

## Decoding Protein/DNA Functions Through Frequencies and Resonances

Within last decades there have been enormous developments in the area of biotechnology and drug design. Millions of protein/DNA structures and functions have been discovered and classified and now even the whole human genome has been deciphered. Although, we know all of these protein and DNA structures and functions, we still do not know the language of how biological function is written within the sequence of amino acids and nucleotides. Without this knowledge it is very difficult to design *de novo* proteins, peptides or DNA fragments with desired biological function and activity. Thus, peptides/protein drug design technology is tapping in the dark by randomly selecting sequences and performing thousands of tests in an attempt to design drugs with desired biological function. So, there is a need for an approach that will provide an understanding of how biological function is imbedded within the sequence of amino acids and nucleotides, with the aim to find out the critical selective parameters that drives their interactions within biological processes. There have been a number of attempts to use information technology approaches to identify such critical parameters, but without much success, as there was no meaningful physical and biological background in these approaches. Here, we present our own biophysical and mathematical approach, the Resonant Recognition Model (RRM). The RRM is a biophysical and mathematical approach, which identifies the critical parameters that drives protein/DNA selective interactions within biological processes using frequencies and resonances. The RRM has already been developed and tested experimentally over the last few decades and its applications are now being commercialised through Tithon Biotech Inc.

The selectivity and specificity of biological processes is driven by the information contained within linear macromolecules: DNA and proteins. While information in DNA is written within the long sequences using different combinations of four different nucleotides, information in proteins is also written within long sequences, but using different combinations of twenty different amino acids. While DNA carries the complete backup information of any organism, proteins are macromolecules that read the necessary parts of DNA information to perform all selective biological activity through a number of very specific interactions. The RRM model proposes that macromolecular selective interactions are based on electromagnetic resonant energy transfer between macromolecules in the range of infra-red, visible and ultra-violet light.

The RRM is based on the findings that certain periodicities within the distribution of energy of free electrons along protein/DNA molecule are critical for protein/DNA biological function and/or interaction with their targets. If charge transfer through these macromolecules is introduced, then charge moving through the macromolecular backbone can produce electromagnetic radiation, absorption and resonance with frequency characteristics corresponding to the periodicities in energy distribution. Furthermore, it has been shown that interacting proteins and their targets share the same characteristic frequency but have opposite phase at that characteristic frequency. 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. The whole RRM model can be graphically presented in Figure 1, where extra cellular proteins can interact with cell membrane receptors at one frequency and then the activated cell membrane receptor can interact with intra cellular proteins at the same frequency or some other frequency and so on in cascade along a whole functional pathway, sometimes all the way up to interaction with DNA.

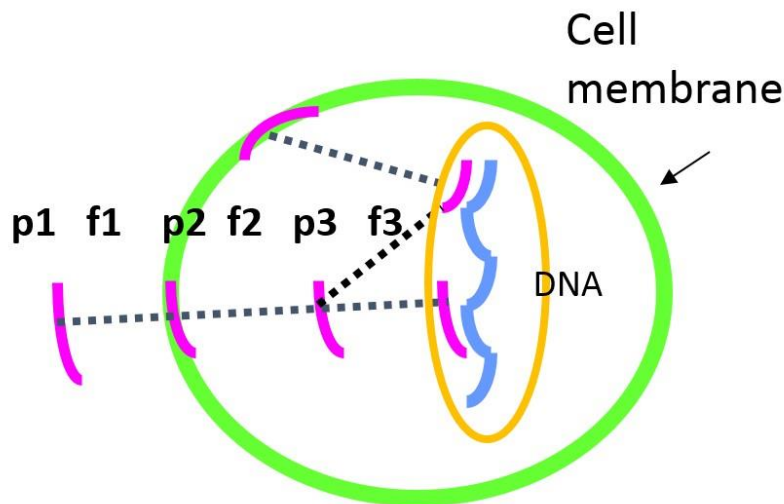


Figure 1. Graphical presentation of the RRM model.

