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REVIEW

Optimality, cost minimization and the design of arterial networks

Alun D. Hughes

Institute of Cardiovascular Sciences, University College London, London, WC1E 6BT, UK

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Abstract The arterial circulation acts as a network to deliver nutrients and oxygen to cells. The design of the cardiovascular system is subject to a variety of constraints and costs. It has been postulated that the design of the arterial network might be understood in terms of the need to minimize competing 'costs' within the context of physical or material limits to the system. These designs can also be envisaged as being subservient to space filling or fractal considerations. The signalling mechanisms underlying these designs remain to be fully characterized although shear stress, wall tensile stress and metabolic stimuli are likely candidates. I will also review evidence that deviations from a minimal cost condition or optimal design may provide both a measure of disease severity and insights into the underlying disease mechanism.

Introduction

In branching cones the living web expands[a]

Lymphatic ducts, and convoluted glands;

Aortal tubes propel the nascent blood,

And lengthening veins absorb the refluent flood;

The aim of this paper is to review ideas regarding the design of arterial networks in relation to optimal design and cost minimization. I will also discuss some evidence that disease is associated with deviations from an 'optimal' design. I will

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E-mail address: alun.hughes@ucl.ac.uk.

[a] From The Temple of Nature: Or the Origin of Society: A Poem with Philosophical Notes (1803) by Erasum Darwin. (Darwin's notes) In branching cones, l. 259. The whole branch of an artery or vein may be considered as a cone, though each distinct division of it is a cylinder. It is probable that the amount of the areas of all the small branches from one trunk may equal that of the trunk, otherwise the velocity of the blood would be greater in some parts than in others, which probably only exists when a part is compressed or inflamed.

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not review the genetic, epigenetic, or signalling mechanisms putatively involved in establishing and maintaining optimal design or issues related to optimal coupling of the heart and vascular system. For these topics readers are referred to other articles.[1–6]

Design of arterial networks

The idea that morphology and function are causally interrelated can be traced back at least to Hellenistic philosophy[7,8]; however attempts to make quantitative links between morphological design and function based on mechanistic arguments or analysis emerged in the Enlightenment, following the work of Galileo, Borelli, Newton and Harvey.[9]

In 1515 Leornardo da Vinci described tree boughs as preserving cross-sectional area at branches[b], but as far as I know the first attempt to quantify relationships between blood vessels at bifurcations in an arterial network was made by James Keill in 1708. Keill made anatomical measurements of arteries from dog, calf and man with the aim of calculating '*the Quantity of Blood in the Humane Body*'. He found that the ratio of vessel cross-sectional areas at a bifurcation was typically 41616:52126[c] (i.e. 1: 1.25) and used this ratio in combination with geometric scaling laws to give crude estimates of total blood volume and blood flow velocity in capillaries. Woldenberg[10] has provided a detailed critical description of Keill's work on the arterial network, and his relationship to the English 'iatromechanists',[d] and to other scientists, such as Hales and Young. Young refers to Keill's data in his 1808 Croonian Lecture[11] where he assumes a consistent increase in area of 1:1.26 at each arterial bifurcation. Young makes no comment on the possible significance of this relationship ($1:2^{1/3}$), although it seems unlikely that it could have escaped his notice.[12] Roux, in his doctoral thesis later in the 19th century, undertook a detailed study of the relationships between diameters and the angles subtended by arteries at bifurcations.[13] He concluded that '*the shape and direction of the lumen of the blood vessels at their branch points is mainly determined by the action of hydrodynamic forces*'. Roux is probably best known the founder of the Entwicklungsmechanik[e], a 'Kantian Mechanist' programme for embryology and development.[14] Roux envisaged that development was shaped by the interaction between forces and 'Darwinian' selection *within* an organism operating at a cellular level.[15] Roux's views were very influential in the late 19th and early 20th century and contributed to a greater integration of physics and mathematics into biological analysis.[16] In 1901 Richard Thoma[17] proposed that the size of arteries depended on the velocity of blood flow in the vessel. He proposed that the diameters between parent and offspring branches conformed to an exponential relationship

$$r_0^x = r_1^x + r_2^x$$

where r_0, r_1 and r_2 are the radii of the parent, and offspring branches at a bifurcation and x is the branching exponent (also termed the bifurcation or junction exponent). Based on measurements in chick embryo and human aorta he suggested that x fell between 2.5 and 3, with values being closer to $x = 3$ in early embryonic life. In 1903 Hess[18] extended Roux's work on branching and suggested that a typical branching angle of around 70° could be explained by minimization of energy losses; stating that '*the most favourable branch angle is the angle whose cosine is equal to the ratio of the energy loss the blood undergoes in the parent vessel compared to a branch of the same length*'. Thompson[19] referred to both Roux's and Hess' work and reproduced Hess' diagrams and calculations in the first edition of his classic work 'On Growth and Form' published in 1917. Ultimately the most influential studies of this era were those of Murray who published three articles[20–22] that are now widely viewed as the seminal early works on optimality principles in vascular design and gave rise to the eponymous 'Murray's Law'.

In the first pair of papers[20,21] Murray aimed to find physical laws that described the organization of the vascular system in relation to oxygen transport and exchange at the capillary level. He envisaged this as '*a problem of maxima and minima*' and employed the idea of two competing economic factors: the cost of blood flow (i.e. power[f] expended) and the cost of the blood volume. Using an assumption of Poiseuille flow and that the cost of the blood volume per unit length was proportional to the area of the vessel, Murray calculated that for maximal efficiency (in terms of blood flow and volume) blood flow should be proportional to the cube of the radius of the vessel, r, hence for a bifurcating network minimization of cost would be achieved if

$$r_0^3 = r_1^3 + r_2^3$$

where 0, 1 and 2 denote parent and offspring branches respectively. Murray demonstrates that this gives reasonably plausible estimates of blood flow in small blood vessels; however he notes that this simple model does not hold for the aorta and ascribes this to the pulsatile nature of flow in this artery. In a third paper[22] Murray extended his analysis to look at the angles subtended by branches with respect to the axis of the parent. Using the optimality arguments developed in his earlier paper he calculated that

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[b] "Every year when the boughs of a tree have made an end of maturing their growth, they will have made, when put together, a thickness equal to that of the main stem." Leonardo da Vinci (1515).

[c] Keill is vague on units but Woldenberg (Woldenberg MJ. James Keill (1708) and the morphometry of the microcosm. Geometric progression laws in arterial trees. In: Stoddart DR, ed. Process and form in geomorphology. London; New York: Routledge; 1997) suggests that these are square inches.

[d] For further information on the iatromechanists in 17th century see Brown, T. M (1970). The College of Physicians and the acceptance of iatromechanism in England, 1665-1695 Bulletin of the History of Medicine, 44(1), 12–30.

[e] Literally translated as 'Developmental Mechanics'; however Roux had a more causal perspective than this translation might imply.

[f] Murray terms this factor work, but as Zamir (Zamir M. Optimality principles in arterial branching. J Theor Biol. 1976; 62:227–251) points out he is really describing power.