

Roll of Temperature in Living Systems Analysed Using the Resonant Recognition Model

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Abstract: Temperature plays some significant role in biological processes. Electromagnetic energy could be related to temperature. Here, we have established the relationship between temperature role in living biological processes and Resonant Recognition Model, which proposes that proteins specific biological activity is based on electromagnetic resonant energy transfer.

Keywords: Biological Temperature, Bioelectromagnetism, Resonant Recognition Model

Introduction

It is well known that temperature plays significant role in biological functioning of living organisms. Besides the fact that most of proteins important for controlling the living processes cannot function above temperature of about 44°C due to protein denaturalisation, many other temperature related biological processes are not well understood. For example, it is not yet well understood why mammalian organisms need specific temperature of about 37°C to function and grow properly, why sex of reptile eggs is very finely defined by environmental temperature or why function of faulty CFTR protein with deletion at F508 can be restored at specific temperature of about 28°C, etc. Here, we try to explain the temperature role in living processes within organisms, using the previously established Resonant Recognition Model (RRM) [1-3], which proposes that proteins specific biological activity and selective interactions are based on electromagnetic resonant energy frequencies specific for each biological function. This electromagnetic energy could be related to temperature and we have established here this possible relationship.

There is general relationship between different electromagnetic radiation frequencies and temperature, so called Wien's displacement law, which states that the peak wavelength of electromagnetic radiation is inversely proportional to temperature, and the peak frequency of electromagnetic radiation is directly proportional to temperature [4,5]. We used this proportionality to find the relationship between RRM frequency characterizing the different protein biological functions and temperature that can influence these functions.

Methods

Resonant Recognition Model (RRM)

The RRM is based on the findings that certain periodicities within the distribution of energy of delocalised electrons along protein/DNA/RNA molecule are critical for protein/DNA/RNA biological function and/or interaction with their targets [1-3]. If charge transfer through these macromolecules is introduced, then charge moving through macromolecular backbone can produce electromagnetic radiation, absorption and resonance with spectral characteristics corresponding to the energy distribution along macromolecule [1-3,6,7].

The RRM enables the calculation of these spectral characteristics, by assigning each amino acid within the protein sequence a physical parameter representing the energy of delocalised electrons of each amino acid [1-3]. Comparing Fourier spectra for this energy distributions by using cross-spectral function, it has been found that proteins sharing the same biological function/interaction share the same periodicity (frequency) within energy distribution along the macromolecule [1-3]. Furthermore, it has been shown that interacting proteins and their targets share the same characteristic frequency but have opposite phase at that characteristic frequency [1-3,8]. Thus, it has been proposed that the RRM frequencies characterise, not only general function, but also recognition and interaction between the particular macromolecule and its target, which then can be considered to be resonant recognition. This could be achieved with resonant energy transfer between the interacting macromolecules through oscillations of physical field, which is electromagnetic in nature. Since there is evidence that proteins and DNA have certain conducting or semi-conducting properties, charge moving through the macromolecular

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backbone and passing different energy stages, caused by different side groups, can produce sufficient conditions for specific electromagnetic radiation or absorption. The frequency ranges of this radiation depend on the charge velocity. The RRM proposes that the charge is traveling through the protein backbone at the estimated velocity of $7.87 \times 10^5 \text{ m/s}$ [1-3]. For this velocity and with the distance between amino acids in protein molecule of 3.8 \AA , the frequency of protein interactions was estimated to be in the range between 10^{13} Hz and 10^{15} Hz [1-3]. Therefore, the estimated frequency range for amino acid macromolecules includes infra-red, visible and ultra-violet light. This idea has been supported by number of published experimental results including [1-3]: laser light growth promotion of cells, chymotrypsin activation achieved by laser light radiation, activation of highly homologous plant photoreceptors which, although being very homologous, absorb different wavelengths of light and photo activated proteins, e.g. rhodopsin, flavodoxin, etc. Based on these examples, the strong linear correlation between electromagnetic wavelengths and RRM frequencies has been established with the slope factor of $K=201$ [1-3]. This correlation can be represented as following:

$$\lambda = K / \text{frm}$$

where λ is the wavelength of light radiation in nanometres (nm), which can influence particular biological process, frm is RRM numerical frequency and K is coefficient of this linear correlation.

