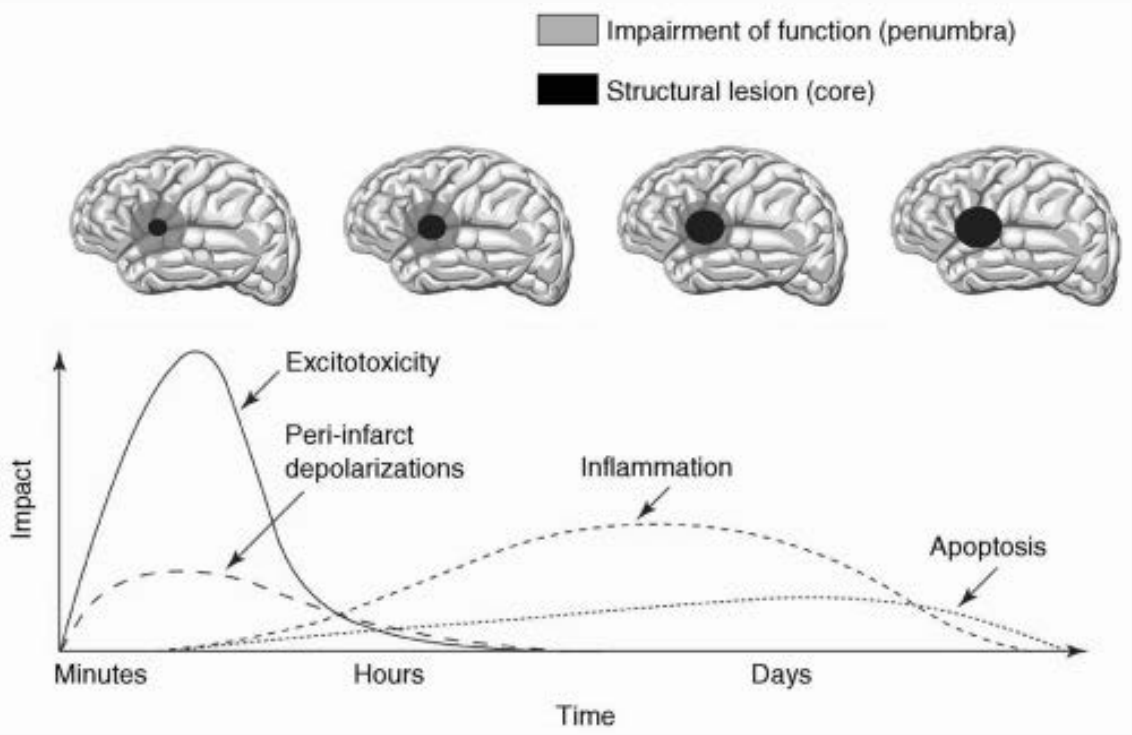


Each year, 52% of new ischaemic strokes occur in men, 48% in women.

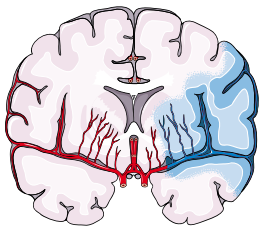
Annually, over 2.7 million people die from ischaemic stroke.

