Computational modelling of oxygen transport in the whole kidney

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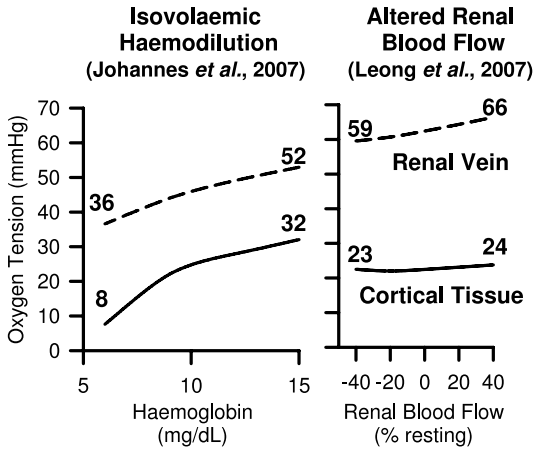
The traditional view is that oxygen homeostasis is achieved in the kidney by matching changes in renal oxygen delivery with proportionate changes in kidney oxygen consumption (VO_2). We have amassed evidence that this view of oxygen regulation is incomplete (Evans *et al.*, 2008), and that the parallel architecture of the renal vasculature facilitates dynamic regulation of kidney oxygenation by enabling oxygen shunting between arteries and veins, such that a significant portion of oxygen in renal arterial blood bypasses kidney tissue. To integrate this new evidence into the conventional model of renal oxygen homeostasis and so achieve a deeper understanding of the processes involved, we have developed a computational model of the parallel-branched vessel architecture for vessel sizes between 10-450 μm (in radius).

In our model the renal vasculature is represented by eight compartments of counter-current systems connected in series. That is, within each compartment an artery and a vein are in parallel configuration with opposing fluid velocities. These compartments correspond directly to the average vessel dimensions at eight of the eleven Strahler orders (branch level in vasculature) identified by Nordsletten *et al.,* (2006) in their structural analysis of the renal vasculature. Further, to account for the intimate association of the arteries and veins at each branch level (the vein is often seen to wrap around the artery) we use a concentric tube with an artery running down the centre of a vein. The Navier-Stokes equation is used to describe blood flow in each vessel and the reaction-advection-diffusion equations are used to model oxygen transport within and between vessels. These equations are numerically solved within each compartment and information on oxygen concentration is fed forward to the neighbouring branch. The binding of oxygen to haemoglobin is included in the model, as is VO_2.



As shown in the Figure, our computational model is able to predict changes in the venous PO_2 and tissue PO_2 for a range of RBF and haemoglobin concentrations consistent with available experimental data (Johannes *et al.,* 2007; Leong *et al.*, 2007). The model predicts a venous PO_2 greater than tissue PO_2 (consistent with oxygen shunting), relatively stable tissue PO_2 in the face of moderate changes in RBF, and that oxygen shunting renders the kidney susceptible to hypoxia during haemodilution. Further, our simulations have revealed that shunting provides a system level robustness which helps to ensure renal tissue PO_2 remains stable in the face of changes in RBF for wide range of combinations of VO_2 to RBF. That is the matching of changes in VO_2 and RBF required by the conventional model of renal oxygen regulation is relaxed by oxygen shunting to allow for a wider range of combinations of VO_2 and RBF.

In summary, the computational model of the parallel countercurrent renal vasculature we have developed has allowed us to integrate several complex processes involved in oxygen transport in the mammalian kidney. This model is able to reproduce existing experimental data and has provided a platform for testing and formulating hypotheses and development of a new understanding of renal oxygen regulation.

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Johannes T, Mik EG, Nohe B, Unertl KE, Ince C. (2007) *American Journal of Physiology*, **292:** F796-803.

Leong C-L, Anderson WP, O'Connor PM, Evans RG. (2007) *American Journal of Physiology*, **292:** F1726-33.

Nordsletten DA, Blackett S, Bentley MD, Ritman EL, Smith NP. (2006) *American Journal of Physiology* **291:** H296-309.