Chapter 7
Exploring Structural and Dynamical Properties Microtubules by Means of Artificial Neural Networks

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ABSTRACT

Microtubules (MTs) are cylindrical polymers of the tubulin dimer, are constituents of all eukaryotic cells cytoskeleton and are involved in key cellular functions and are claimed to be involved as sub-cellular information or quantum information communication systems. The authors evaluated some biophysical properties of MTs by means of specific physical measures of resonance and birefringence in presence of electromagnetic field, on the assumption that when tubulin and MTs show different biophysical behaviours, this should be due to their special structural properties. Actually, MTs are the closest biological equivalent to the well-known carbon nanotubes (CNTs), whose interesting biophysical and quantum properties are due to their peculiar microscopic structure. The experimental results highlighted a physical behaviour of MTs in comparison with tubulin. The dynamic simulation of MT and tubulin subjected to electromagnetic field was performed via MD tools. Their level of self-organization was evaluated using artificial neural networks, which resulted to be an effective method to gather the dynamical behaviour of cellular and non-cellular structures and to compare their physical properties.

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INTRODUCTION

Background

Microtubules

Microtubules (MTs) are key constituents of all eukaryotic cells cytoskeleton. They are involved in the regulation of essential cellular functions such as the transport of materials within the cell, the movement of cytoplasmic organelles or vesicles and the cell division (Hyams & Lloyd, 1994).

MTs are stiff cytoskeletal filaments characterized by a tubelike structure. The building block of a MT is a 110-kDa heterodimeric protein said tubulin, that is the association product of two different subunits, designated α and β tubulin (Postingl, Krauhs, Little, & Kempf 1981, Krauhs, Little, Kempf, Hofer-Warbinek, Ade, & Postingl 1981) and encoded by separate genes. The word tubulin always refers to the αβ heterodimer, that is usually considered as one unit, although the association is only due to non-covalent interactions. Each monomer of α and β tubulin is a compact ellipsoid of approximate dimensions 46 x 40 x 65 A° (width, height, and depth, respectively); while dimensions of α β-heterodimer are 46 x 80 x 65 A°. Both α- and β- tubulin is composed of approximately 450 amino acids.

Recently important information about tubulin conformational changes during the MTs polymerization have been obtained through X-ray crystallography (Ravelli, Gigant, Curmi, Jourdain, Lachkar, Sobel, & Knossow 2004).

The general structure of MTs has been established experimentally (Amos & Amos1991, Chrétien & Wade 1991). MTs have been considered as helical polymers and they are built by the self-association of the αβ-heterodimer through a process of polymerization and depolymerization.

This dynamic nature makes MTs sensitive to several pharmacological agents, i.e. some classes of anticancer agents that are able to destroy or stabilize their structure.

The polymerization occurs in a two-dimensional process that involves two types of contacts between tubulin subunits. The first process involve head-to-tail binding of heterodimers and it results in polar protofilaments that run along the length of the MT. The second process involve lateral interactions between parallel protofilaments and it completes the MT wall to form a hollow tube (Nogales, Whittaker, Milligan & Downing 1999). The longitudinal contacts along protofilaments appear to be much stronger than those between adjacent protofilaments (Mandelkow, Mandelkow, & Milligan 1991).

All protofilaments in a MT have the same orientation.

Assembly mechanism of α- and β- tubulin gives rise *in vitro* to a variety of cylindrical structures that differ by their protofilament and monomer helix-start numbers (Binder & Rosenbaum, 1978, Burton & Himes 1978, Chrétien, Metoz, Verde, Karsenti & Wade 1992, Linck & Langevin 1981, Pierson, Burton & Himes 1978, Chrétien 2000). In contrast, most MTs assembled *in vivo* seem to be composed of 13 protofilaments, although many exceptions have been noted in different species and cell types.

The lengths of MTs vary but commonly reach 5-10 μm dimensions; and their diameter depends on the protofilament number. For example in the case of 13 protofilaments the tube has an outer diameter of 23 nm and an inner diameter of roughly 15 nm.

Microtubules Quantum Theories

In the last decade many theories and papers have been published concerning the biophysical properties of MTs including the hypothesis of MTs implication in coherent quantum states in the brain evolving in some form of energy and information transfer.

The most discussed theory on quantum effects involving MTs has been proposed by Hameroff and Penrose that published the OrchOR Model