Kidney function:
An interplay between structural network topology and network dynamics

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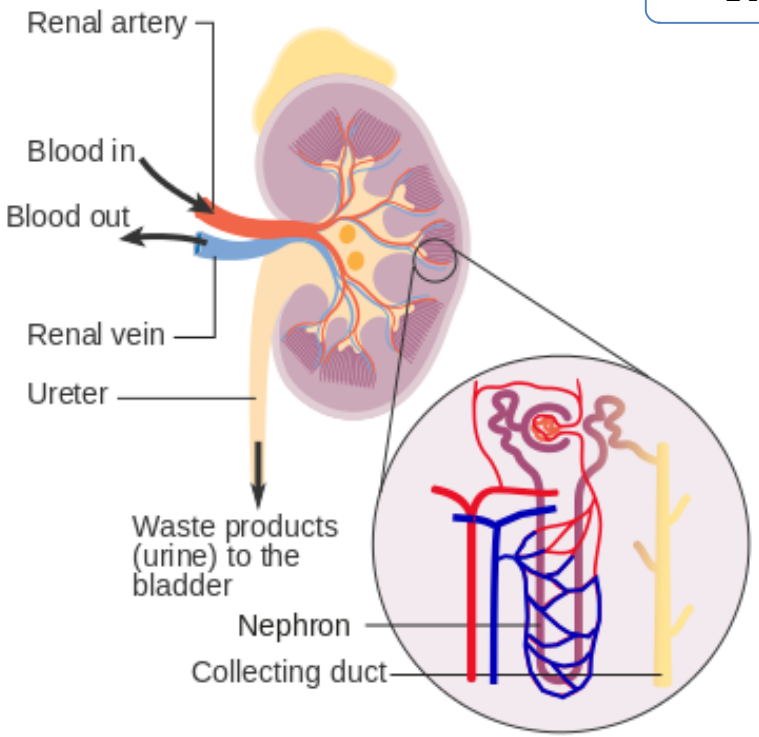
Associate Professor

Kidney function

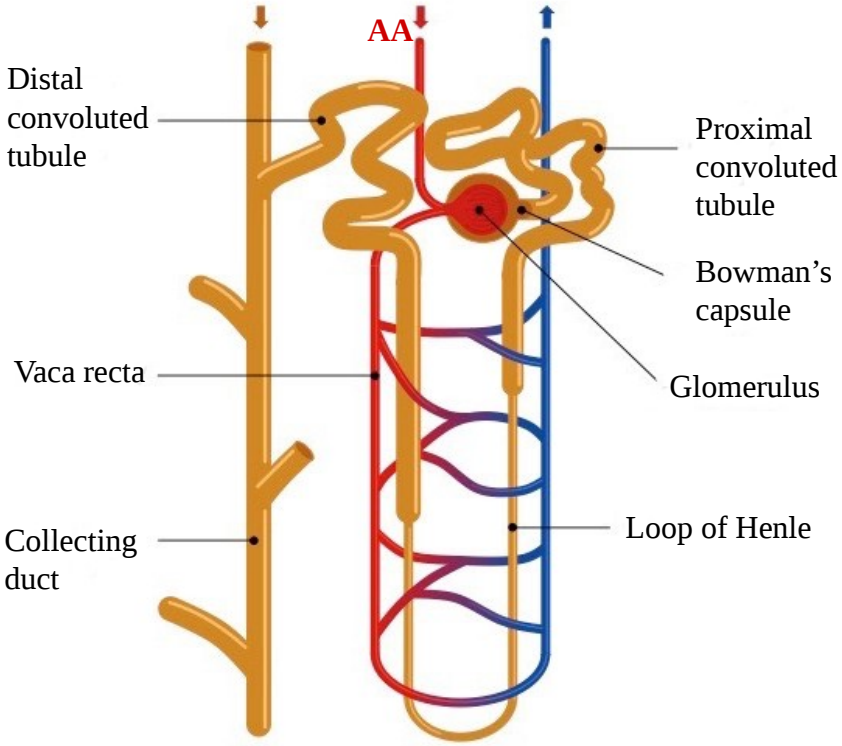


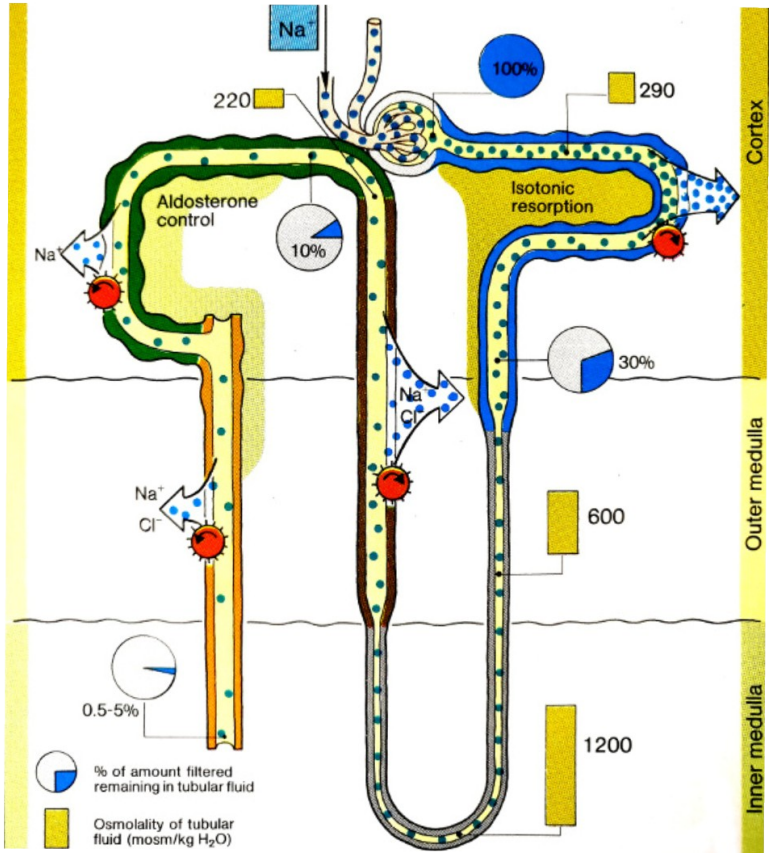
- Regulation of water and electrolyte balance
- Excretion of metabolic products
- Secretion of hormones
- Regulation of arterial pressure

Nearly 500 million people globally (which nearly 10% of global adult population) suffer from some kind of kidney problem/damage.

