Remarks on the number of tubulin dimers per neuron and implications for Hameroff-Penrose Orch OR

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Abstract

Stuart Hameroff has wrongly estimated that a typical brain neuron has 10^7 tubulin dimers and wrongly attributed this result to Yu and Baas, J. Neurosci. 1994; 14: 2818-2829. In this letter we show that Hameroff's estimate is based on misunderstanding of the results provided by Yu and Baas, who actually measured the total microtubule length in a single axonal projection with length of 56 µm in a differentiating in vitro stage 3 embryonic hippocampal neuron. In order to visualize how big Hameroff's error is, we have reconstructed two of the studied by Yu and Baas embryonic hippocampal neurons with Neuromantic v1.6.3 and compared them with previously published reconstructions of adult hippocampal neurons. Correct calculations show that an adult differentiated pyramidal neuron in vivo has approximately 1.3×10^9 tubulin dimers incorporated in cytoskeletal microtubules. This estimate has profound implications for the Hameroff-Penrose Orch OR model, because it sets limitations on the number of quantum coherent neurons and implies that if 100% of the neuronal microtubules are quantum coherent for 25 ms then Hameroff-Penrose Orch OR conscious events should involve only 15 pyramidal neurons.

Keywords: tubulin dimer, pyramidal neuron, embryonic neuron

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The Hameroff-Penrose Orch OR model has been criticized by various authors in terms of biological feasibility, decoherence issues, etc. However it is highly surprising to find out that Hameroff-Penrose Orch OR model is built upon false statements of the type "*A typical brain neuron has roughly 10^7 tubulins (Yu and Baas, 1994)*" or "*Each brain neuron is estimated to contain about 10^7 tubulins (Yu and Bass, 1994)*", which can be found in virtually every article written by Hameroff (cf. Hameroff and Penrose, 1996; Hameroff 1998a,b). Moreover, this error propagates in articles of researchers who discuss Hameroff-Penrose model and they incorrectly cite Yu and Baas (1994) as the scientists who have measured the value of 10^7 tubulin dimers per typical brain neuron (cf. Mureika, 2007).

A direct check of the original article by Yu and Baas (1994) shows two alarming things – (i) nowhere in the article is estimated that there are 10^7 tubulin dimers per neuron; and (ii) the authors investigated embryonic hippocampal neurons in culture in vitro, which start differentiation from rounded cells (stage 1), then transform to cells with few micro-processes (stage 2), and after that become cells with few micro-processes and one longer projection that is going to be an axon (stage 3). Actually a central result of Yu and Baas (1994) article is that the authors "*reconstructed the microtubule (MT) arrays of a 56 µm axon from a cell that had undergone axon differentiation*" and this reconstructed axon "*contained 1430 MTs ... and the total MT length was 5750 µm*". Microtubules in vivo have 13 protofilaments (n_{PF}=13) and each tubulin dimer is l_{TUB}=8 nm long, therefore the number of tubulins in this 56 µm long axon is:

$$(1) \quad n_{TUB} = \frac{n_{PF} \times l_{MT}}{l_{TUB}} = \frac{13 \times 5750 \times 10^{-6}}{8 \times 10^{-9}} \approx 10^7$$

Therefore it is Hameroff who calculated the number of 10^7 dimers per neuron, based on misunderstanding of Yu and Baas (1994) paper. In order to see what kind of neuron and what kind of compartment has the number of 10^7 tubulin dimmers, we refer the reader to Fig.1c,d in Yu and Baas (1994) article, which shows microscopic images of the studied embryonic hippocampal neurons. In the current work, we have reconstructed these embryonic neurons with Neuromantic v1.6.3 (cf. Myatt, 2008) and compared them to previously published reconstruction of hippocampal CA1 neuron by Pyapali et al. (1998), see Figure 1.

Essentially the question how much tubulin dimers are there per differentiated pyramidal neuron could be answered if one combines the data from Yu and Baas (1994), and Pyapali et al. (1998). The volume of the reconstructed hippocampal CA1 neuron N122 is 4961.6 µm^3 (as measured with L-Measure software). The volume V of the measured by Yu and Baas axonal projection with length l=56 µm and diameter d=0.9 µm (as measured from Yu and Baas, 1994; Fig.1c,d with ImageJ software) is:

$$(2) \quad V = \frac{\pi d^2 l}{4} \approx 35.63 \ \mu m^3$$

Assuming that both the embryonic hippocampal neuronal axon and the differentiated CA1 pyramidal neuron have the same microtubule total length per unit volume, we can calculate that the differentiated pyramidal neuron in vivo has 1.3×10^9 tubulin dimers incorporated in the cytoskeletal microtubules. A caveat is necessary - this estimate does not include free tubulin dimers in the cytosol. Instead it measures only tubulin dimers incorporated in stable

microtubules that can survive the fixation before being studied by electron microscopy.

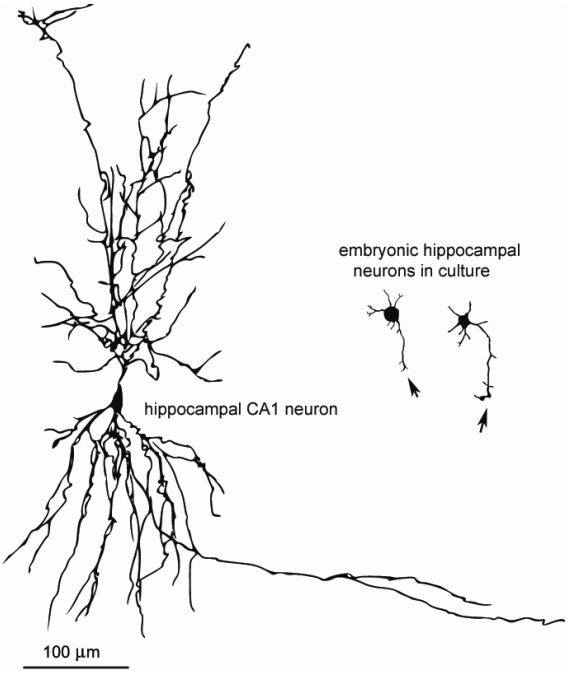

Figure 1. Cultured in vitro embryonic hippocampal neurons reconstructed from Yu and Baas (1994, Fig.1c,d) and compared to hippocampal CA1 neuron (we have used the N122.swc file available at Duke-Southampton Archive of Neuronal Morphology; originally published in Pyapali et al., 1998). The reconstructed embryonic cells have axons with length 50 µm and 74 µm respectively and these should be compared with the scale of the real in vivo neurons. The scale bar is 100 µm.

The estimate is essential for Orch OR because according to Hameroff (1998b) the number of tubulins participating in a single Orch OR event is 2×10^{10}, which gives 20000 neurons in quantum coherence for 25 ms. However, if one takes the correct number of 1.3×10^{9} tubulin dimers per neuron and assumes that 100% of the tubulins are in quantum superposition it will come out that only 15 neurons participate in each conscious event. From these 15 neurons Hameroff should start his “inflation argument” in the form: assuming that only 10% of the tubulins of the neuron are quantum coherent, then 150 neurons will be necessary for a single Orch OR event, etc. And it is difficult to see how from 15 neurons one can “inflate” the argument so that to incorporate thousands of neurons in quantum coherence. Moreover, one is puzzled: where are left the tubulins and the microtubules from the ten times more numerous glial cells, which according to Hameroff increase the computational power of the brain via their gap junction interconnected network?

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