

# Network Physiology aspects of diabetic kidney disease

*Olga Sosnovtseva*  
*Associate Professor*

UNIVERSITY OF COPENHAGEN



**COMFORTING TRUTH**

# Drink or not drink

What is the reason most people dye during a marathon?

Should you drink 2-3 l of water per day?

Should I drink alkaline water to ensure right pH?

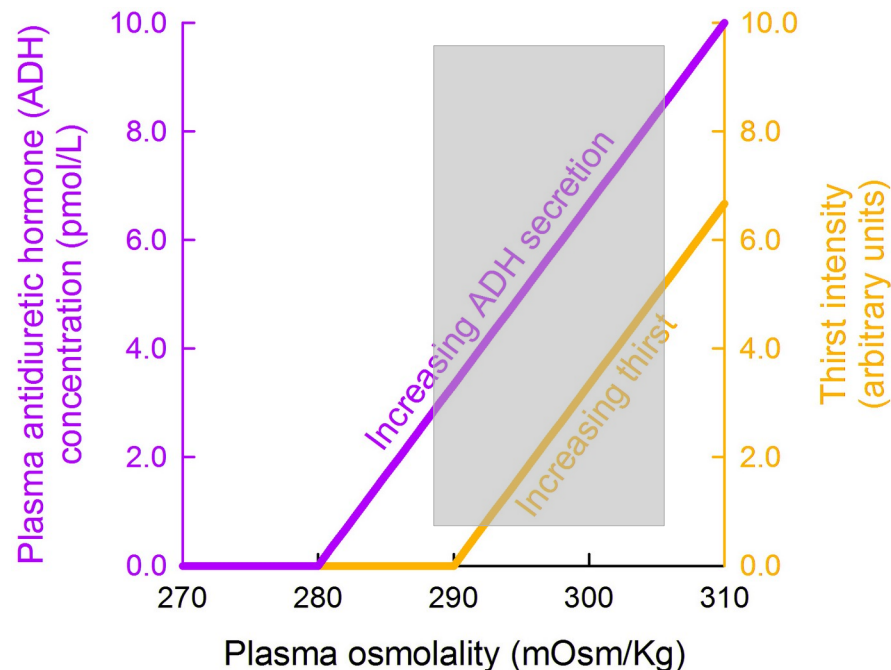
# Drink or not drink

## Daily problems

Decreased pressure/volume  
Water-salt imbalance  
Increased pressure  
Decreased blood oxygen

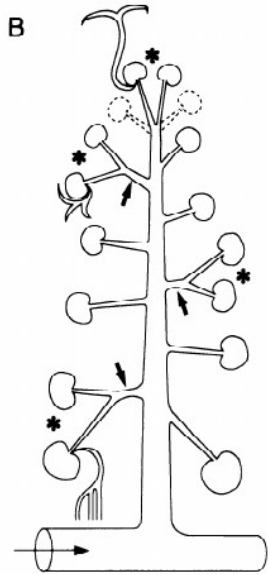
## Kidney provides solutions

Renin → Ang II and aldosterone  
Antidiuretic hormone  
Autoregulation  
Erythropoietin



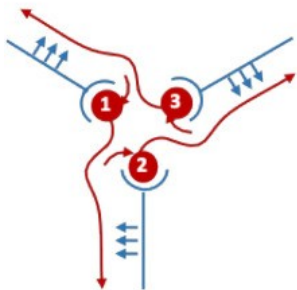
# **OPTIMAL VASCULAR DESIGN**

# Renal microcirculation

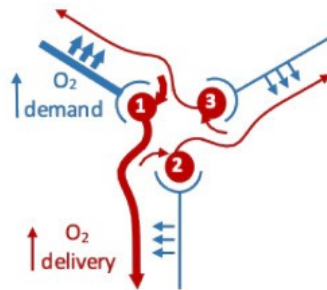


About 50% are organized as arteriolar pairs/triplets.  
This may enhance the efficiency of autoregulation and possibly renin production.