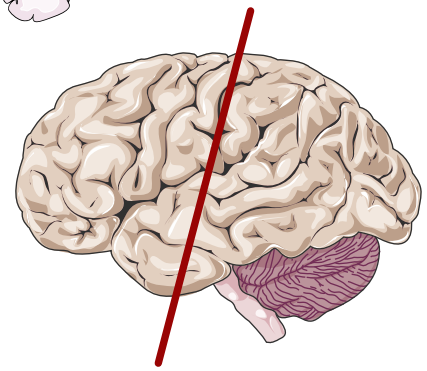
**DALY - disability-adjusted life-year*

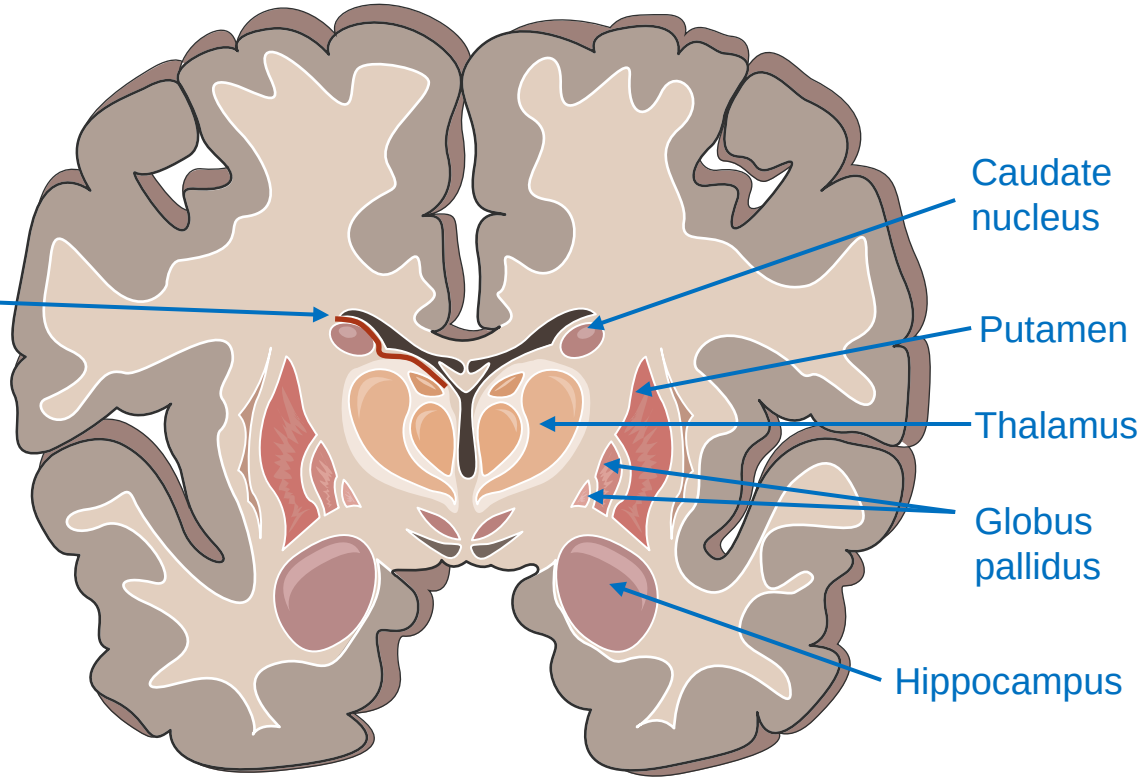
Time is brain



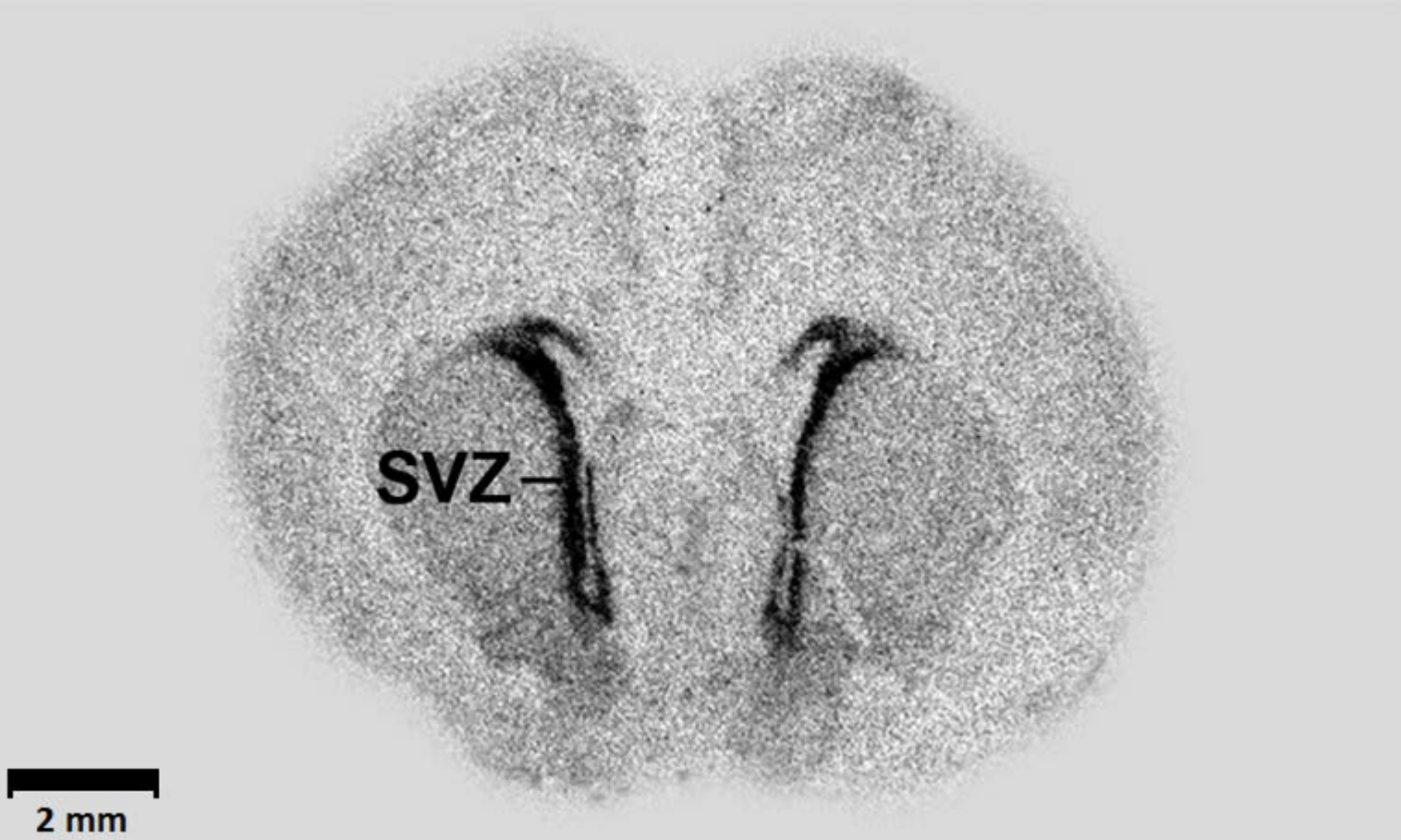
Subventricular zone



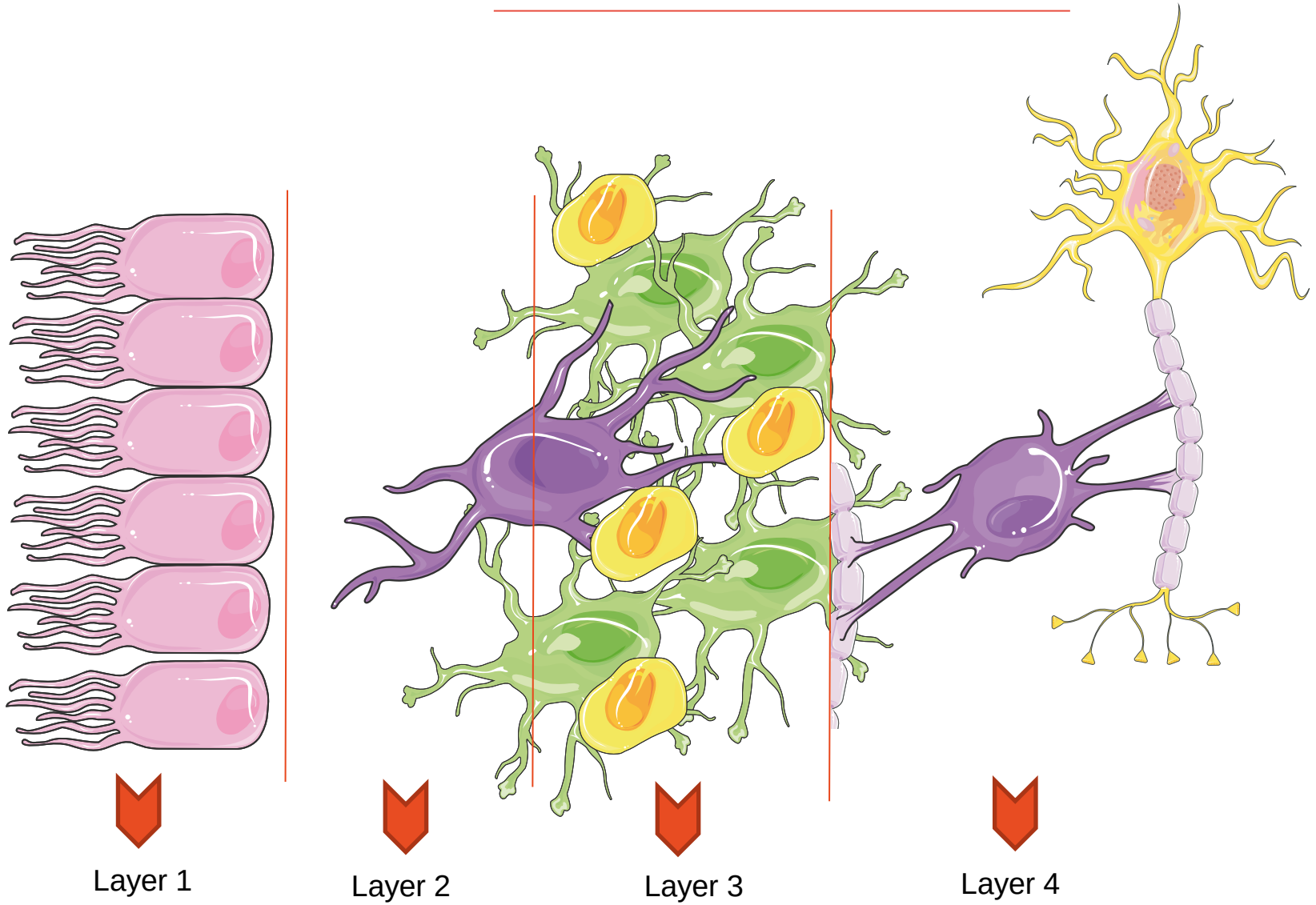




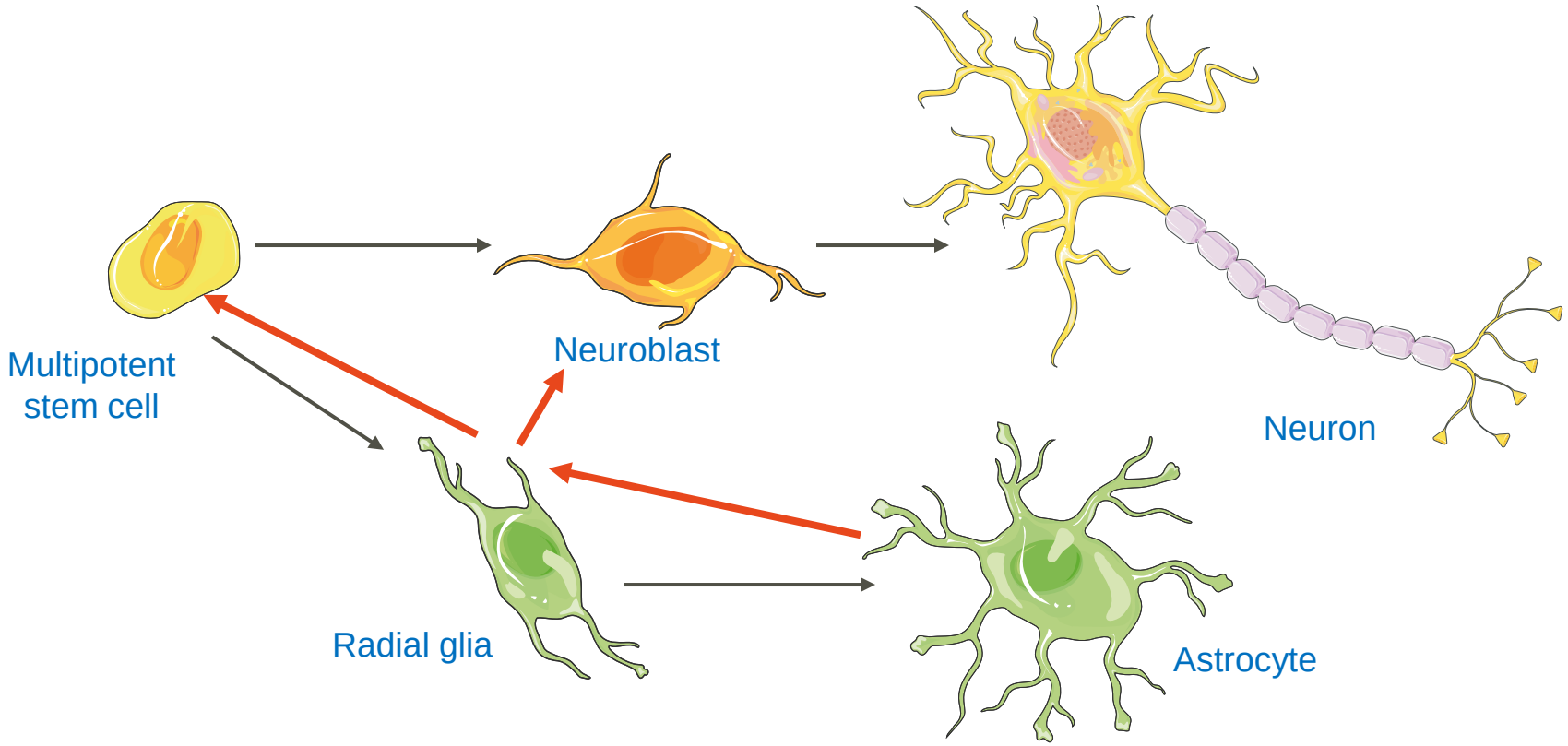
Mouse subventricular zone



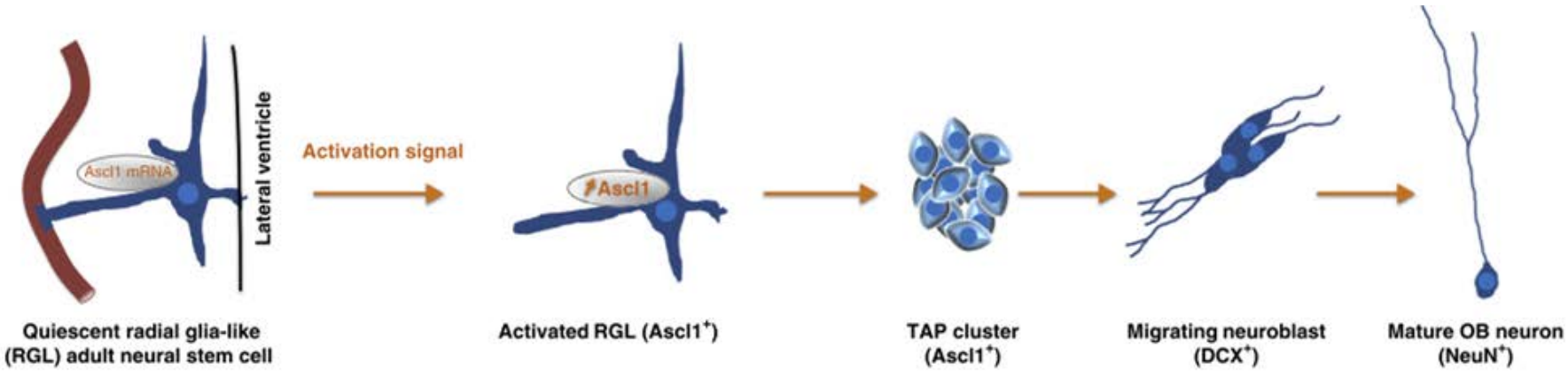