Modified original image released as part of an open knowledge project by Cancer Research UK http://www.cancerresearchuk.org/ and Wikimedia Commons https://commons.wikimedia.org/

Nephron function





The kidney contains 1 million nephrons

Two mechanisms of autoregulation: myogenic and tubuloglomerular feedback

Color atlas of physiology, Thieme, 1991

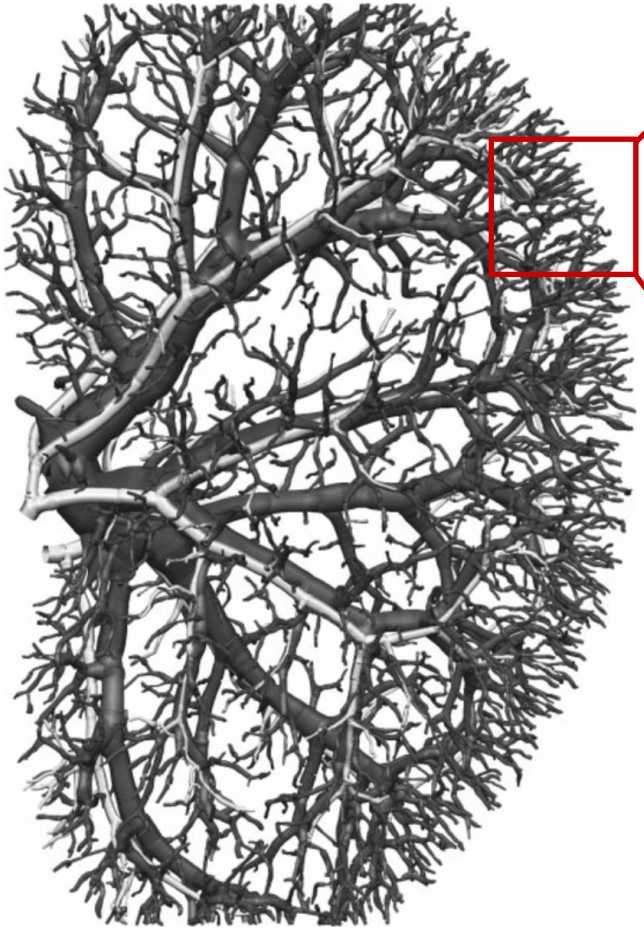
Kidney in numbers

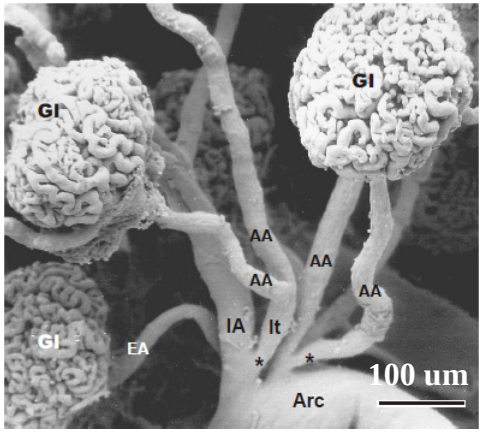
For a healthy person weighing 70 kg, the blood volume is 5 L (the cardiac output at rest is about 5 L/min). The kidneys receive 20% of cardiac output. Blood consists of 60% of plasma and 40% of hematocrit. The kidneys filter 20% of plasma. The kidneys reabsorb and redistribute 99% of the plasma volume and only 1% of the blood filtered becomes urine.

Calculate:

- How much blood do the kidneys receive per minute?
- How much plasma is filtered per minute?
- How much plasma is filtered per day?
- How many times blood volume is filtered by the kidneys a day?
- How much urine is formed per day?