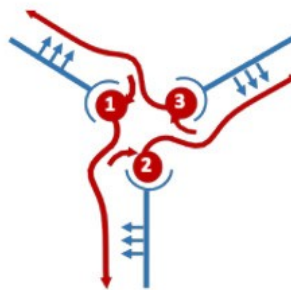
A Baseline conditions



B Flow/GFR not distributed, perfusion/O<sub>2</sub> mismatch in nephron 1



C Flow/GFR distributed, perfusion/O<sub>2</sub> match in all nephrons

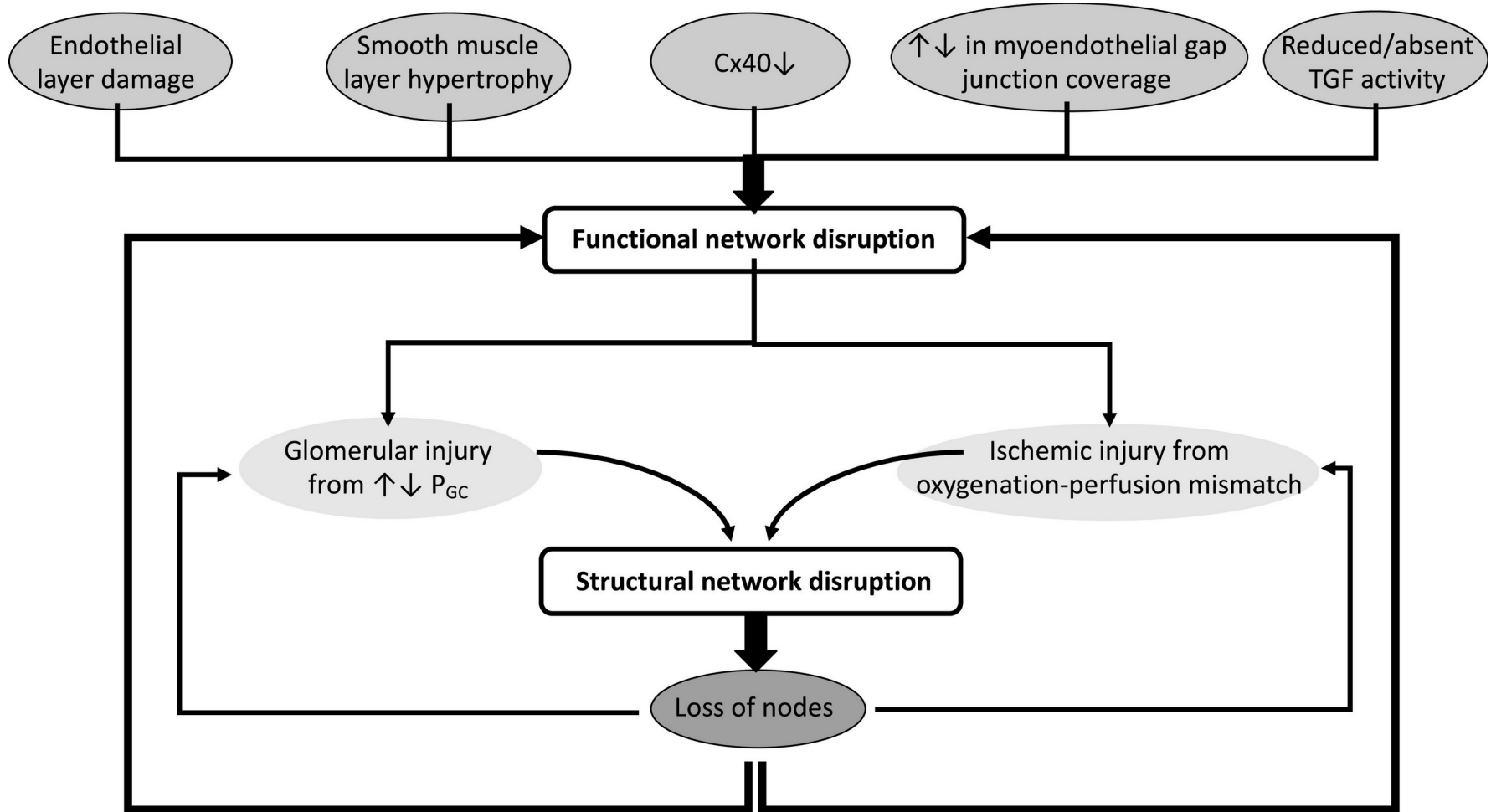


Post-glomerular blood flow from 90 % of glomeruli perfuse other nephrons, not the same nephron?