This formula has been also tested experimentally on L-Lactate Dehydrogenase activity [9], on experimental measurements of photon emission from dying melanoma cells [10], on photon emission from lethal and non-lethal Ebola strains [11], as well as on classic signalling pathway, JAK-STAT composed of nine sequential protein interactions [12]. Even more, the RRM model, for the first time, explains how and why external light can influence human health exemplified in the treatment of Crigler-Najjar syndrome by blue light [13].

As on one hand, temperature is important for activation of certain biological processes and on the other hand, we found that certain wavelengths of electromagnetic radiation are also important for activation of proteins and related biological processes, we made here an attempt to correlate biologically important temperatures with related RRM frequencies (electromagnetic wavelengths).

Results and Discussion

Here, we have analysed the certain number of examples where temperature is critical for activation of biological processes and compared them with characteristic RRM frequencies for the same processes.

Cystic Fibrosis

The cystic fibrosis is genetic disease characterised by build-up of thick mucus in the lungs, which causes difficulties in breathing. This disease is caused by mutations in CFTR proteins. The most common mutation that causes the cystic fibrosis is deletion of amino acid, phenylalanine (F) at 508th position of the CFTR protein. However, the number of experiments in cell cultures have shown that specific temperature of about 28°C can restore effect of F508 deletion in CFTR proteins [14-16]. The fact that temperature can restore the function of mutated proteins gave us an idea that activity of CFTR proteins can be manipulated by energy levels in the environment, which might be done using electromagnetic radiation. To understand such process, we analysed CFTR proteins and their mutants using the RRM approach [17].

We analysed twelve healthy CFTR proteins from UniProt database (Q00552, Q2QLE5, Q5U820, P26361, P13569, Q6PQZ2, Q00554, Q2QLA3, P35071, Q2IBF6, Q00555 and P34158) and found the most prominent common frequency at $f1=0.0444 \pm 0.0007$ with high signal-to-noise ratio of 863, as presented in Figure 1. This result indicates that frequency f1 is characterising CFTR protein's healthy activity. According to conversion formula between numerical RRM frequency into the electromagnetic wavelength in nanometres (nm) the frequency f1 corresponds to electromagnetic radiation of 4527 nm , which is within far infra-red spectrum.

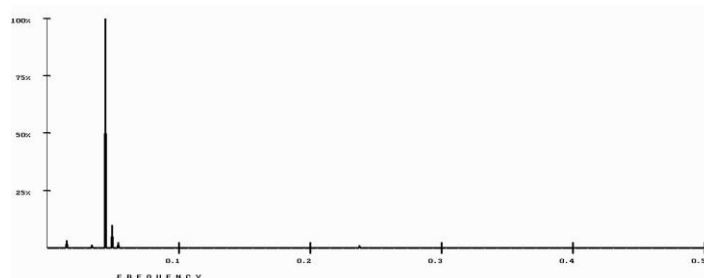


Figure 1. RRM cross-spectrum of twelve healthy CFTR proteins. The common characteristic frequency is at $f1=0.0444 \pm 0.0007$, with signal-to-noise ratio of 863. Frequency f1 represents electromagnetic radiation wavelength of 4527 nm .

When we analysed same twelve CFTR proteins, but with deletion F508, using the RRM, the same most prominent common frequency has been found at $f1=0.0444 \pm 0.0007$, but with much smaller signal-to-noise ratio of 686. This result indicates that mutated proteins have much lower amplitude at RRM characteristic frequency f1, indicating lower activity in mutated proteins and thus could explain why CFTR protein with F508 deletion is malfunctioning.

All these results are indicating that frequency f_1 is critical for normal healthy functioning of CFTR proteins. As specific temperature of about 28°C can restore the healthy function of mutated CFTR protein with F508 deletion, we propose that this temperature is related to RRM characteristic frequency for healthy functioning of CFTR proteins at $f_1=0.0444\pm 0.0007$ (4527nm).

