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Bronchial asymmetry and Fibonacci scaling

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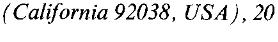
Summary. The irregular branching pattern of the bronchial tree in multiple mammalian species is consistent with a process of morphogenetic self-similarity described by Fibonacci scaling.
Key words. Bronchial tree; Fibonacci scaling; fractal; lung.

The bronchial system is a branching network of tubes. A key feature of this dendritic structure is its irregularity[1,2]. Over multiple generations, each tube gives rise to a conjugate pair of daughter structures of unequal lengths, beginning with the trachea which bifurcates into a long (left mainstem) and short (right mainstem) bronchus. Based on Weibel's data[2] (including figures 85 and 90) the ratio of the shorter to longer conjugate element, for the fifth through the seventh generations of the bronchial tree in a single human lung cast, was 0.62 ± 0.02 (mean ± SEM). The ratio of the right (~ 37 mm) to the left (~ 60 mm) mainstem bronchus was also ~ 0.62 in this cast.

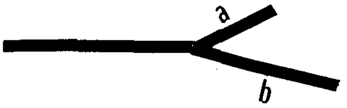
While the irregular pattern of branching of the human bronchial tree is well-recognized[1,2], its theoretical basis remains unexplained. We conjecture that this asymmetry may be a manifestation of the self-similarity principle of morphogenesis advanced by D'Arcy Thompson[3]. A simple model of one type of self-similar scaling can be obtained by starting with a rod of unit length and dividing it into two sections of respective lengths a and b such that the ratio of the total length (a+b) to the longer section b will be equal to the ratio b/a:



It is then readily demonstrated[4] that $(a+b)/b = b/a = (1+\sqrt{5})/2 \approx 1.62$ which is referred to as the golden mean or divine proportion and is designated as φ. Inversely, $a/b = 1/\varphi \approx 0.62$.

The same self-similarity ratio is obtained by generating a series of positive integers such that each integer is the sum of the two preceding integers: 1, 1, 2, 3, 5, 8, 13, 21, 34, ... These numbers are referred to as the Fibonacci numbers: the ratio of one number to its immediate predecessor approaches φ as a limiting value.

In the case of the bronchial tree, since each tube bifurcates into two branches



a self-similarity argument can be used to predict Fibonacci scaling in the length ratio of daughter tubes a and b. The ratios computed from Weibel's data, cited above, are suggestive in this regard.

To further test this hypothesis, data from Raabe et al.[5] which provide detailed morphometric measurements of silicone rubber bronchial casts from four mammalian species were analyzed. Computations were made from bronchial tree measurements of two adult male humans, two male beagle dogs, a female Long-Evans rat and a female Syrian hamster (table). We assessed the short:long branch length ratios in each cast by two methods. Method A: mean ±SEM values were computed from the ratio of short:long conjugate tube lengths for each bifurcation for which measurements were available in bronchial generations one (right and left mainstem bronchi) through seven of the bronchial tree. Method B: the sum of all short (Σ short) and all long (Σ long) branches in bronchial generations one through seven was obtained. The ratio Σ short/Σ long was then calculated for each generation and the overall mean ± SEM computed for these seven generations.

The data in the table along with Weibel's data are compatible with the hypothesis that the Fibonacci ratio is a universal scaling ratio in the bronchial tree. It should be emphasized that these values represent the mean ratios derived from multiple conjugate branch pairs in each of the human and animal lung casts. As expected, there is considerable biologic variability around the 'ideal' (i.e. average) ratio of 0.62 for any single branch pair ratio. The consistency of the mean ratio derived from four species, however, is highly suggestive of a Fibonacci scaling mechanism. In a different analysis of bronchial structure, Horsfield[6,7] generated a Fibonacci sequence by using a numbering system for successive branches in a bifurcating tree. However, this model

Bronchial length ratios (computed from Raabe et al.[5])

Lung cast	Method A*	Method B* (n = 7)
Human HM-2-72	0.66 ± 0.02 (n = 109)	0.62 ± 0.03
Human HM-3-73	0.64 ± 0.02 (n = 117)	0.62 ± 0.03
Dog DN-2-72	0.67 ± 0.02 (n = 110)	0.68 ± 0.02
Dog DN-5-75	0.67 ± 0.02 (n = 104)	0.66 ± 0.03
Rat RF-3-72	0.63 ± 0.03 (n = 100)	0.55 ± 0.05
Hamster HaF-4-73	0.62 ± 0.02 (n = 107)	0.59 ± 0.07

*See text for details. For method A, n = total number of conjugate bronchial branch pairs for which data were available in the first seven generations of bronchial tubes. For method B, n = 7 generations. Values are given as mean ± SEM.

did not acount for the asymmetrical relationship between conjugate branch pairs. Our observation of a self-similarity ratio for conjugate tube lengths also complements descriptions of the fractal architecture of the lung which implies a scaling relationship from one generation of tubes to the next[2,8,9].