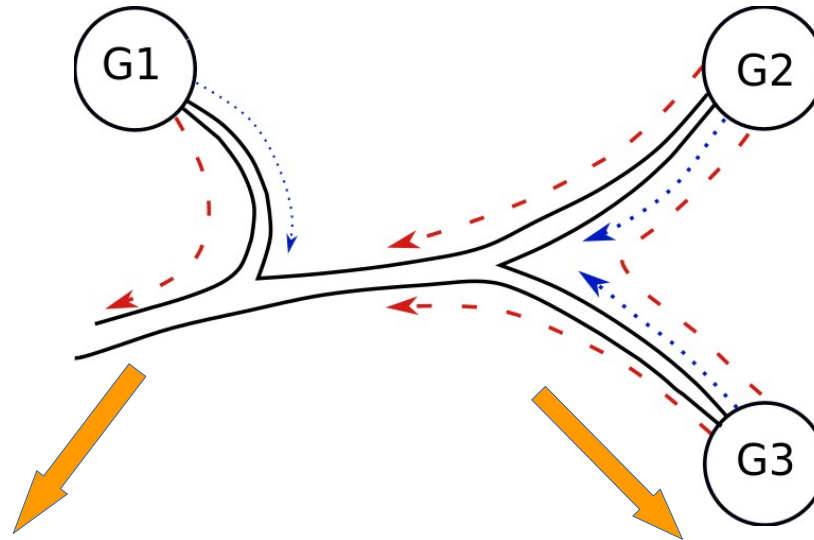
D. Caselas, Am. J. Physiol. 267 1994

T. Zehra et al. JASN 32: 1293–1304 , 2021

# Structure vs function



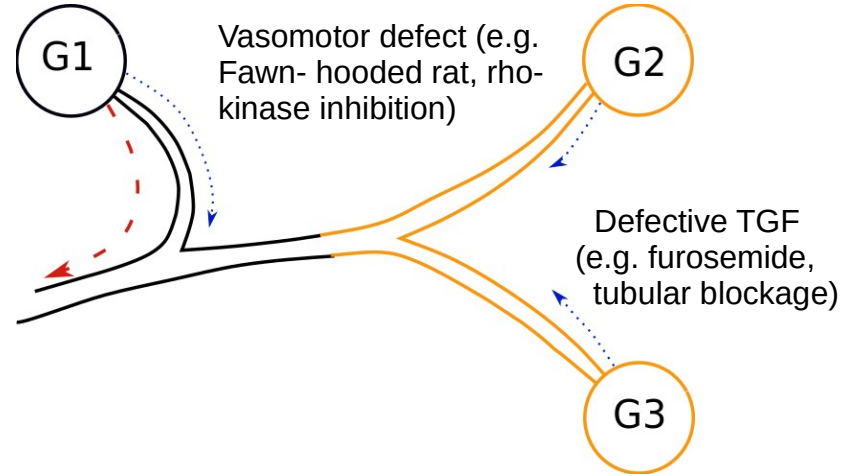
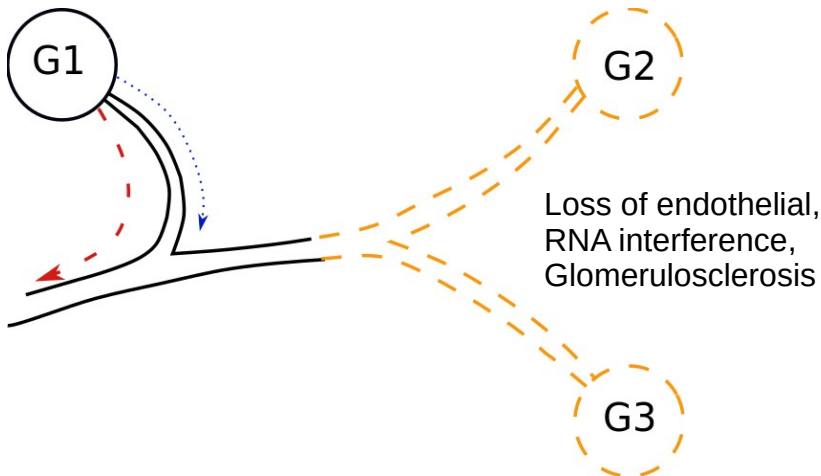
# Disruption of microcirculation