To support the idea, that protein/DNA interactions are based on resonant electromagnetic energy transfer between interacting macromolecules, the RRM computational predictions have been compared with a number of published experimental results including: laser light cell growth promotion, chymotrypsin activation, activation of plant photo receptors and photo activated proteins. The RRM concept has been also experimentally tested by influencing L-Lactate Dehydrogenase activity with electromagnetic radiation of predicted frequency. This concept has also been tested independently on experimental measurements of photon emission from dying melanoma cells, on photon emission from lethal and non-lethal Ebola strains, as well as on classic signalling pathway, JAK-STAT composed of nine sequential protein interactions. 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.

Keeping all this in mind, it is proposed that the RRM concept is an excellent predictor for proteins and DNA functions, selective interactions, biological processes and pathways in living cells. By applying the RRM, it is possible to identify and calculate relevant frequencies critical for resonant activation of specific biological activities of proteins and DNA. In our previous work, we have calculated a large number of specific frequencies for different protein and DNA biological functions and interactions, as presented in Figure 2.

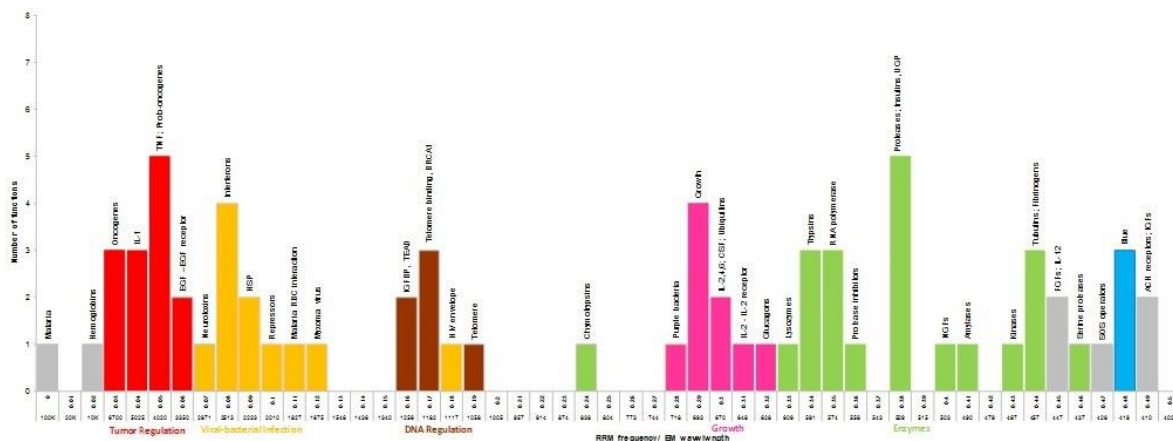


Figure 2. Number of functional groups within each RRM frequency range of 0.01. X axis represents RRM frequencies in increments of 0.01, as well as corresponding electromagnetic frequencies in nm. Y axis represents the number of functional groups. Names of functional groups are written on the top of each bar. Functional super families are differently coloured and labelled below the X axis.

Identifying the characteristic frequency of a particular protein biological function, creates the possibility to predict which amino acids prevail in the sequence and predominantly contribute to this frequency and consequently to the observed function. Even more, when the characteristic RRM frequency for desired protein biological function is identified, then it is possible to design *de novo* peptides/proteins using this frequency component and consequently achieving desired biological function. This RRM design approach has already been successfully applied and experimentally tested in design of fibroblast growth factor analogue, HIV envelope protein analogue and peptide to mimic myxoma virus oncolytic function.

With all these research results in mind, it is obvious that the biophysical, mathematical, RRM approach is not only excellent in analysing protein/DNA functions and interactions but can also be used in targeted, rational, *de novo* peptide/protein drug design, as well as influencing health conditions using specific electromagnetic radiation. By applying the RRM approach for cell membrane bound receptors and their biological functions with the scientists at Tithon Biotech Inc, a number of potential peptide drugs have been designed and are about to be tested to combat glaucoma, fibrosis, osteoporosis, autoimmune disease and cancer, as well as nanophotonic particles that resonate with RRM characteristic frequency, that are being tested to demonstrate the ability to stimulate both plant and fish growth. Some preliminary experiments on plant growth, based on nanophotonic particles designed via the RRM approach, have yielded fascinating results, as can be observed with the photograph of tomatoes, presented in Figure 3.