Sex Determination in Alligators

Some reptiles including alligators have temperature dependant sex determination, where environmental temperature of the developing eggs determines the sex of new born babies. In the case of american alligators, eggs incubation at 33°C produces mostly males, while incubation at 30°C produces mostly females. It has been found that thermo-sensitive protein TRPV4 is crucial for male sex determination pathway at molecular level during thermal sex determination of the alligators [18]. Alligator TRPV4 protein is responsive to temperatures near to mid thirties and by inducing calcium ion influx can activate cell signalling, which is important for male development within the developing eggs [18].

To find out if there is relationship between sex determination temperature in alligators and corresponding RRM characteristic frequency for TRPV4 proteins, we have analysed alligator TRPV4 protein in tetramer form, as its active structure. When we analysed alligator TRPV4 protein as tetramer from reference [18], we found the most prominent common frequency at $f_2=0.1738\pm 0.0020$, as presented in Figure 2. According to conversion formula between numerical RRM frequency into the electromagnetic wavelength in nanometres (nm) the frequency f_2 corresponds to electromagnetic radiation of 1156nm, which is within infra-red spectrum.

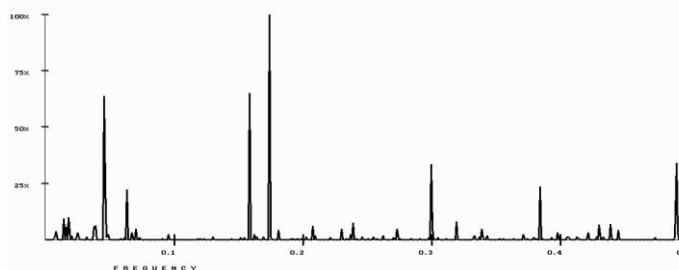


Figure 2. RRM cross-spectrum of alligator TRPV4 protein as tetramer. The common characteristic frequency is at $f_2=0.1738\pm 0.0020$. Frequency f_2 represents electromagnetic radiation wavelength of 1156nm.

Thus, we propose that frequency f_2 is characterising temperature related sex

determination and can be correlated to temperature of 33°C.

Heat Shock Proteins

The heat shock proteins (HSPs) are essential factor for cellular responses to hyperthermia and other environmental stressors. The transcription of HSPs is mainly controlled by heat shock transcription factor 1 (HSF1). It has been shown experimentally in cell culture that heat shock factors are produced using heat shock treatment at 43°C in water bath [19].

When we analysed four HSF1 proteins, from UniProt database (P38532, Q00613, Q08DJ8 and P38529), as trimers which is their active form [18], we found the most prominent common frequency at $f_3=0.4144\pm 0.0020$, as presented in Figure 3. According to conversion formula between numerical RRM frequency into the electromagnetic wavelength in nanometres (nm) the frequency f_3 corresponds to electromagnetic radiation of 485nm, which is within blue light spectrum.

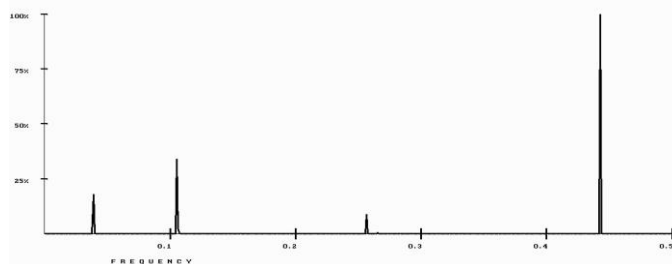


Figure 3. RRM cross-spectrum of four HSF1 proteins as trimers. The common characteristic frequency is at $f_3=0.4144\pm 0.0020$. Frequency f_3 represents electromagnetic radiation wavelength of 485nm.

Thus, we propose that frequency f_3 is characterising activation of heat shock proteins by HSF1 proteins and can be correlated to temperature of 43°C.

Growth Factor

In our previous extensive work [1-3,7], we have identified RRM characteristic frequency of $f_4=0.2929$ as the main characteristic frequency for the number of growth factors and thus we proposed that it is characterising general growth function in mammalian cells. It is also well known that temperature of about 37°C is optimal temperature for biological processes within mammalian cells, particularly for their growth. Thus, the temperature of 37°C can be related to general RRM characteristic frequency of $f_4=0.2929$ for mammalian cell growth.