Subventricular zone cell layers

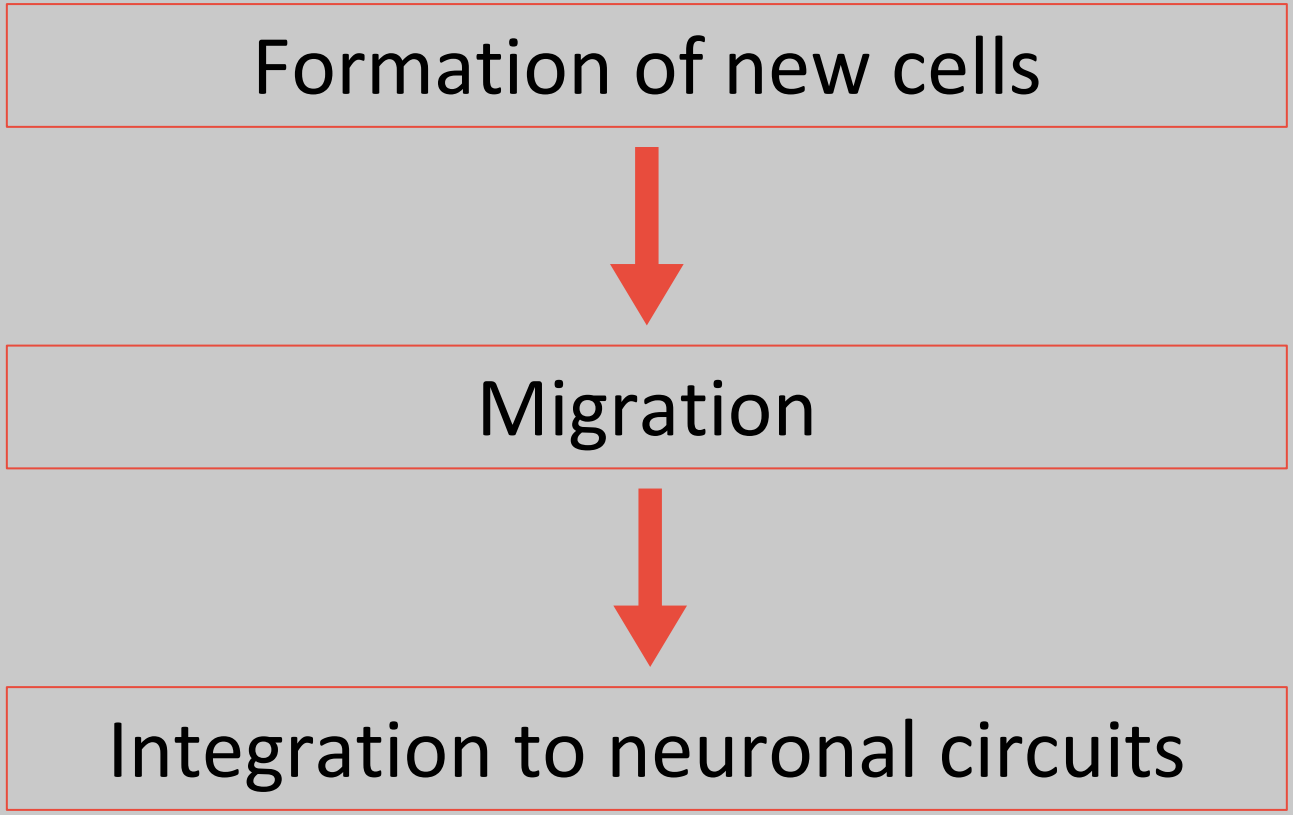


Possible way to recruit SVZ potential



Subventricular zone niche




Formation of new cells
Migration
Integration to neuronal circuits

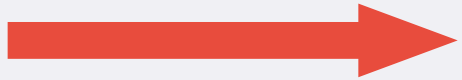
The nature of stroke induced cell proliferation

- Tumor necrosis factor(*Iosif et al 2008*)
- Indomethacin (*Hoehn et al. 2005*)
- Erythropoietin (*Wang et al. 2004, Tsai et al. 2006*)
- Exercise activity, Functional electrical stimulation (*Zhang et al. 2013 and Liu et al. 2013*)
- GDNF, BDNF, cerebrolysin, citicoline (*Kobayashi et al. 2006, Keiner et al. 2009, Zhang et al., 2010, Diederich et al. 2012*)

NEUROGENESIS-Phase1

The nature of stroke induced cell migration and maturation

- Chemokines, growth factors and metalloproteases (Robin et al., 2006)
- Differentiation of newborn cells into GABAergic, cholinergic neurons and also different type of interneurons (Hou et al., 2008, Marin et al., 2000)
- GFAP-expressing cell aggregates in the striatum (Yamashita et al., 2006)
- SVZ neuroblasts begin to express calretinin (Liu et al., 2009)

