

Measurement of Electromagnetic Activity of Living Cells

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Abstract— Living cells display mechanical vibrations excited by energy supply. The majority of biological molecules and structures are electrically polar and vibrations generate an electromagnetic field. Microtubules are the generating structure in eukaryotic cells. The generated electromagnetic field can be measured at the plasma membrane by a micro sensor integrated with an input amplifier and evaluated by a real time spectrum analyser controlled by computer.

1. INTRODUCTION

Biological activity is conditioned by continuous energy supply which enables formation and maintenance of the state far from the thermodynamic equilibrium, a crucial condition of life. Transformation of energy is an essential process of living activity. Organization of bodies with macroscopic dimensions and synchronization of mutually dependent activity requires forces of corresponding extension. Excitation of coherent electromagnetic (EMG) field is considered to be an essential mechanism of biological functions. Energy stored in oscillating systems represents a source of forces for biological utilization. H. Fröhlich formulated a hypothesis of coherent electric polar vibrations in biological systems with energy condensation in a mode of motion and correlated over macroscopic region [1, 2]. Fröhlich's hypothesis has a strong support in experimental results on mechanical vibrations in living cells. Nanoscale vibrations are an expression of metabolic activity and a signature of life [3]. The majority of biological macromolecules and structures are electrically polar and, therefore, EMG activity belongs to the signature of life too. EMG activity in the frequency range 8–9 MHz in the M phase depends on development of the mitotic spindle [4]. Microtubules represent the oscillating structure in eukaryotic cells. Sahu et al. [5, 6] measured resonant frequencies of isolated microtubules in the classical frequency range below 20 GHz, in the far infrared region in the range of 300–1500 cm⁻¹, and the UV absorption-emission spectrum. The frequency spectrum from 20 GHz to 100 GHz should be also analysed.

Energy supply is a necessary condition of life and, therefore, any disturbance of energy metabolism has to initiate a pathological state. Defective processes of energy supply and transformation cause pathological states, in particular cancers [7].

2. GENERATING STRUCTURES-MICROTUBULES

In eukaryotic cells microtubules form a filamentous structure which has an essential role in cell activity. The microtubule system is a primary organizer of the cytoskeleton. Microtubules are hollow tubes of a circular cross section with the inner and outer diameter 17 and 25 nm, respectively (Figure 1). In the interphase they form radial fibers growing outward from the centrosome, a spherical structure in the center of the cell. The essential part of microtubules is bonded to structures at the membrane. In the M phase the microtubules of the mitotic spindle emanate from two centrosomes.

Microtubule physical characteristics correspond to requirements for generating the EMG field: they are electrically polar, nonlinear, and excited by energy supply. Microtubules are built of tubulin heterodimers forming an organized structure (Figure 1). Each heterodimer is an electric dipole whose dipole moment is about 1000 Debye, i.e., 10⁻²⁶ Cm [8, 9]. Several mechanisms were described for energy supply for excitation of polar vibrations. The energy is supplied by hydrolysis of GTP to GDP in β tubulins after polymerization [10, 11], energy losses at motion of motor proteins along microtubules [12], and very likely also by non-utilized energy liberated from mitochondria [13]. Photons released from chemical reactions may supply energy in the UV and visible wavelength regions.

Sahu et al. [5, 6] measured resonant frequencies of isolated microtubules in the frequency range 10–30 MHz, 100–200 MHz, 3–18 GHz (Figure 2), at about 20 THz (the wavenumber about 700 cm⁻¹),

and the UV absorption-emission spectrum at about 276 nm. Oscillations depend on the water content in the microtubule cavity. The water core inside the microtubule resonantly integrates all proteins around it such that the nanotube irrespective of its size functions like a single protein molecule. Therefore, the water channel inside the microtubule cavity displays a control in governing the electronic and optical properties of microtubule. Sahu et al. [9] claim that the energy levels of a single tubulin protein and of a single microtubule made of 40,000 tubulin dimers are identical.

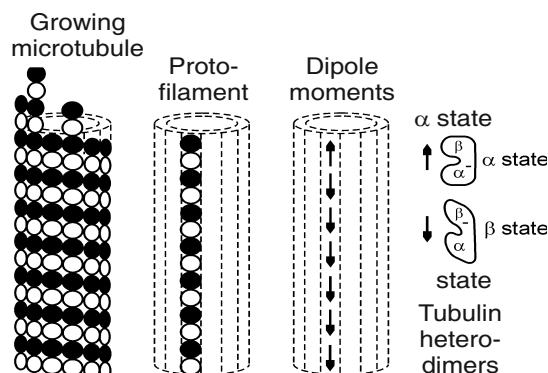


Figure 1: Structure of a microtubule. Microtubule is a tube with inner and outer diameter 17 and 25 nm, respectively, composed of heterodimers which are electric dipoles. After polymerization of hetero-dimers the guanosine triphosphate in the β tubulin is hydrolysed and polarization reversed. Orientation of electric dipoles in the microtubule is visualized by arrows.