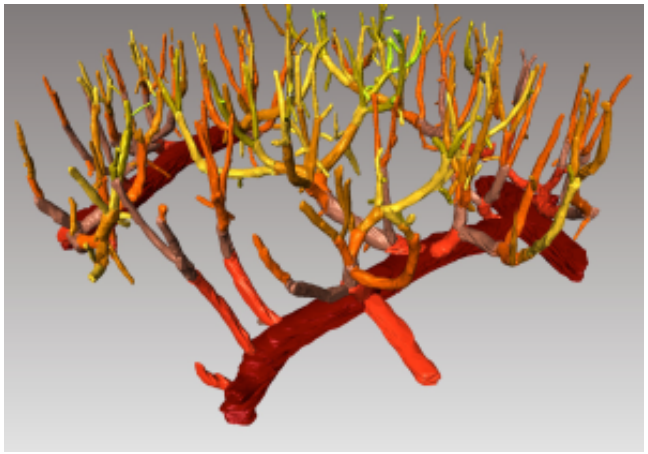
Renal vascular tree

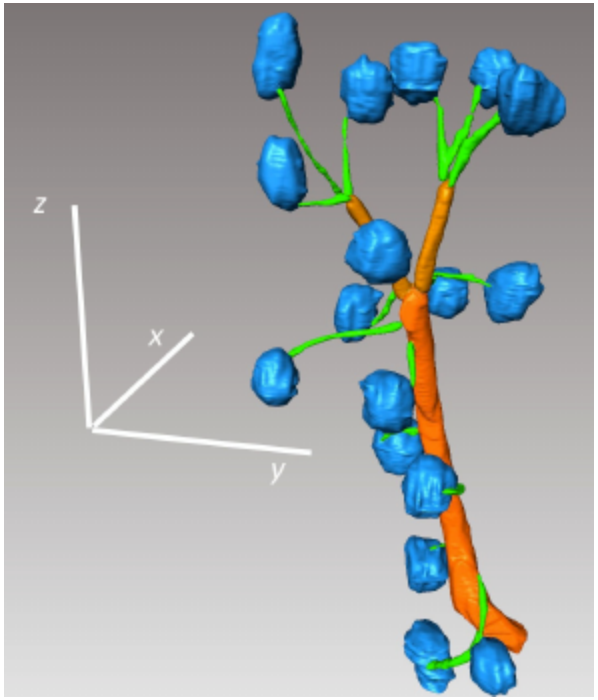


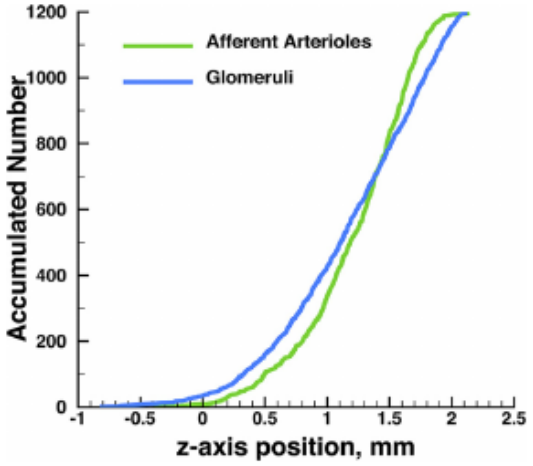


Nordsletten et al, Am. J. Physiol. 291, 2006
Vodenicharov, Bulg. J. Vet. Med. 10, 2007

Renal vascular tree







7th Order
6th Order
5th Order
4th Order
3rd Order
2nd Order
1st Order
Arcuate Artery

Marsh et al. Am J Physiol. 313, 2017

Renal vascular tree

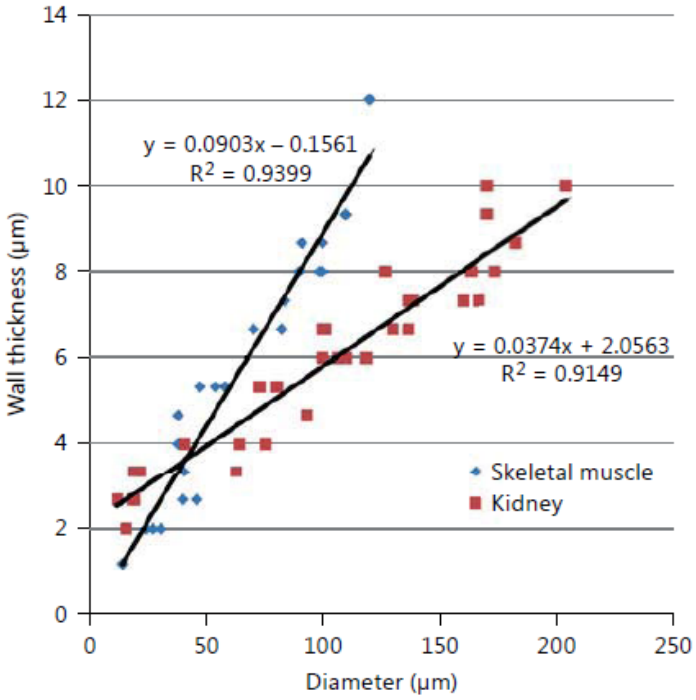


Table 2. *Length of terminal arteries at the top of the arterial tree and the number of afferent arterioles they form*

Branch Order No.	No. of Arteries	Avg Length, µm	No. of Afferent Arterioles	Afferent Arterioles/Artery
2	3	662 ± 195	24	8.0
3	25	517 ± 288	127	5.1
4	41	427 ± 250	176	4.3
5	37	352 ± 189	146	3.9
6	31	277 ± 203	125	4.0
7	10	168 ± 126	31	3.1