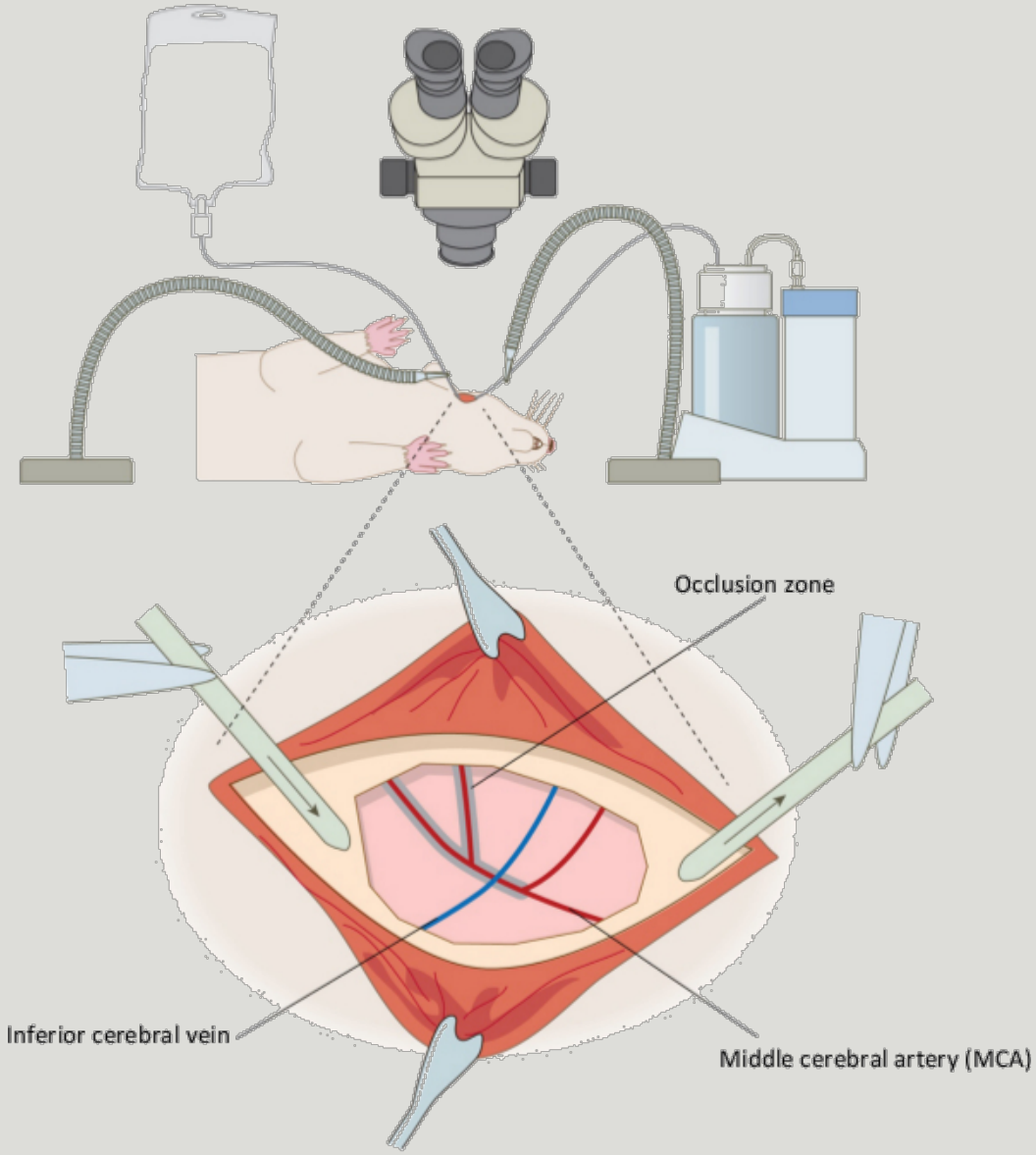


Neurogenesis – Phases 2,3

We propose that combined strategy of stimulation and neuroprotective drug delivery will enhance the capability of ischemia induced NSCs to migrate to damaged area and efficiently recruit in on-site neural circuits

1. Development of animal stroke model via DMCAO.
2. Recording of electrical activity in the ischemic and healthy brain tissue and data analysis
3. Multimodal strategy development to efficiently recruit activated NSCs.
4. Model as well as treatment effectiveness evaluation.

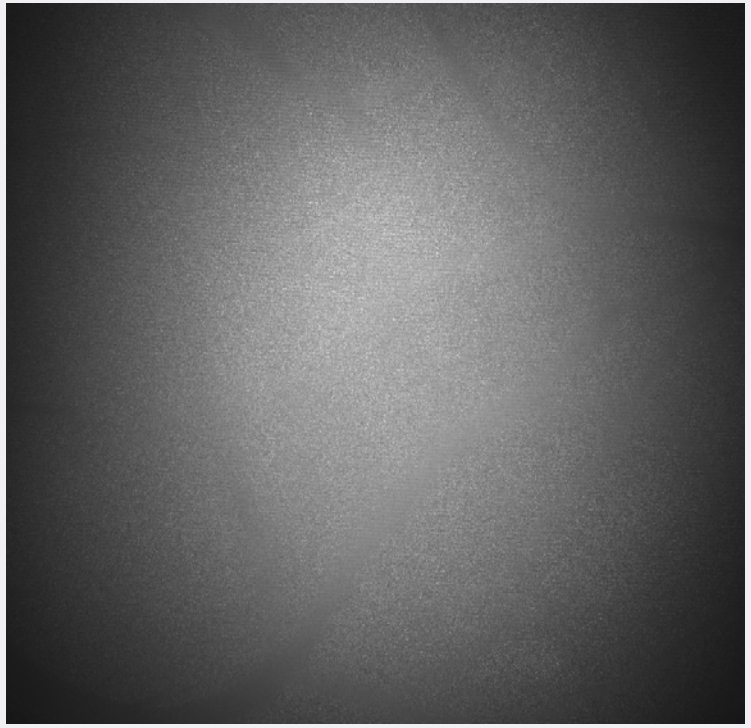
STROKE MODEL(d-MCAO)



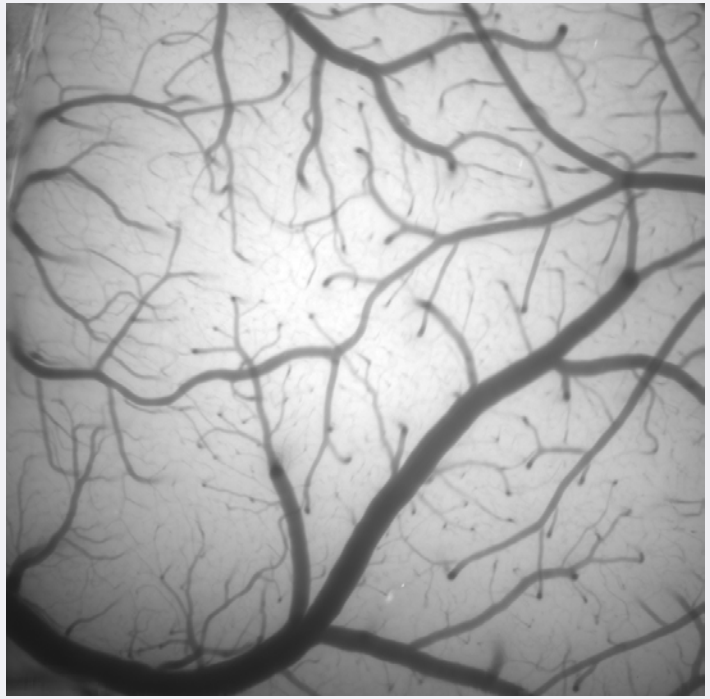
Speckle imaging

- Coherent scattering light forms speckles on rough surfaces
- If the rough surfaces moves the speckles get blurred and won't resolved by the camera anymore
- Quantification: determine the local contrast in each pixel: the more movement the lower the contrast in image