Anatomical lesion of glomerulus, afferent arteriole, or cortical radial artery

No interaction

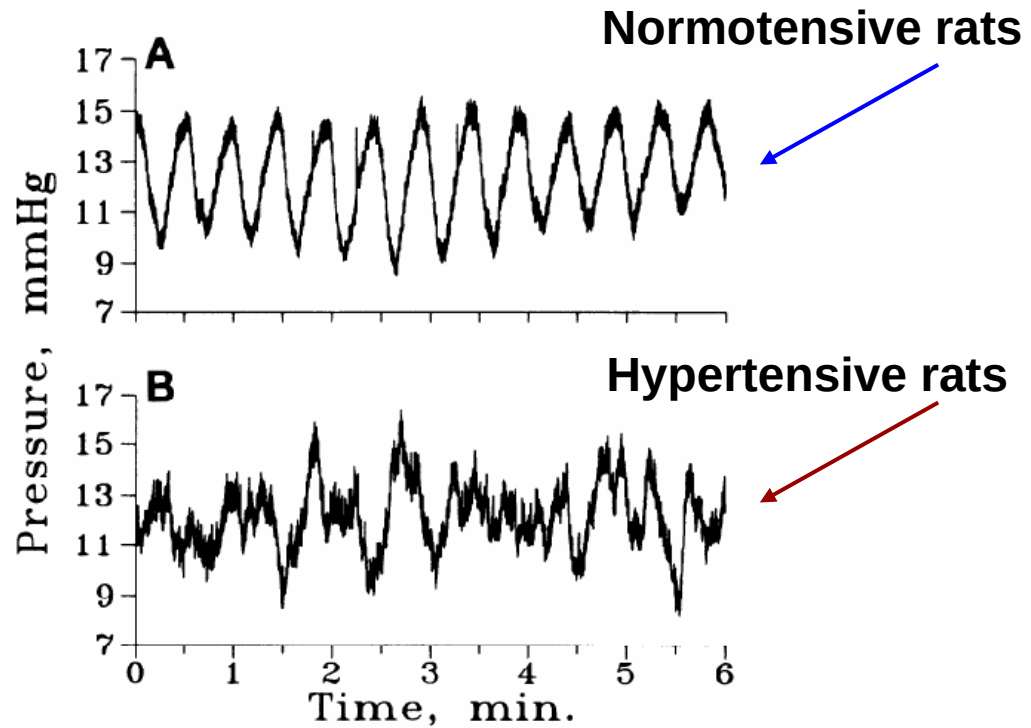
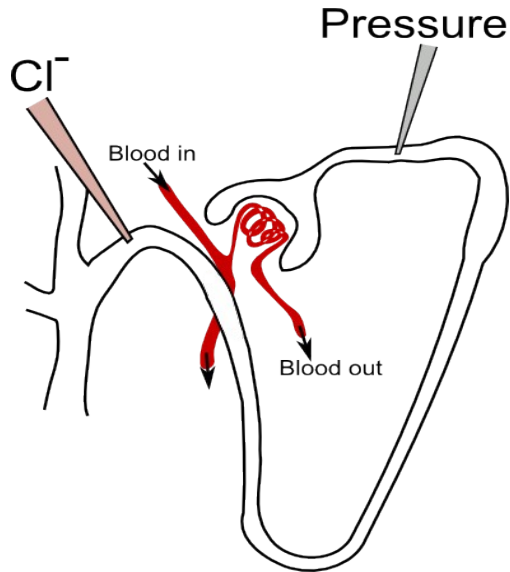
Functional disruption of TGF, myogenic mechanism or afferent arteriole