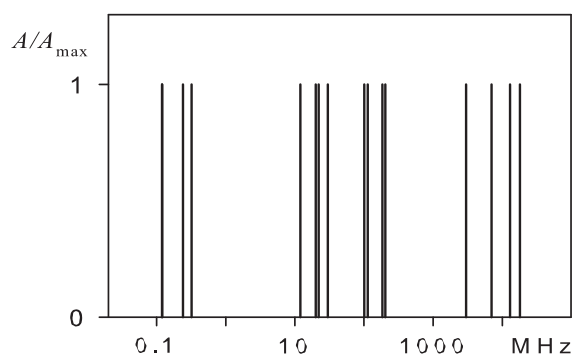


Figure 2: Spectrum of resonant frequencies of the electromagnetic activity of microtubules in the classical frequency range below 20 GHz. A microtubule forms a vibration resonant string with oscillations approximately along longitudinal axis. The amplitudes of the resonant peaks are displayed as relative values ($A/A_{\max}$). After Sahu et al. [5, 6].

The power supply to the electric polar vibrations in a cell is assumed to be of the order of magnitude of 0.1 pW (10^{-13} W). If the number of microtubules in a cell is 400 then the power supply to a single microtubule is of the order of magnitude 0.1 fW (10^{-16} W). For a quality factor of about 80 the power of electric polar vibrations in one microtubule is about 10 times higher (i.e., 1 fW). The power of EMG component of oscillations is smaller than 1 fW.

3. MEASUREMENT OF MICROTUBULE EMG FIELD

EMG field generated by microtubules in living cells may be measured at the plasma membrane in the points where the microtubules are attached to structures at the membrane inside the cell. Dimension of the detection contact of the sensor (Figure 3) has to correspond to the cross section of the microtubule to receive the maximum value of the signal. The distance between the ends of the neighbouring microtubules depends on the cell size and number of microtubules in the cell. Its value is of the order of magnitude of μm 's. The intensity vector $\mathbf{E}$ of the near EMG field has longitudinal orientation along the microtubule axis. For a dipole source the amplitude E_R is given

by the equation

$$E_R = P/(2\pi\epsilon\epsilon_0 R^3)$$

where P is the amplitude of the dipole moment of the microtubule and R is the distance from the end of the microtubule along its axis. The detection contact of the sensor must be in touch with the plasma membrane to reduce decrease of the measured signal by increased R .

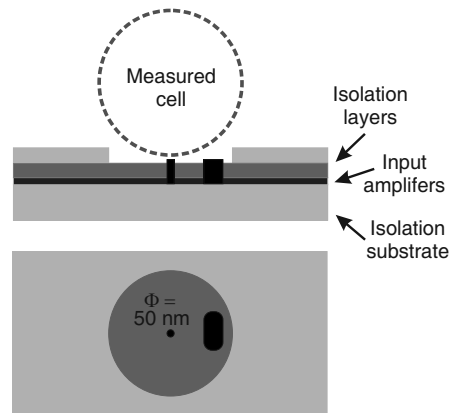


Figure 3: A schematic picture of a suggested sensor for detecting cellular electromagnetic activity. Dimension of the detector gold contact in the centre of circular opening for a living cell has to correspond to microtubule cross section. Function of the gold contact with a diameter about 50 nm was experimentally verified. The input amplifier has to be integrated with the detector part to increase the signal to noise ratio. The measured signal processed and amplified by the input amplifier may be embedded in noise.

A block diagram of the experimental system for detecting EMG oscillations of living cells is shown in Figure 4. The sensor with an input amplifier together with a subsequent preamplifier should be placed in a shielded box. Two or three screening layers for electric and magnetic screening should be used to eliminate disturbances and electromagnetic noise from the ambient medium. Real time spectrum analyser makes possible effective analysis of coherent oscillations. The essential part of the experimental system is the sensor integrated with the input amplifier. The detection contact and connection with the input amplifier must have not only small resistance but also small capacitance. Moreover, the sensor with the input amplifier has to meet other requirements to detect the cellular signals. High signal to noise ratio and intact cellular functions during measurement are necessary conditions.