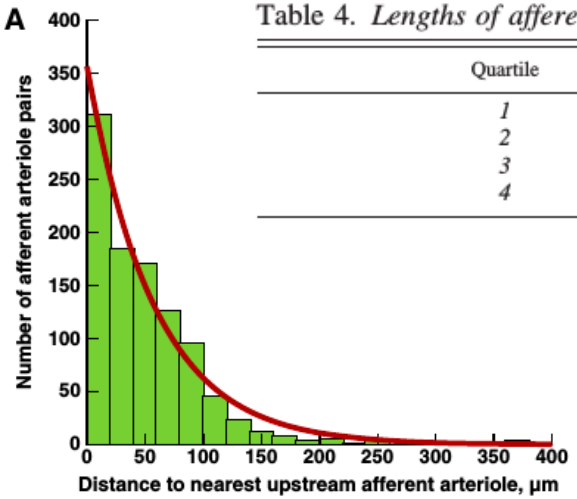
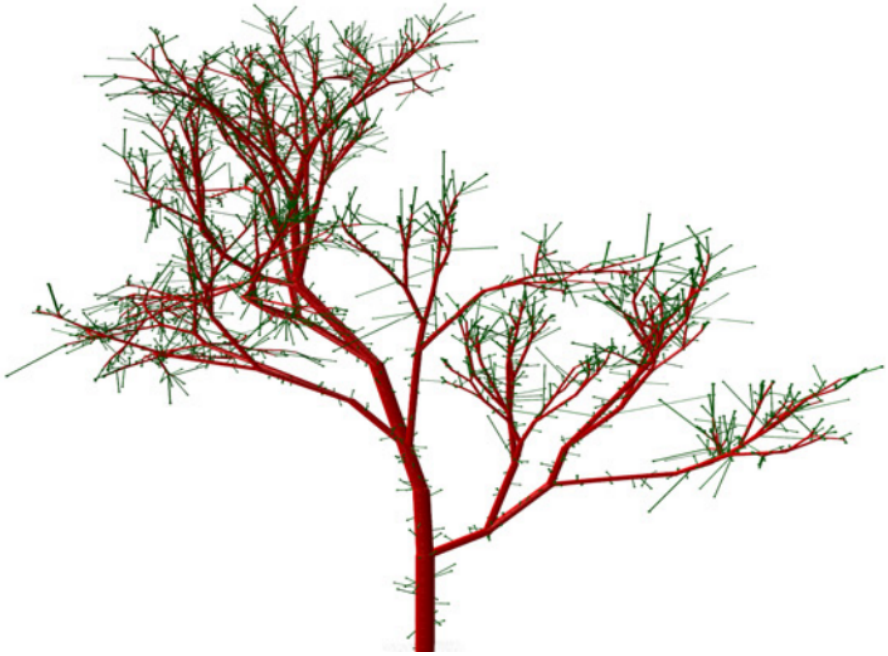


Table 4. *Lengths of afferent arterioles*

Quartile	Length, µm
1	232 ± 123
2	168 ± 75
3	172 ± 85
4	183 ± 80

Marsh et al. Am J Physiol. 313, 2017
Postnov et al. PLoS Comput. Biol. 2016

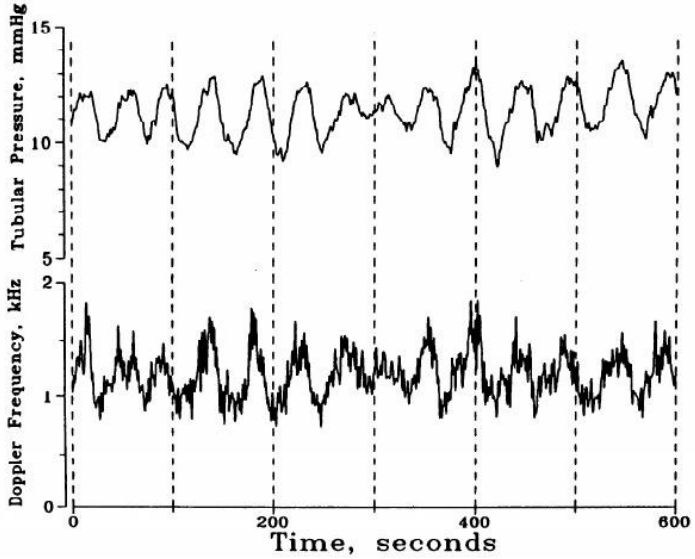
How can autoregulation work in such irregular environment?

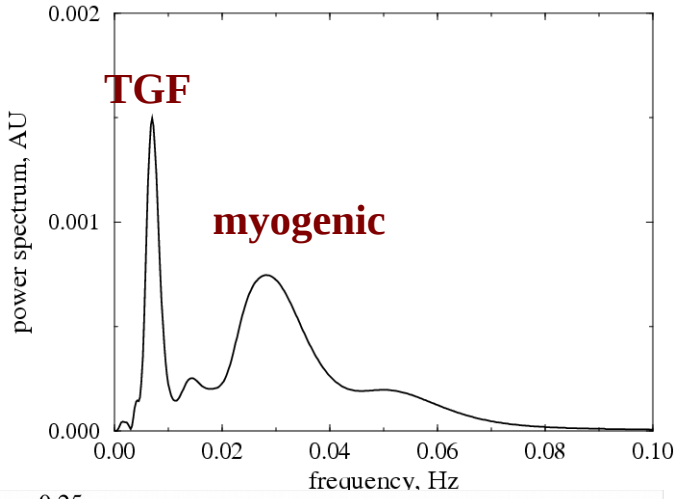


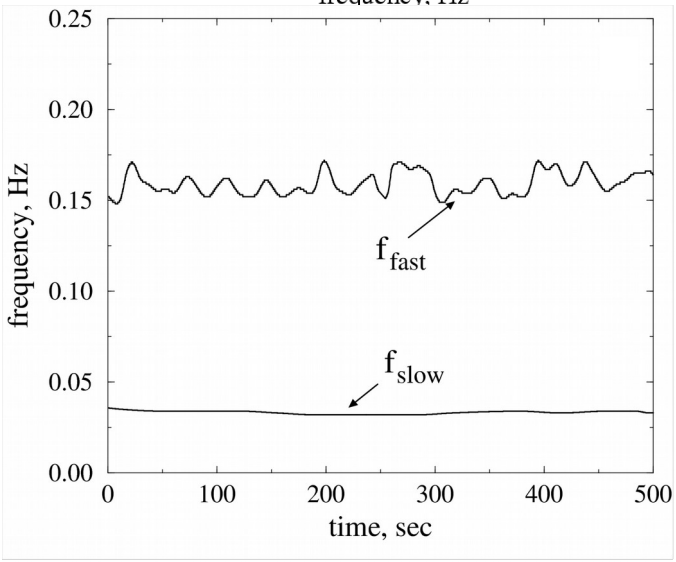
- How can the kidney achieve homogeneous perfusion despite being regulated locally at the most distal site in a highly variable arterial tree?
- What are the means of communication if post-glomerular blood flow from 90 % of glomeruli perfuse other nephrons, not the nephron from the same glomerulus?
- How can each nephron maintain the same pressure when branching is so irregular?