Speckle imaging



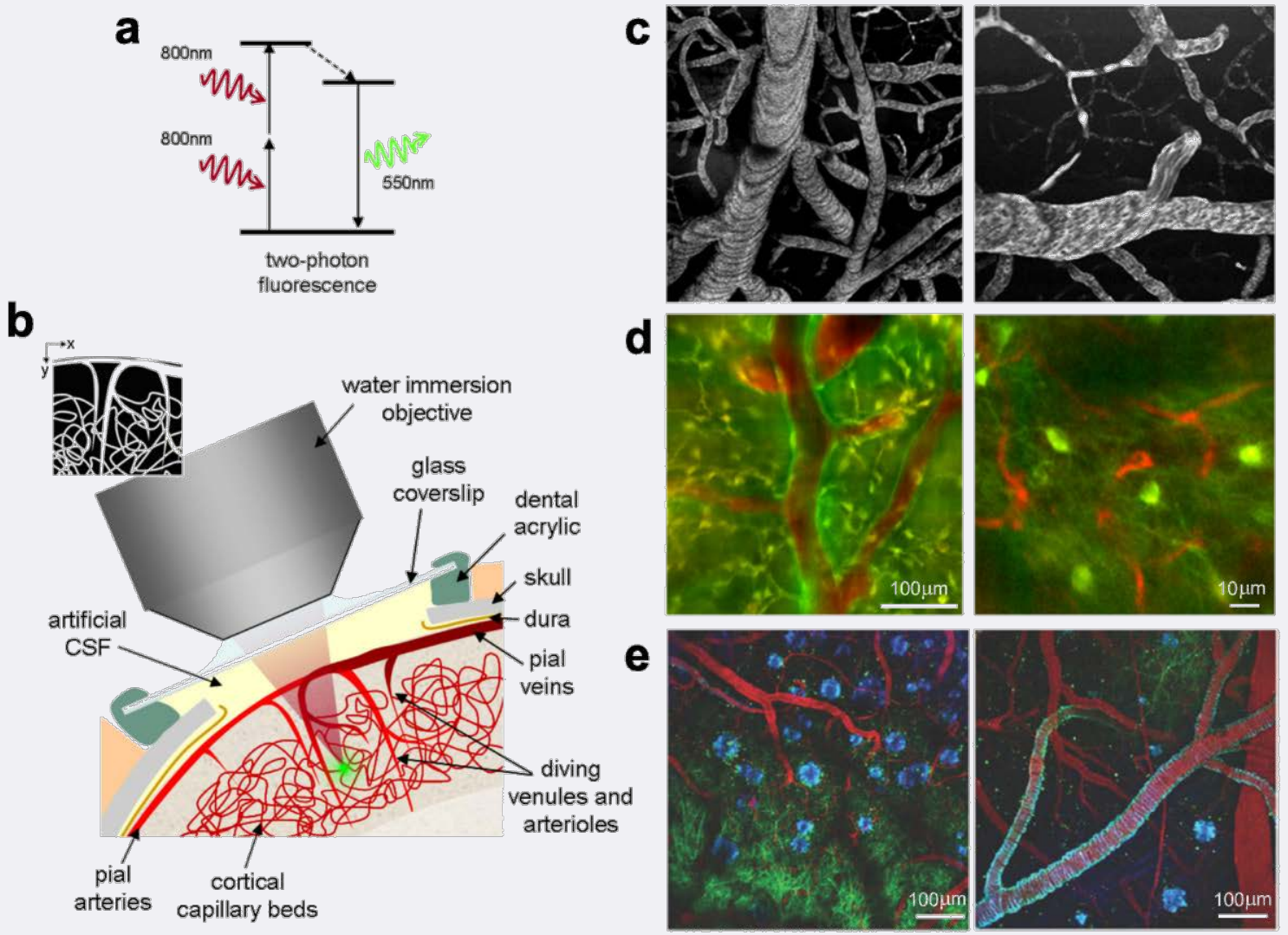
Laser Speckles:
Real time movie of laser light scattering in blood vessels.



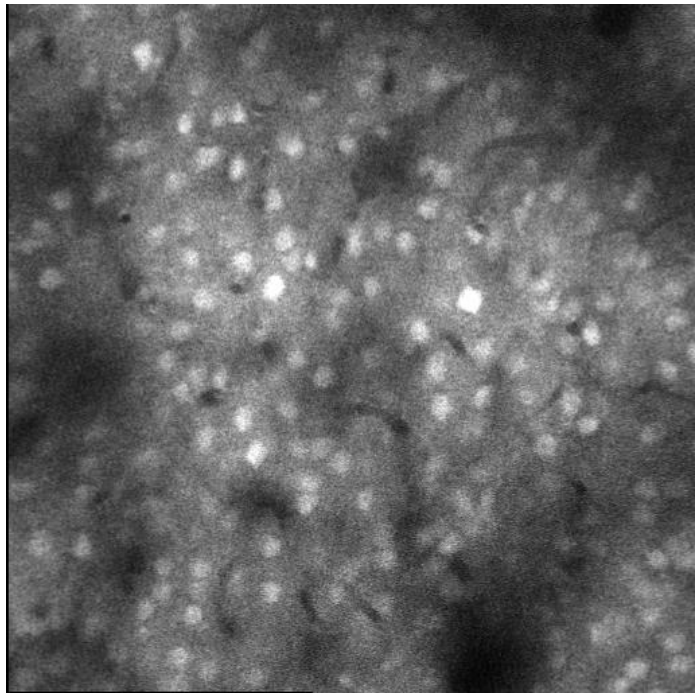
Vessel map
(light reflection)