The main problem of detection the cellular EMG field is the level of noise. First of all the level of signal and noise in the cell should be discussed. Coherent EMG field is assumed to have an essential function in cellular activity-in working and information processes. Information management in living cells is an essential condition for the existence of life. It is assumed that biological systems need not store data in many memory elements, and utilize parallel or repeated processing. But the present knowledge of information storage in cellular memory, its reading and processing is remarkably limited. Biological cells operate at the boundary of the nano and micro worlds. Noise in biological cells is assumed to be at acceptable level due to water ordering, and cellular processes can distinguish signal from noise. During the measurement, the signal to noise ratio is mainly deteriorated by the input amplifier.

Impedance matching of the input amplifier to cellular source is a special problem. The sensor measures the potential difference of the near field excited by electric polar vibrations in microtubules between two points at the membrane. The input impedance of the preamplifier should correspond to the impedance of the plasma membrane in the region of the sensor. Nevertheless, reaction of the living cell to power losses caused by preamplifier consumption is an unknown factor. Living cell is an active substance which senses even small disturbances caused by surrounding medium. The cell may react by increase of energy supply to cover the loss or in an opposite way by decrease of energy supply to defective parts of the microtubule system. Changes of the power in the nonlinear oscillating system cause frequency shifts.

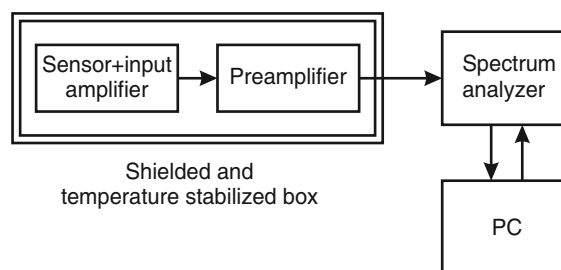


Figure 4: A block diagram of the experimental system for detecting cellular EMG. Sensor integrated with the input amplifier is shown in Figure 3. Measured cells, sensor with input amplifier, preamplifier and batteries have to be shielded to limit disturbances caused by external signals and noise. The computer controls the experimental system and stores the measured data.

4. VERIFICATION OF THE METHOD

Experimental results obtained on synchronized yeast cells *S. cerevisiae* (mutant *tub2-401*) in the M phase are plotted in Figure 5. Average values of signals above a threshold level (circular symbols connected with a solid line) and standard deviations (diamond symbols connected with dashed lines) from six measurements are plotted versus time (one period corresponds to about 3.5 min). The vertical lines at T_1 and T_2 denote time points when the majority of cells had a complete mitotic spindle and when they were in the anaphase A, respectively (after published data [4]). The increased activity at the period 4 might correspond to formation of the mitotic spindle, 10 to metaphase, and 12 to anaphase A. However, the number of measurements is too low and adequate control measurements were not performed. The measurement might be also distorted by changed electric parameters of the medium around detection contacts caused by cellular activity. Temperature in the shielded box during measurements was $28 \pm 2^\circ\text{C}$. Our sensor and input amplifier were not integrated and a spectrum analyzer Agilent E4448A was used.

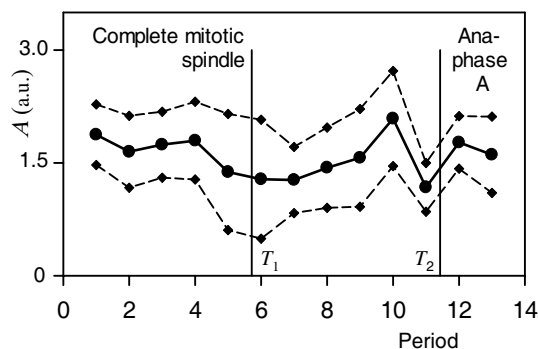


Figure 5: Experimental verification of the method. Electric signals detected by the sensor at yeast cells (synchronized in the M phase) in the cell suspension. Amplitude in arbitrary units versus time in 3.5 min periodss.

5. CONCLUSION

Energy supply to living systems excites a state far from thermodynamic equilibrium which is an essential condition of life. EMG field generated by electric polar vibrations in microtubules can be measured by a low noise microelectronic system containing a sensor detecting cellular signal, integrated with an input amplifier, and a real time spectrum analyser controlled by a computer. We have built a preliminary experimental setup and experimentally verified the method.

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