Nephrons need to operate in larger groups!

Oscillations

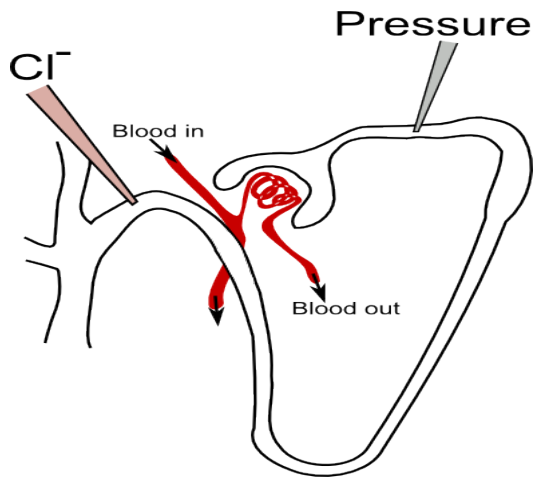


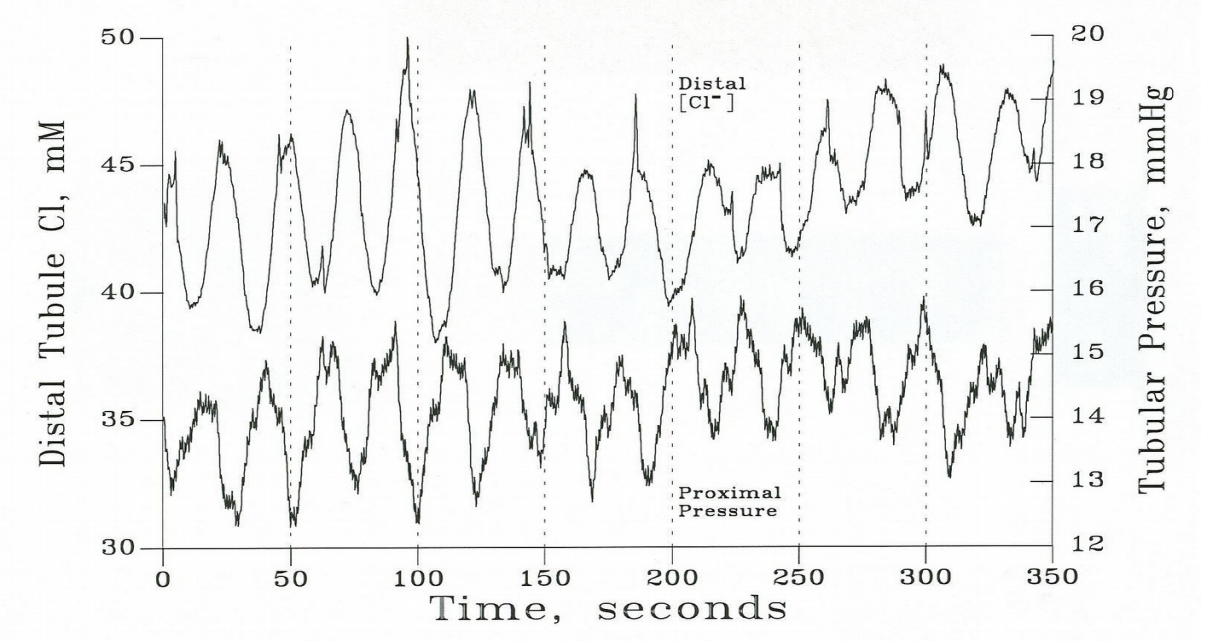




K.-P. Yip et al, Am. J. Physiol. 264, 1993

Oscillations

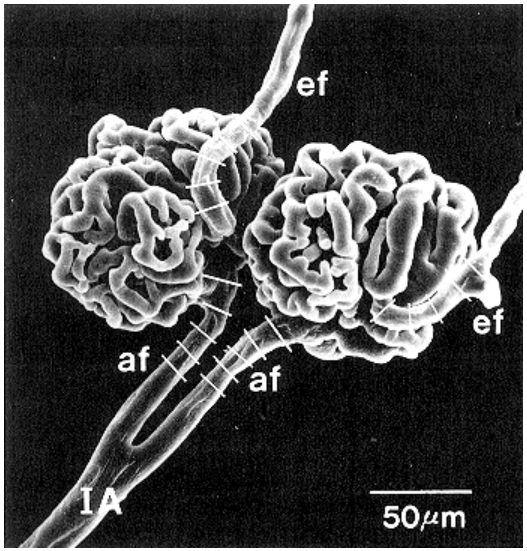


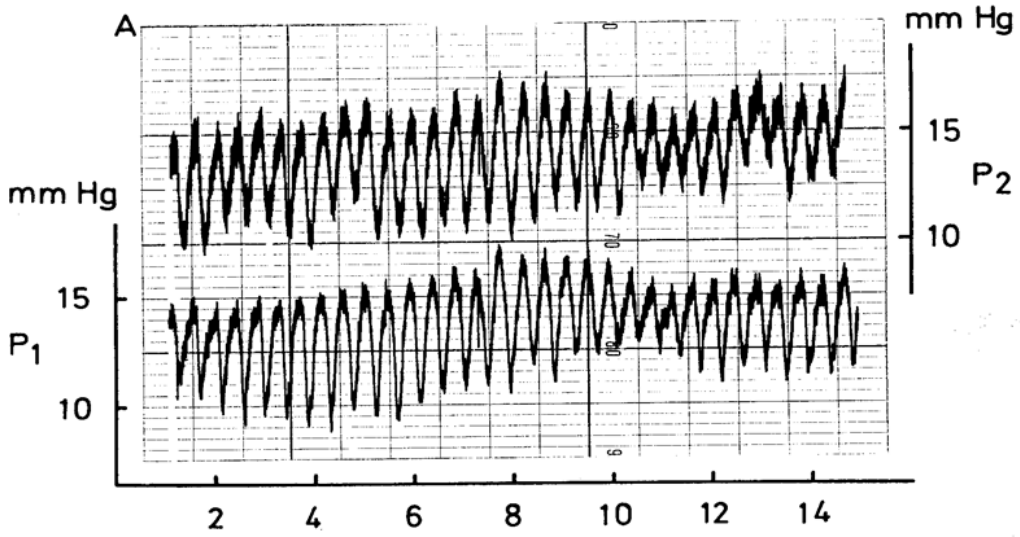


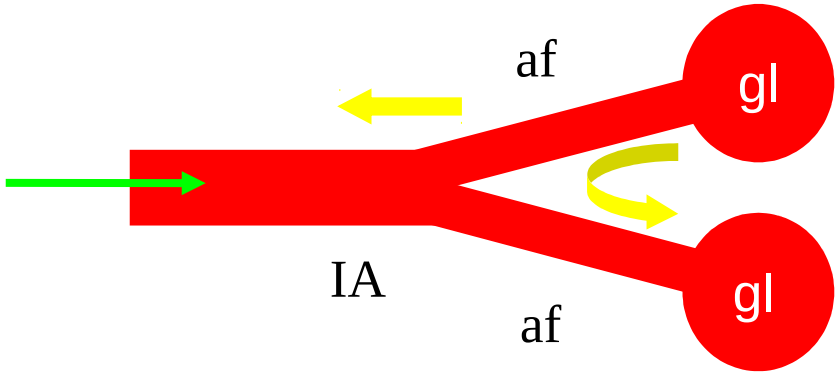
- Regular self-sustained oscillations in normotensive rats
- Highly irregular oscillations in hypertensive rats