Skin Temperature in Mammals

According to Wien’s displacement law, as described in introduction, one of the examples is that mammals with a skin temperature of about 300°K (27°C) emit pick radiation at around 1000nm within the far infra-red spectrum [4,5]. According to RRM conversion formula between wavelength of electromagnetic radiation and RRM frequency, as described in methods, this wavelength corresponds to RRM frequency of $f_5=0.0201$.

Temperature of Protein Denaturalisation

It is well known that proteins cannot naturally function above temperature of about 44°C due to protein denaturalisation. This temperature could be considered as the maximum for protein natural activity, without help of any chaperones and thus could be related to the maximum frequency of RRM spectrum, which is $f_{max}=0.5$.

Correlation between Temperature and RRM Frequencies

Here, we have presented number of very different biological processes that are related to temperature, including recovery of critical mutation within CFTR proteins related to cystic fibrosis, temperature induced sex determination in alligators, heat shock protein temperature characteristics, temperature induced growth, mammal skin temperature electromagnetic radiation, as well as temperature of protein denaturalisation. All these examples are related to RRM characteristic frequencies, either through RRM characteristics of relevant proteins or through electromagnetic radiation that can be related to RRM. When those biologically relevant temperatures are correlated with related RRM characteristic frequencies the striking linear correlation was found with correlation coefficient of over 0.99 and slope factor of 36.2 as presented in Table 1 and Figure 4.

Table 1. Correlation between temperature and RRM frequencies.

RRM Frequency	Temperature [°C]	Biological Effect
0.0444	28	CFTR proteins (cystic fibrosis)
0.1738	33	alligator sex determination (TRPV4)
0.4414	43	heat shock proteins (HSF1)
0.2929	37	mammalian cell growth
0.0201	27	mammalian skin temperature
0.5000	44	maximum RRM frequency / maximum protein functional temperature

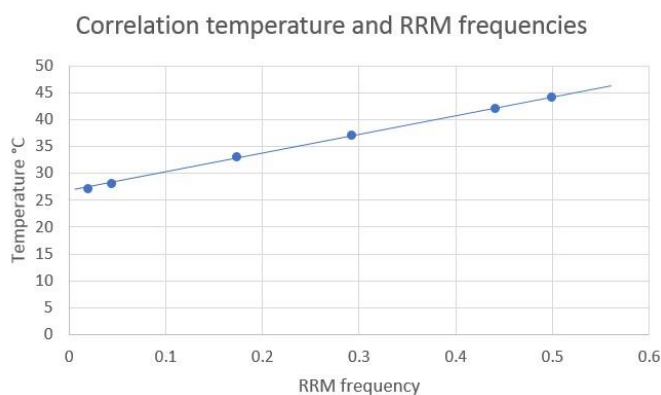


Figure 4. Graphical presentation of correlation between temperature and RRM frequencies.

Such striking correlation can support the idea that RRM frequencies are related to temperature, possibly through electromagnetic radiation that is related to protein functions and interactions. This relationship can explain why certain temperatures have specific effect on certain biological activities. If this relationship is universally true, it would mean that biological functions of proteins can be influenced, not only by electromagnetic radiations of specific frequencies, as has been shown previously within RRM, but also by specific temperatures.

Conclusion

We have presented here the number of examples where the specific temperature can influence the specific biological processes. When these temperatures are compared with the RRM characteristic frequencies for the same biological processes the striking linear correlation has been found with correlation coefficient of 0.99 and slope factor of 36.2. This correlation can indicate that there is definite relationship between electromagnetic frequencies that are characterising biological function of proteins and temperature that can influence the same function. Such findings can introduce completely new view into how biological functions of proteins can be influenced by not only electromagnetic radiation, but also temperature. This finding could open whole new area in treatment of diseases and health conditions.

Competing Interests

Authors declare they have no competing interests.

Contributions

All authors have contributed equally to this article.

