Measuring and modeling electromagnetic properties of cytoskeletal proteins and their filaments

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Abstract – We provide an overview of the experiments and computer modeling on microtubules, actin filaments and cancer cells exposed to various frequencies of electric and electromagnetic fields. Conductivity and capacitance of tubulin and microtubules have been measured and modeled at frequencies between 100kHz and 1 MHz. significant mechanistic explanation of the observed effects. Similar measurements were performed for G- and F-actin. Experiments were also performed using exposure of microtubules and actin filaments to infrared fields, THz electromagnetic waves, visible light and ultraviolet laser light. Finally, conductivity measurements combined with imaging for cancer cells exposed to TTFields indicate important interactions of the cellular cytoskeleton with electric and electromagnetic fields and provide a mode of action of these fields used therapeutically.

Keywords – cytoskeleton; microtubules; actin filaments; ionic conductivity; capacitance, cancer cells

I. INTRODUCTION

Microtubules and actin filaments, as key components of the cytoskeleton, have aroused great interest due to their numerous functional roles in eukaryotic cells, including intracellular electrical signaling. Their electrical conductivity and response to electromagnetic fields are topics of current interest, which may shed light on the functioning of both normal and cancer cells.

II. TUBULIN AND MICROTUBULES

We have measured [1-7] and modeled [8] the following properties of tubulin and microtubules: (1) the hydration shell around tubulin ranges from 1 nm to several nm when ionic concentration is reduced, indicating that the environment may controllably tune electrical and electromagnetic properties of tubulin and its assemblies; (2) the net electric charge of tubulin has been shown to be also tunable by the environment such that tubulin which is normally highly negatively charged, can reverse its charge and become positively charged when pH<5; (3) polarizability and the index of refraction have been measured as a function of pH and calculated. Polarizability has been found to vary in the range (4 to 9) x 10^{-34} Cm^2/V, for 6.6<pH<7.4 which accounts for permanent dipole reorientation, induced dipole generation and ionic bilayer formation around the protein surface. The dielectric constant in the same range of pH varies between 2 and 4. Electrochemical impedance spectroscopy was used to measure the impedance of microtubule networks at physiologically relevant tubulin concentrations. While polymerized microtubules increased solution capacitance, it was seen that unpolymerized tubulin at the same concentrations did not. This indicates the role of microtubules as potential intracellular ion storage devices. Additionally, we have found through exposure of microtubules to high intensity THz pulses that these protein filaments can be disintegrated in a matter of minutes by electromagnetic waves in the low THz range [9].

III. ACTIN FILAMENTS

We characterized the AC conduction characteristics of both globular and polymerized actin and compare their values to those theoretically predicted earlier. Actin filaments have been demonstrated to act as conducting bionanowires, forming a signaling network capable of transmitting ionic waves in cells. Measurements at different concentrations of actin, for both unpolymerized and polymerized actin identified revealed two relevant characteristics: (1) actin filaments have a lower impedance than its globular counterpart; (2) an increase in the actin concentration leads to higher conductivities. We developed a quantitative model representing the electrical properties of actin in a buffer solution as electrical resistor-inductor-capacitor (RLC) circuits, where the resistive contribution is due to the viscous ion flows along the filaments; the inductive contribution is due to the solenoidal flows along and around the helix-shaped filament and the capacitive contribution is due to the counterion layer formed around each negatively charged filament.

IV. CANCER CELLS

Every cell in the human body possesses electrical properties that are essential for its proper behavior. It is not yet clear whether these changes correlate with cell mutation in cancer cells, or only with their subsequent development. These aspects merit further investigation and a comprehensive understanding of the current knowledge regarding the electrical landscape of cells is much needed. To this end, we performed conductivity measurements [10] at different electrical field intensities and frequencies of TTFields on HeLa, GBM and MCF7 cells with GFP-labelled tubulin, Time-lapse imaging experiments were performed using Hela cells stably expressing EGFP-Tubulin and individual cells were tracked during exposure to TTFields. We discovered that TTFields-treated cells exhibited prolonged mitosis as well as prolonged cytokinesis.

V. CONCLUSIONS

We propose an electro-energetic model of the cancer cell which accounts for a reduction in the transmembrane potential, a drop in the extracellular pH value and their consequences for the glycolytic shift due to the reduction in the proton-motive force.

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