Holstein-Rathlou, Am. J. Physiol. 256, 1989

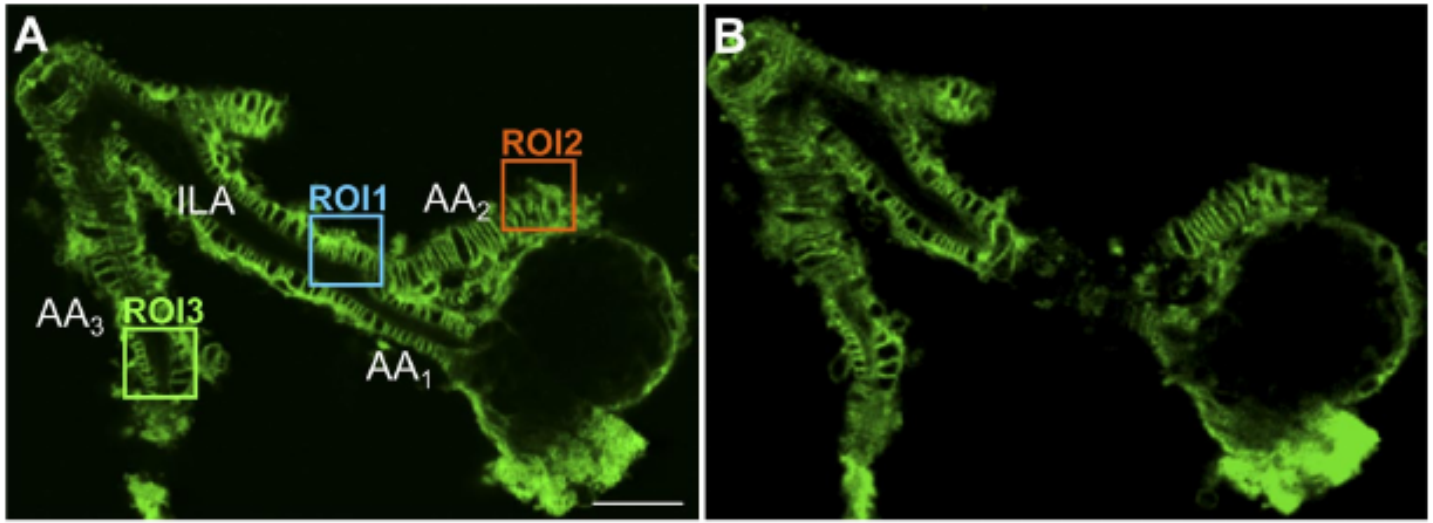
Nephron synchronization

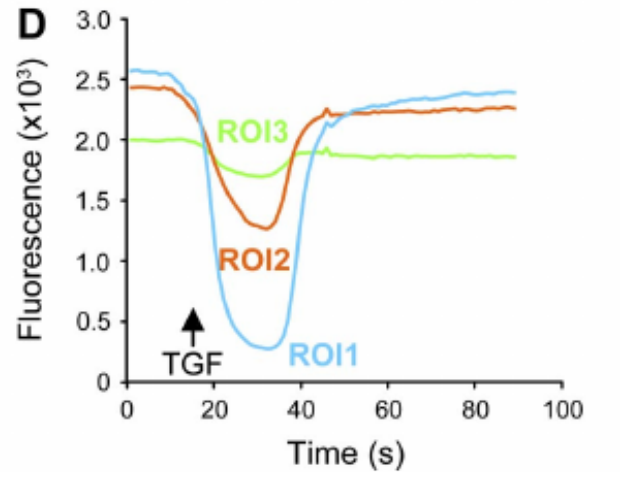






Nephron communication

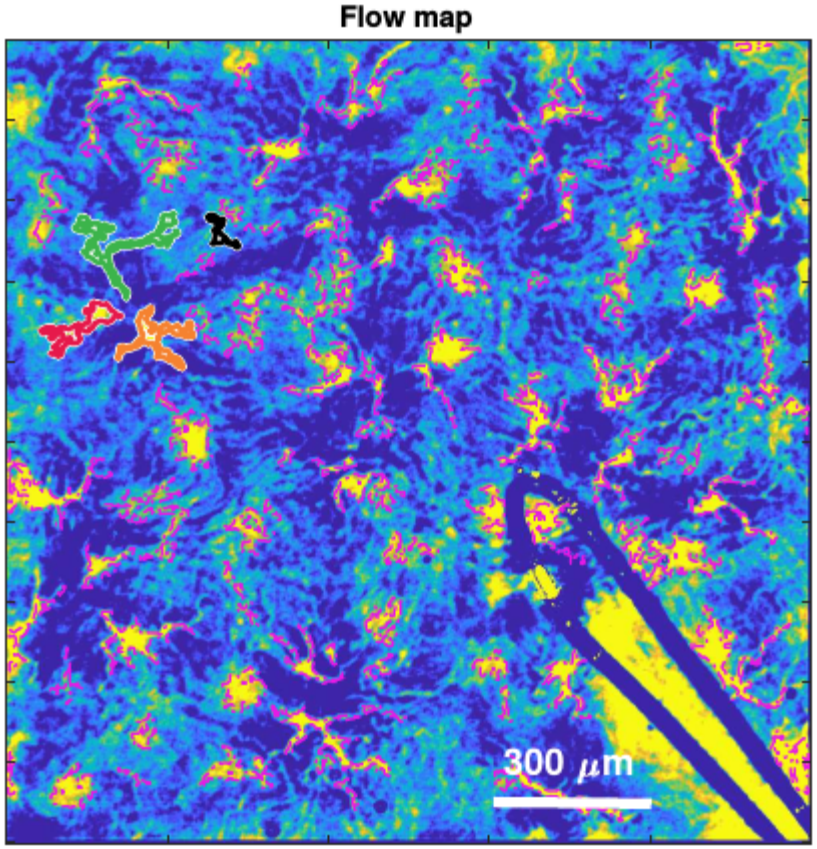