References

- Cosic I. Macromolecular Bioactivity: Is it Resonant Interaction between Macromolecules? -Theory and Applications. *IEEE Trans on Biomedical Engineering*. 1994; 41:1101-1114.
- Cosic I. Virtual spectroscopy for fun and profit. *Biotechnology*. 1995; 13:236-238.
- Cosic I. The Resonant Recognition Model of Macromolecular Bioactivity: Theory and Applications. Basel: Birkhauser Verlag. 1997.
- Wikipedia. Wien's Displacement Law. 2018.
- Walker J. *Fundamentals of Physics*. 8th ed. John Wiley and Sons. 2008; 891.
- Cosic I, Cosic D, Lazar K. Is it possible to predict electromagnetic resonances in proteins, DNA and RNA?. *Nonlinear Biomedical Physics*. 2015; 3, doi: 10.1140/s40366-015-0020-6.
- Cosic I, Cosic D, Lazar K. Environmental Light and Its Relationship with Electromagnetic Resonances of Biomolecular Interactions, as Predicted by the Resonant Recognition Model. *International Journal of Environmental Research and Public Health*. 2016; 13(7):647, doi: 10.3390/ijerph13070647.
- Cosic I, Cosic D, Lazar K. Analysis of Tumor Necrosis Factor Function Using the Resonant Recognition Model. *Cell Biochemistry and Biophysics*. 2015; 11, doi: 10.1007/s12013-015-0716-3.
- Vojisavljevic V, Pirogova E, Cosic I. The Effect of Electromagnetic Radiation (550nm-850nm) on L-Lactate Dehydrogenase Kinetics. *Internat J Radiat Biol*. 2007; 83:221-230.
- Dotta BT, Murugan NJ, Karbowski LM, Lafrenie RM, Persinger MA. Shifting wavelength of ultraweak photon emissions from dying melanoma cells: their chemical enhancement and blocking are predicted by Cosic's theory of resonant recognition model for macromolecules. *Naturwissenschaften*. 2014; 101(2), doi: 10.1007/s00114-013-1133-3.
- Murugan NJ, Karbowski LM, Persinger MA. Cosic's Resonance Recognition Model for Protein Sequences and Photon Emission Differentiates Lethal and Non-Lethal Ebola Strains: Implications for Treatment. *Open Journal of Biophysics*. 2014; 5:35.
- Karbowski LM, Murugan NJ, Persinger MA. Novel Cosic resonance (standing wave) solutions for components of the JAK-STAT cellular signalling pathway: A convergence of spectral density profiles. *FEBS Open Bio*. 2015; 5:245-250.
- Cosic I, Cosic D. The Treatment of Crigler-Najjar Syndrome by Blue Light as Explained by Resonant Recognition Model. *EPJ Nonlinear Biomedical Physics*. 2016; 4(9), doi: 10.1140/epjnbp/s40366-016-0036-6.
- Gomes-Alves P, Neves S, Coelho AV, Penque D. Low Temperature Restoring Effect on F508del-CFTR Misprocessing: A Proteomic Approach. *J Proteomics*. 2009; 73(2):218-230, doi: 10.1016/j.jprot.2009.09.001.
- Wilke M, Bot A, Jorna H, Scholte BJ, de Jonge HR. Rescue of Murine F508del CFTR Activity in Native Intestine by Low Temperature and Proteasome Inhibitors. *PLOSOne*. 2012; doi: 10.1371/journal.pone.0052070.
- Rennolds J, Boyaka PN, Bellis SL, Cormet-Boyaka E. Low Temperature Induces the Delivery of Mature and Immature CFTR to the Plasma Membrane. *Biochemical and Biophysical Research Communications*. 2008; 366(4):1025-1029, doi: 10.1016/j.bbrc.2007.12.065.
- Cosic I, Paspaliaris V, Cosic D. Biophysical Insights into Cystic Fibrosis Based on Electromagnetic Resonances in CFTR Proteins. *International Journal of Sciences*. 2019; 8(9):1-8, doi: 10.18483/ijSci.2148.
- Yatsu R, Miyagawa S, Kohno S, Saito S, Lowers RH, Ogino Y, Fukuta N, Katsu Y, Ohta Y, Tominaga M, Guilete LJ Jr, Iguchi T. TRPV4 Associates Environmental Temperature and Sex Determination in the American Alligator. *Scientific Reports*. 2015; 5:18581, doi: 10.1038/srep18581.
- Wang HY, Fu JCM, Lu PJ. Hyperthermia Stress Activates Heat Shock Protein Expression via Propyl Isomerase 1 Regulation with Heat Shock Factor 1. *Mol Cell Biol*. 2013; 33(24):4889-4899.