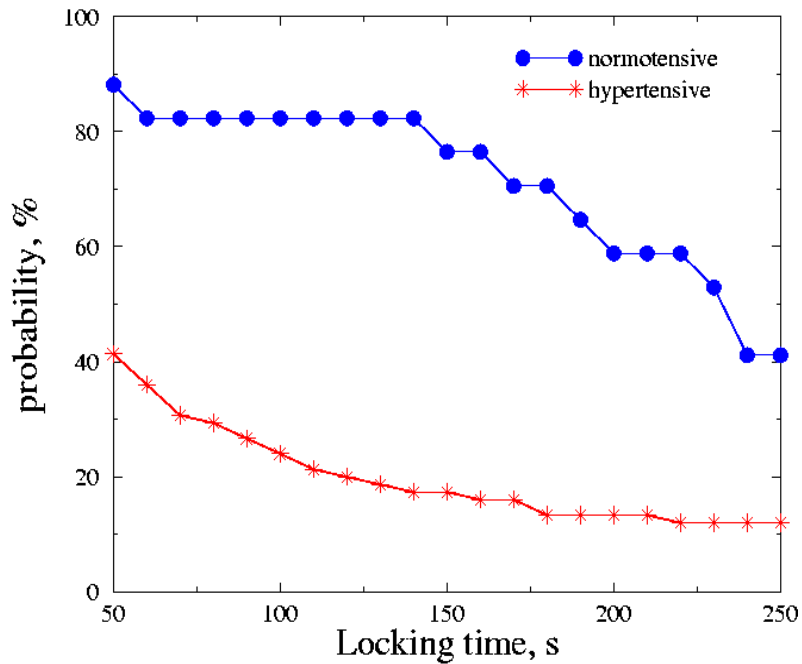
# **KIDNEY WONDERLAND**

# Chronical hypertension

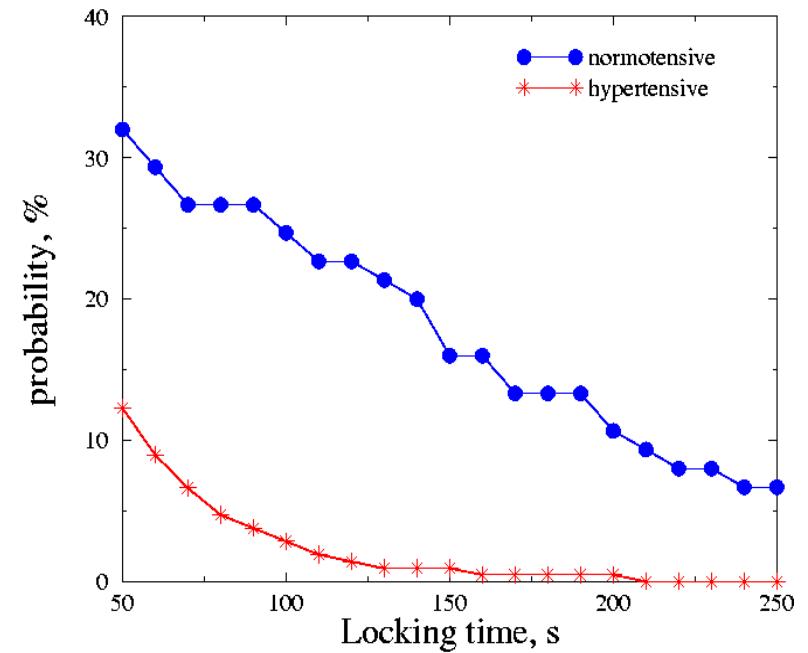


# Chronical hypertension

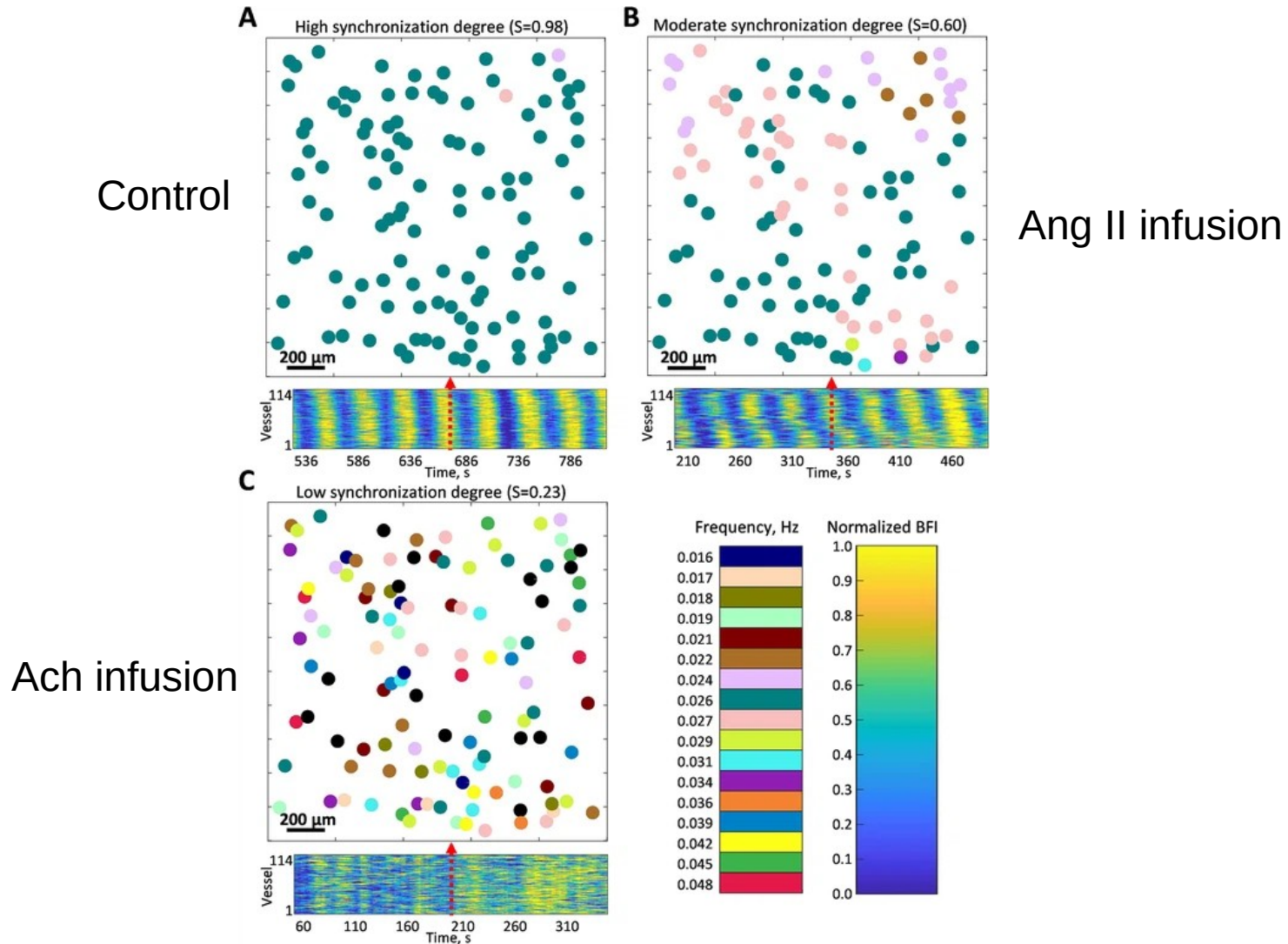