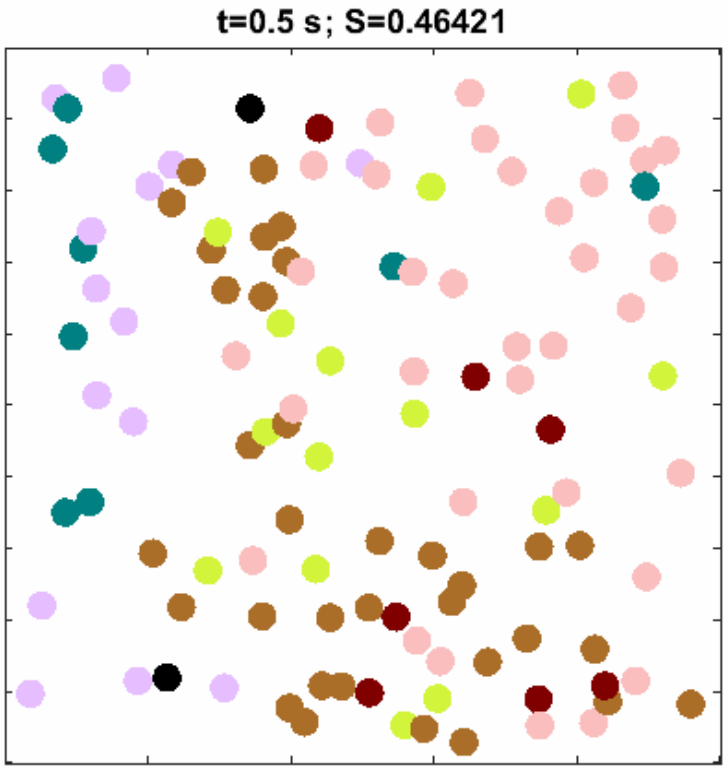


Activation of the TGF mechanism by stimulation of the macula densa in one nephron causes depolarization and contraction of the afferent arteriole in the neighboring nephron.