Figure 3. The four tomatoes at the bottom were picked from a plant that was sprayed with nanophotonic particles and the one at the top was taken from a plant that was not sprayed. The top tomato is about 7 cm in diameter. All plants were grown under the same environmental parameters, soil and watering conditions. Nanophotonic particles were sprayed three times a week on the leaves of the plant, yielding the four tomatoes shown at the bottom.

**Key Words:** protein/DNA structure function; frequencies and resonances in macromolecules; peptide/protein drug design.

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## Relevant References

1. Cosic I: Macromolecular Bioactivity: Is it Resonant Interaction between Macromolecules? - Theory and Applications, IEEE Trans on Biomedical Engineering, 1994; 41, 1101-1114.
2. Cosic I: Virtual spectroscopy for fun and profit, Biotechnology, 1995; 13, 236-238.
3. Cosic I: The Resonant Recognition Model of Macromolecular Bioactivity: Theory and Applications, Basel: Birkhauser Verlag, 1997.
4. Pirogova E, Cosic I: Examination of amino acid indexes within the Resonant Recognition Model, Proc. of the 2nd Conference of the Victorian Chapter of the IEEE EMBS, 2001; 124-127.
5. 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.
6. Cosic I, Lazar K, Cosic D: Cellular Ageing - Telomere, Telomerase and Progerin analysed using Resonant Recognition Model, MD-Medical Data, 2014; 6(3), 205-209.
7. Krsmanovic V, Biquard JM, Sikorska-Walker M, Cosic I, Desgranges C, Trabaud MA, Whitfield JF, Durkin JP, Achour A, Hearn MT: Investigation Into the Cross-reactivity of Rabbit Antibodies Raised against Nonhomologous Pairs of Synthetic Peptides Derived from HIV-1 gp120 proteins, J.Peptide Res, 1998; 52(5), 410-412.
8. Cosic I, Lazar K, Cosic D: Prediction of Tubulin resonant frequencies using the Resonant Recognition Model (RRM), IEEE Trans. on NanoBioscience, 2015; 12, 491-496, doi: 10.1109/TNB.2014.2365851.
9. 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.
10. 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.

11. 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.
12. 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.
13. 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.
14. 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.
15. 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.
16. Pirogova E, Istivan T, Gan E, Cosic I: Advances in methods for therapeutic peptide discovery, design and development, *Current Pharmaceutical Biotechnology*, Bentham Science Publishers Ltd, Netherlands ISSN: 1389-2010, 2011; 12(8), 1117-1127.
17. Cosic I, Pirogova E: Bioactive Peptide Design using the Resonant Recognition Model, *Nonlinear Biomedical Physics*, 2007; 1(7), doi: 10.1186/1753-4631-1-7.
18. Cosic I, Drummond AE, Underwood JR, Hearn MTW: In vitro inhibition of the actions of basic FGF by novel 16 amino acid peptides, *Molecular and Cellular Biochemistry*, 1994; 130, 1-9.
19. Hearn MTW, Biquard JM, Cosic I, Krsmanovic V: Peptides Immunologically related to proteins expressed by a viral agent, having a sequence of amino acids ordered by means of protein informational method, *US Patent* 6, 294, 174, 2001.
20. Achour A, Biquard JM, Krsmanovic V, M'Bika JP, Ficheux D, Sikorska M, Cozzone AJ: Induction of Human Immunodeficiency Virus (HIV-1) Envelope Specific Cell-Mediated Immunity by a Non-Homologous Synthetic Peptide, *PLoS ONE*, 2007; 11, 1-12, doi: 10.1371/journal.pone.0001214.
21. Pirogova E, Istivan T, Gan E, Cosic I: Advances in Methods for Therapeutic Peptide Discovery, Design and Development, *Current Pharmaceutical Biotechnology*, 2011; 12, 1117-1127.
22. Almansour N, Pirogova E, Coloe P, Cosic I, Istivan T: Investigation of cytotoxicity of negative control peptides versus bioactive peptides on skin cancer and normal cells: a comparative study, *Future Medicinal Chemistry*, 2012; 4(12), 1553-1565.
23. Istivan T, Pirogova E, Gan E, Almansour N, Coloe P, Cosic I: Biological effects of a De Novo designed myxoma virus peptide analogue: Evaluation of cytotoxicity on tumor cells, *Public Library of Science (PLoS) ONE*, 2011; 6(9), 1-10.