## Slow TGF dynamics



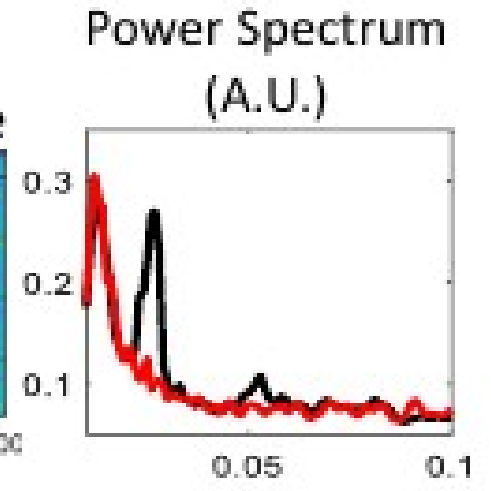
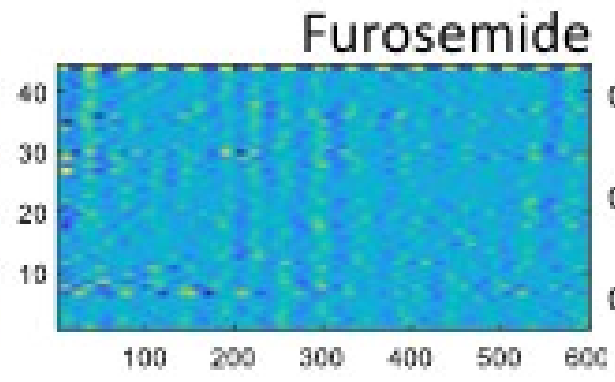
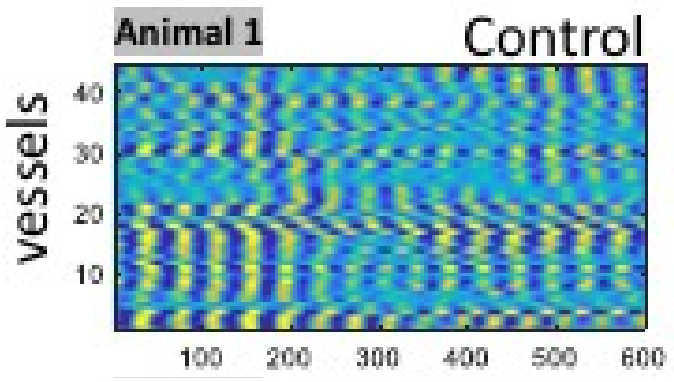
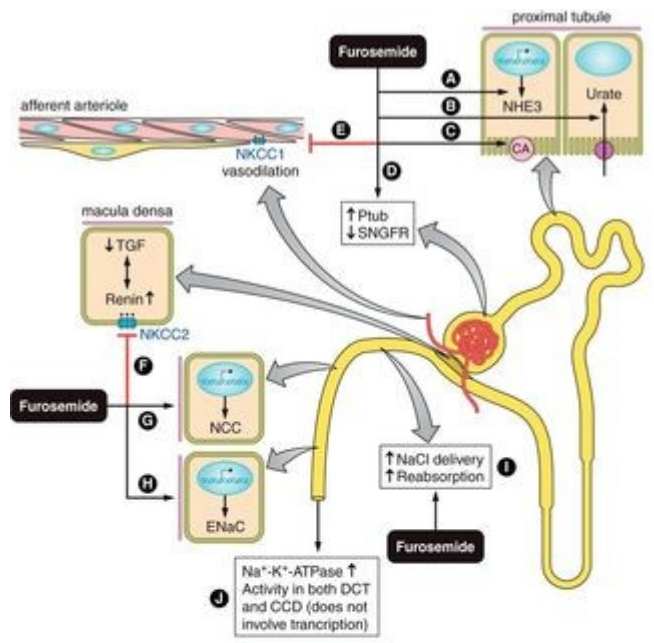
## Fast myogenic dynamics