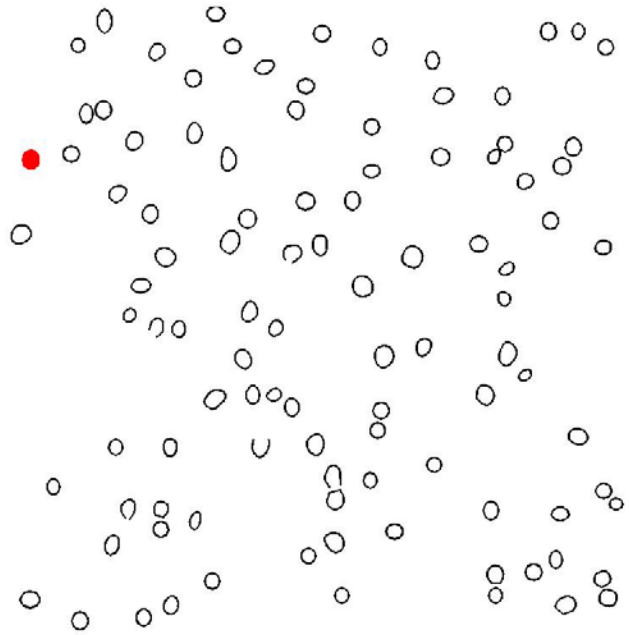
Laser Speckle Contrast
normalized pixel variance in light scattering

Two photon microscopy



Imaging neuronal activity in awake behaving mice





Miller et al, 2014

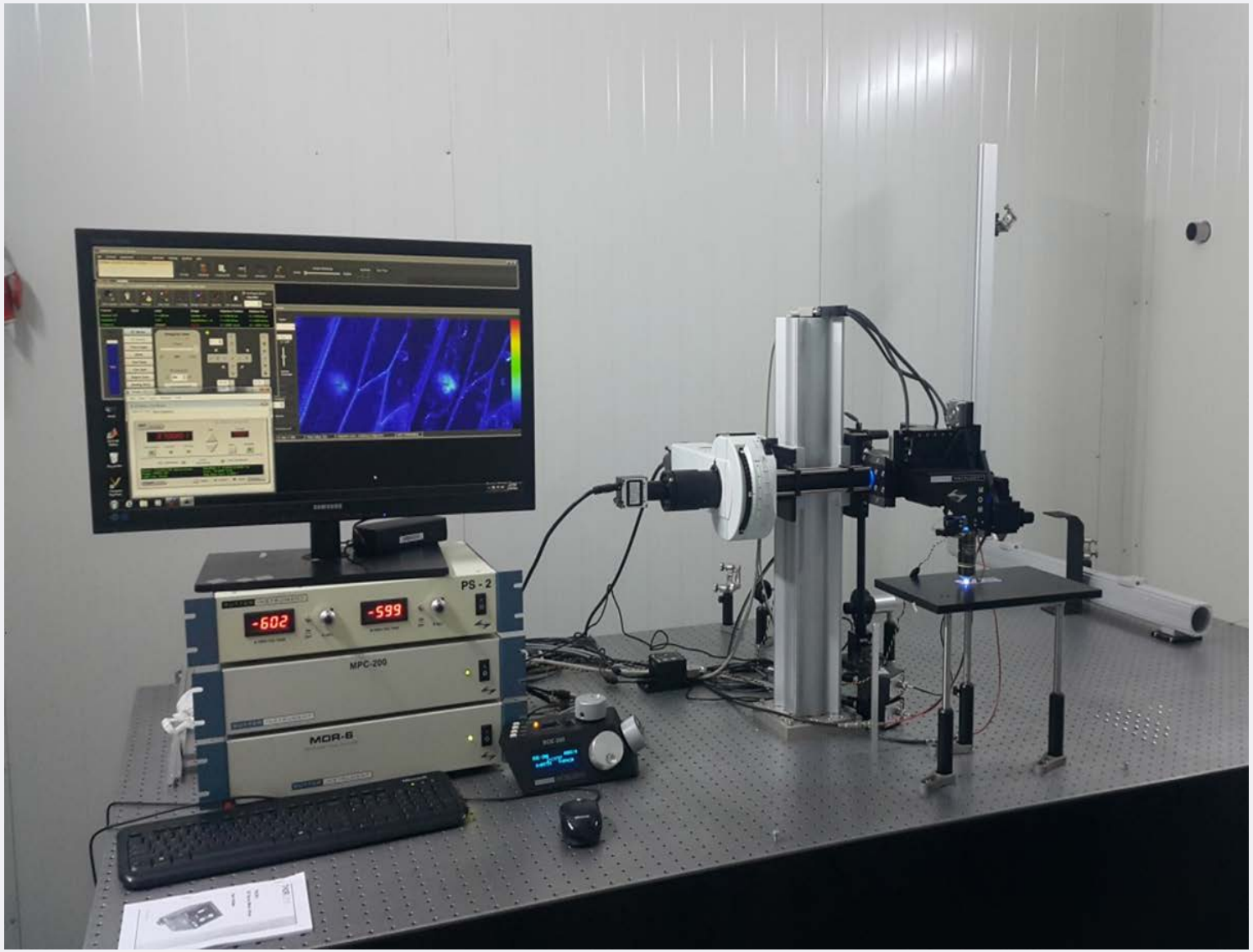
Our experiments

Our experiments

Future perspectives

- Two-photon Calcium sensor imaging implementation
- Vasculature density tracking in subacute and chronic phases of ischemic stroke
- Simultaneous two-photon optogenetics and two-photon imaging *in vivo*

Two-photon microscopy station of CANDLE SRI



Thank you!

We are open to any critique.