Fibonacci scaling has been observed in multiple other biological systems and anatomic relationships[10-12]. For example, the historical observation that the ratio of the total height in humans to the vertical height of the navel approximates the golden mean has been verified in a systematic study[13]. From a morphogenetic viewpoint, the generation of complex, irregular structures based in part on principles of fractal self-similarity[9] and Fibonacci proportionality may serve to minimize constructional error[3]. How the information which regulates this type of stable growth pattern is encoded and processed are major unanswered questions. From an evolutionary point of view such scaling mechanisms are also of interest because they lead to complex anatomic structures without apparent recourse to natural selection. The relevance of natural selection to organismic complexity is a current area of investigation and debate[14]. It remains to be seen whether Fibonacci geometry of the lung will generalize to enhance the understanding of other irregular branching networks, as seen in the nervous system, the vascular tree, the biliary ducts, and the His-Purkinje network.

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Frequency-dependent effect of verapamil on rat soleus muscle

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Summary. In the presence of verapamil (0.1 mM) rat soleus muscle fibers failed to generate action potentials with overshoots. In fibers with their V_m set to a local level of −90 mV, verapamil produces a gradual reduction in the amplitude of the repetitive action potentials; this effect is more pronounced at high rates of stimulation (100 Hz). Our results suggest a local anesthetic action of this drug that could contribute with its calcium channel blocking effect to the diminished mechanical tension observed in the presence of the drug.

Key words. Rat skeletal muscle; verapamil; frequency-dependent effect; mechanical activity; electrical activity.

There are several reports that suggest the necessity for the participation of external calcium ions in activation of mammalian skeletal muscle[2-6]. Recently, we reported a decrease in the twitch and tetanus tension of rat soleus muscle exposed to verapamil[4]; the effect of this calcium channel blocker on the mechanical activity is more pronounced when the muscle is repetitively stimulated. Several hypotheses have been suggested to explain this phenomenon (frequency-dependent or use-dependent effect)[7-10]. In addition, verapamil does not have any significant effect on caffeine contracture tension[4].

It has been suggested that many of these drugs have an anesthetic effect besides their calcium channel blocker effect[11-13]. Verapamil (0.1 mM) does not hinder the generation of single action potentials (APs) recorded in hyperpolarized rat soleus muscle fibers[4] but there are no data available on the iterative generation of APs in the presence of this drug. So it seemed to be of interest to find out whether verapamil would modify the electrical activity elicited at low and high frequencies of stimulation.

Material and methods. Experiments were performed in rat (Wistar strain) soleus muscle in vitro at 32°C. APs were generated and recorded using a double microelectrode technique. The fiber was impaled with two microelectrodes (6–15 MΩ, 3 M KCl); a recording and a stimulating electrode (inserted at about 100 µm from one another). In some cases, the fiber was hyperpolarized to −90 mV with anodal current through the stimulating electrode, 5–10 s before a depolarizing pulse of 2–3 ms duration via a WPI electrometer. The action potential and its

Action potential characteristics in control and verapamil (0.1 mM) solutions

	Control (n:39) without hyperpolarization	with hyperpolarization	Verapamil (n:41) with hyperpolarization
Overshoot (mV)	10.9 ± 5.4	16.5 ± 5.1	11.6 ± 5.0
Duration (ms)	0.9 ± 0.2	0.8 ± 0.2	1.2 ± 0.3
+ dV/dt (V/s)	203 ± 64	309 ± 40	267 ± 26
− dV/dt (V/s)	140 ± 37	157 ± 37	95 ± 19

Values are mean ± SD. The action potentials were measured in fibers with their normal resting membrane potential (without hyperpolarization) and hyperpolarized to − 90 mV (see methods) previous to depolarizing pulse. The duration of the AP was measured at − 40 mV. + dV/dt: maximum rate of rise; − dV/dt: maximum rate of fall.