# Acute hypertension

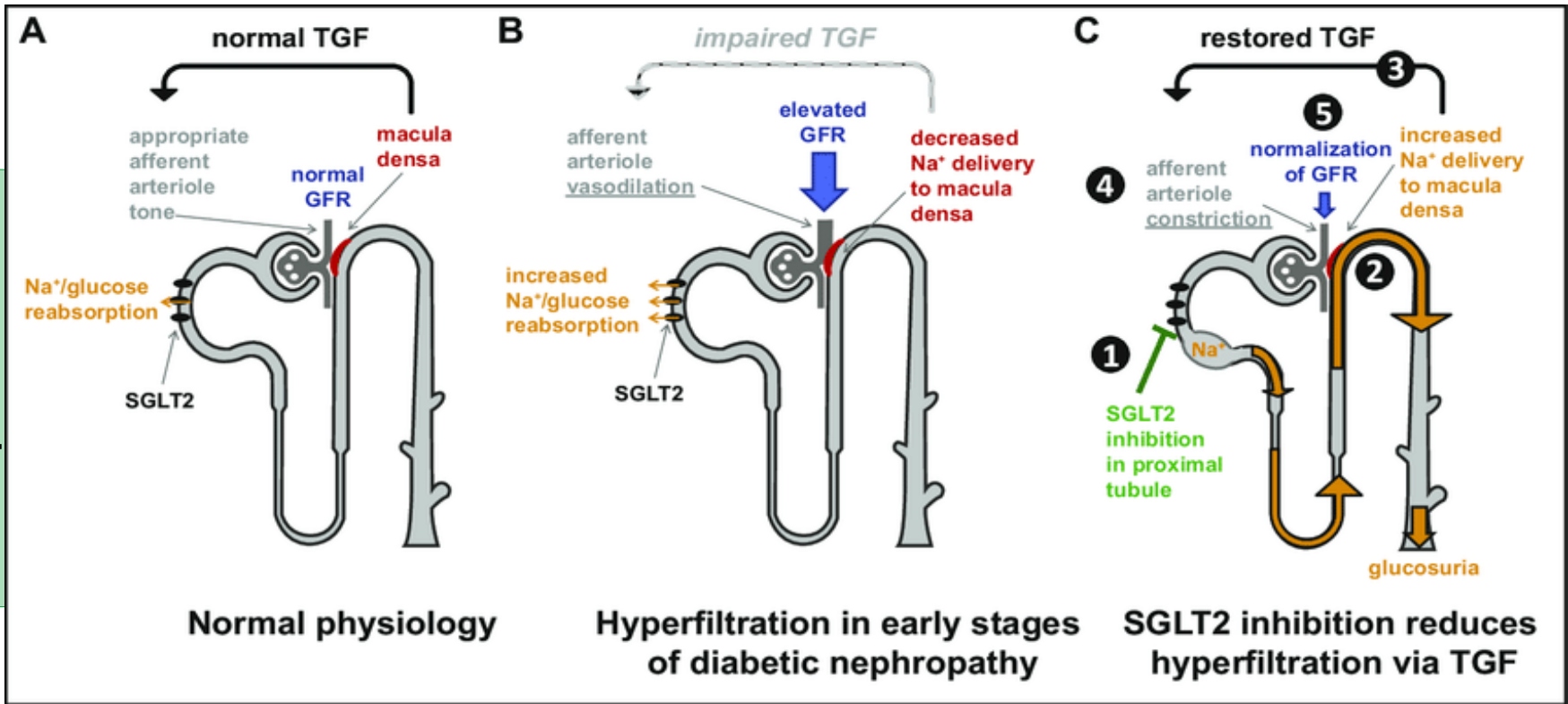


# Na/K/2Cl transporters blockade

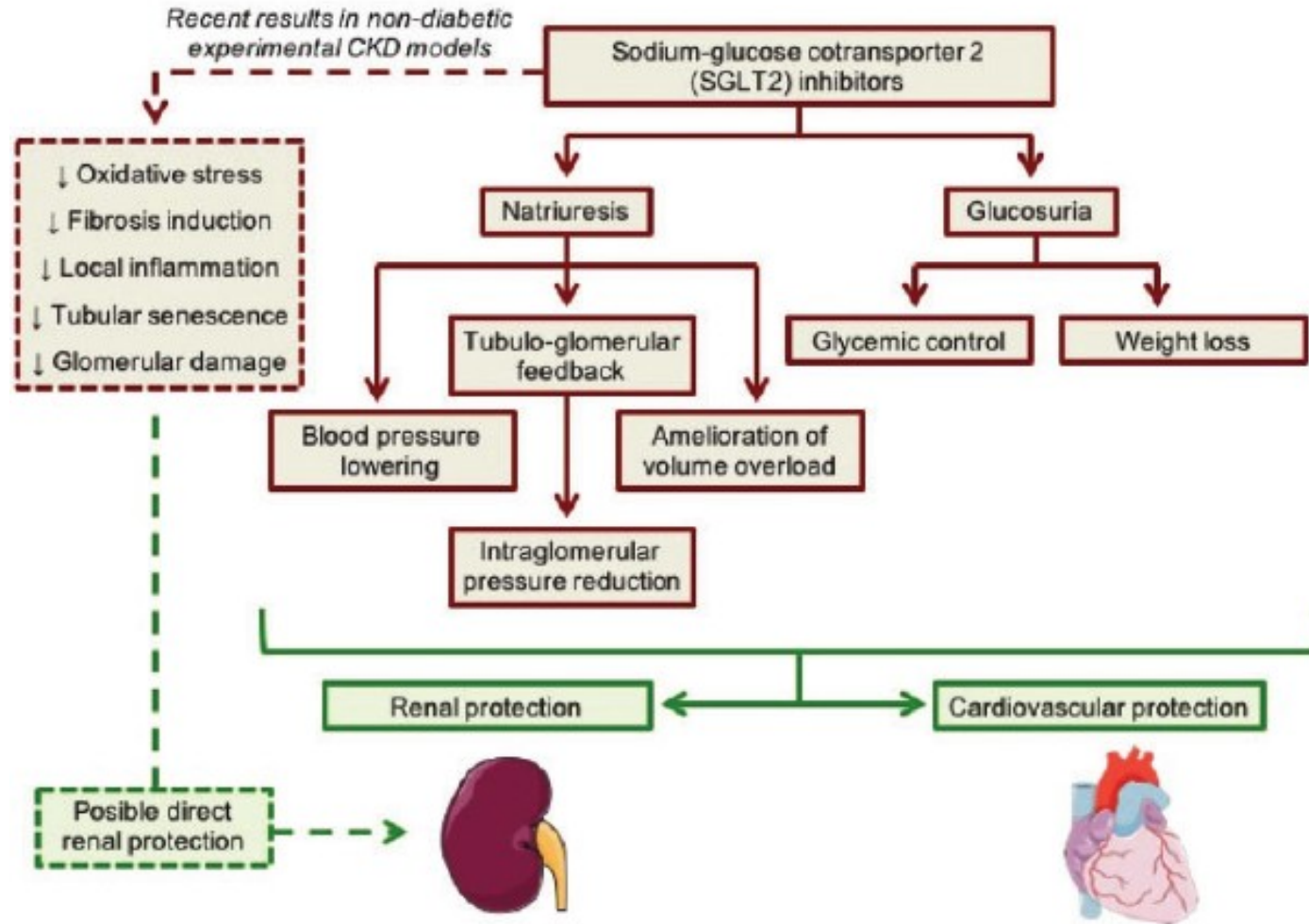


# Diabetic nephropathy

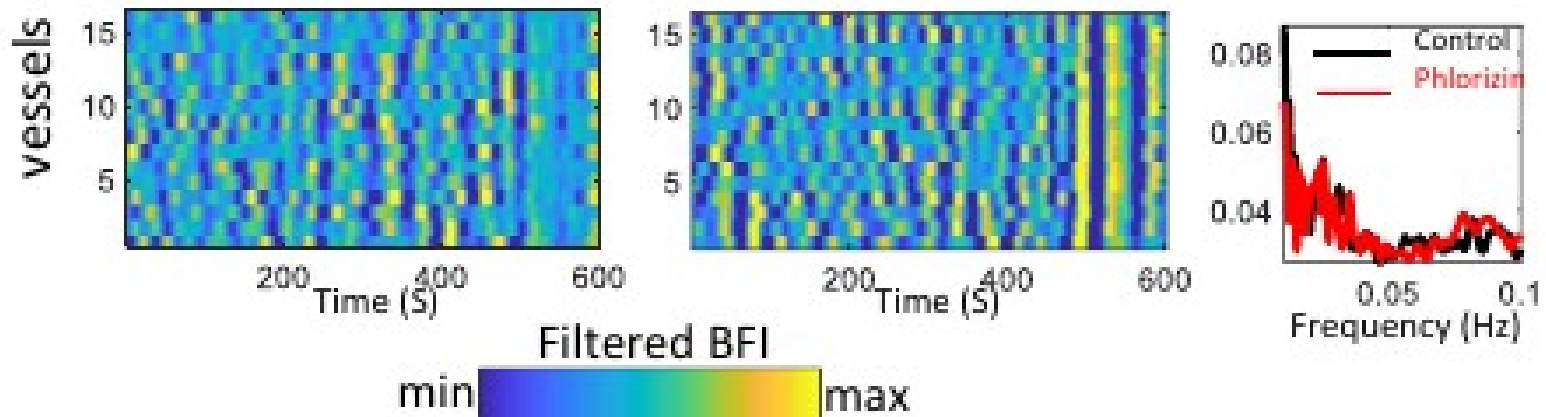
Renoprotection



# Renoprotection

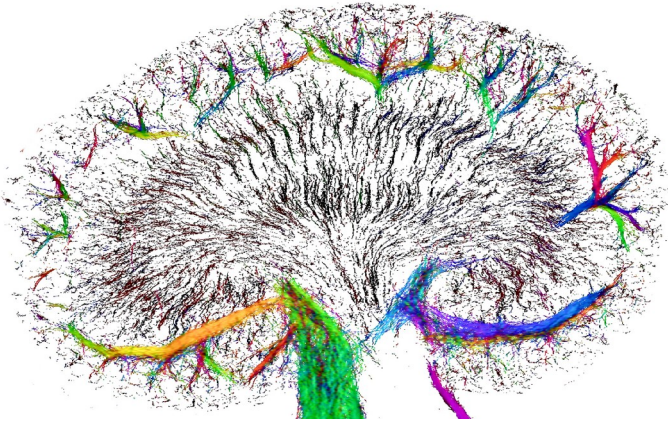


# SGLT transporters blockade





# Open questions



- **What is the microvascular effect of SGLT2 inhibitors with impaired and strong TGF?**
- **Does cooperative dynamics of all nephrons play a renoprotective role?**
- **What are the new targets to slow down diabetic nephropathy?**