Marsh et al. Am J Physiol 296, 2009

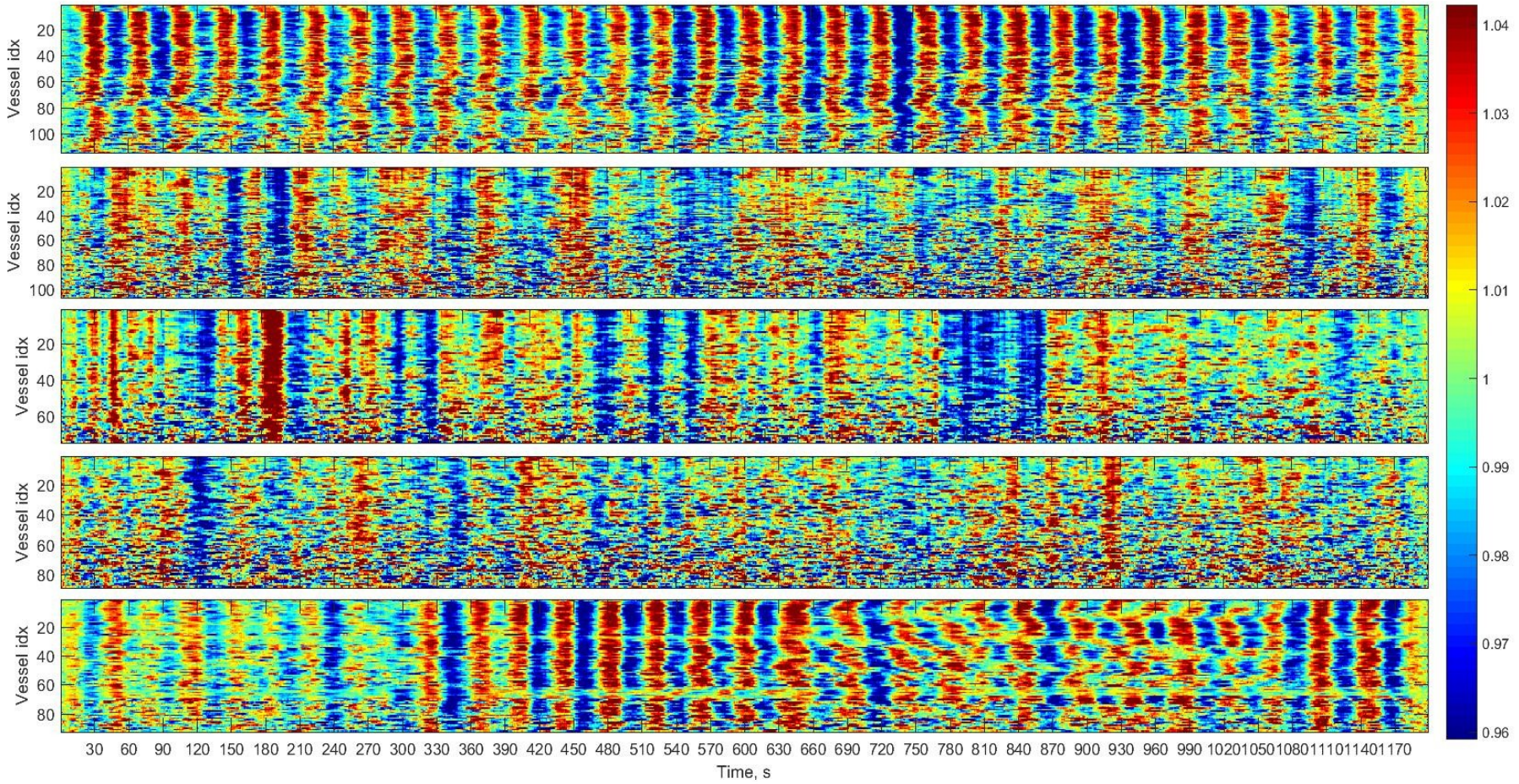
Laser speckle flowmetry





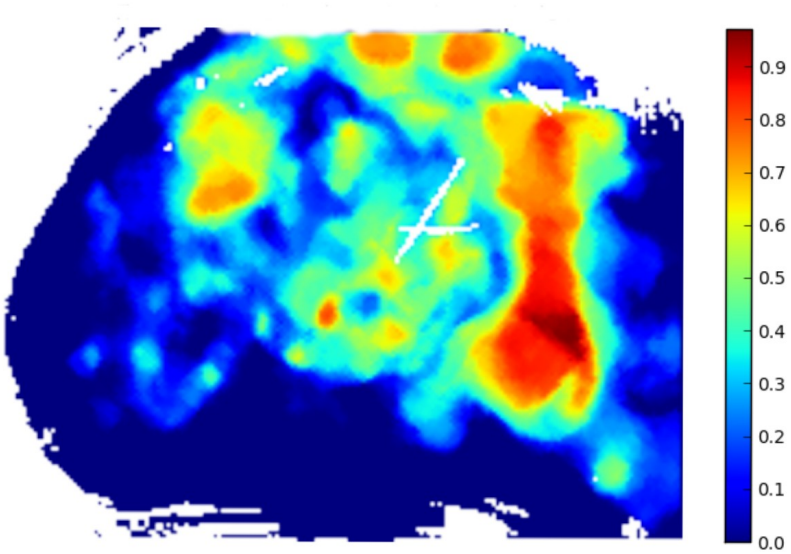
Postnov et al. 2019 (to be submitted)

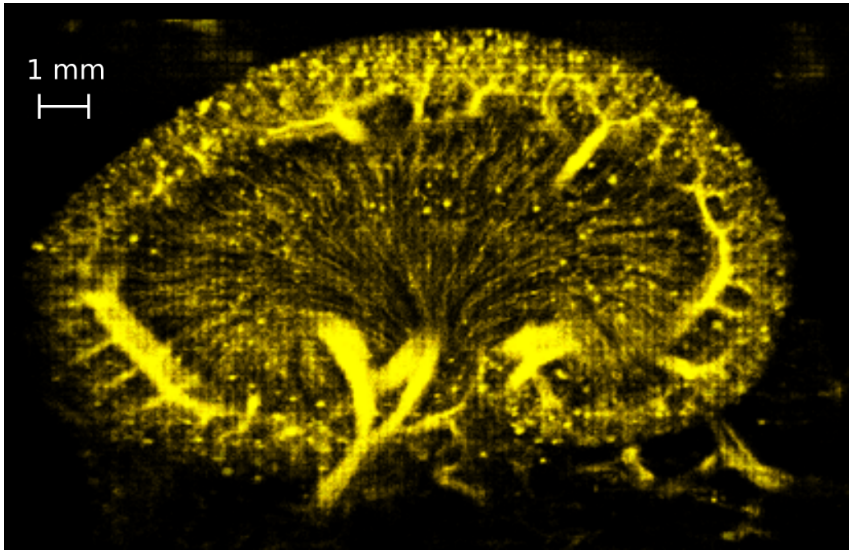
Nephron synchronization



Postnov et al. 2019 (to be submitted)

SynchroGram





- Laser speckle flowmetry
- Optical coherent tomography
- Ultrasound with bubbles

Open questions

- **What does the renal vascular tree actually look like?**
- **How many nephrons are coupled?**
- **How far can the signal travel?**
- **What happens during diabetes and hypertension?**
- **Is a rat really a tiny human?**