Scaling relationships for neuronal circuit wiring set by noise and metabolic cost

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The development of information processing devices, such as computer chips has been profoundly influenced by two basic physical constraints: noise and energy. Here we relate these two constraints to the wires of neural circuits – the axons. Axons carry the fundamental signal of the nervous systems, the action potential (AP) to allow neurons to communicate fast and reliably [1]. Neurons in cerebral cortex achieve axonal wiring densities of 4 km (!) per mm³, by using unmyelinated axons of 0.3 μm average diameter for local cortical, account for about 40% of resting metabolic consumption [2]. Although, as in computer chips, wire miniaturization economizes on space and energy [3,4], it increases the effects of noise introduced by thermodynamic fluctuations in a neuron's “protein transistors,” voltage-gated ion channels – so called channel noise. We previously showed that channel noise causes AP communication to break down in axons and cell bodies below 0.1 μm and 3 μm diameter respectively – a universal limit to neuron size matched by anatomical data across species [1]. In the many thin axons operating close to this limit we demonstrated several mechanisms through which channel noise can destroy information encoded in the timing of APs, by randomly varying the speed of conduction in the order of milliseconds [5].

Here, we explore the basic relationships imposed by noise and energy on axonal connectivity. First, we conducted detailed Monte Carlo simulations of thin axons using the Modigliani stochastic simulator (www.modigliani.co.uk, see [1,5]), which allowed us to establish how the effects of axonal variability scales with respect to axonal geometry. We find that spike time reliability increases as a power-law of axon diameter and decreases as a power-law of axon length (or synaptic distance). This yields a basic relationship between axon diameter, synaptic distance and the achievable synaptic spike time reliability. We match these results to the few existing anatomical data points (maximum synaptic distance, average diameter in cortex and cerebellum) and make testable predictions on cortical axonal geometry and associated synapses (NMDA/AMPA). Second, we use a simple model of metabolic cost, based on an axonal membrane surface area argument[2] which shows that increasing axon diameter or axon length linearly increases the metabolic cost of axons. Thus, choosing a particular combination of axon diameter and axon length/synaptic distance sets up a trade-off between noise and energy in wiring cortical circuits that can be assayed with anatomical data.

Acknowledgments
AAF was supported by Studienstiftung des Deutschen Volkes, Boehringer-Ingelheim Fonds and the BBSRC.

References