

CHD2 Protein Malfunction Causing Neurodevelopmental Disorders and Epilepsy as Analyzed by Resonant Recognition Model

Irena Cosic ^{1,*}, Carolyn Mary Harris ² and Drasko Cosic ¹

¹ AMALNA Consulting, R&I Department, Black Rock, 3193, Australia.

² Independent Researcher, BMBS, FRACGP, Sealcliff, 5049, Australia.

International Journal of Science and Research Archive, 2025, 17(02), 574–579

Publication history: Received on 06 October 2025; revised on 13 November 2025; accepted on 15 November 2025

Article DOI: <https://doi.org/10.30574/ijrsra.2025.17.2.3080>

Abstract

Mutations in CHD2 gene are strongly associated with developmental and epileptic encephalopathy, characterized by early-onset, drug-resistant seizures and neurodevelopmental impairments. In response to the urgent need for novel interventions, we have utilized here, the Resonance Recognition Model (RRM), a biophysical framework that identifies and targets specific protein resonances associated with these pathological conditions. Our analysis revealed a consistent association between CHD2 protein activity and a specific far-infrared resonance, at RRM frequency of 0.0005 corresponding to wavelength of 0.2 to 0.4mm, suggesting that lack of this frequency (wavelength) may represent a biophysical signature of the dysfunctional protein. Based on these results unveiling resonance signature, we also hypothesize potential therapeutic strategies.

Keywords: Epilepsy; Neurodevelopmental impairments; CHD2 protein; Molecular modeling; Resonant Recognition Model.

1. Introduction

The impact of catastrophic epilepsies on the people with them and their families is devastating. These severe neurological disorders, often characterized by early onset, drug resistance, and profound cognitive and developmental impairments, pose immense challenges to both clinical management and quality of life. Among them, CHD2-related epileptic encephalopathies represent a particularly complex subset, marked by photosensitivity, intellectual disability, and frequent seizures that are refractory to conventional treatments [1].

CHD2 (Chromodomain Helicase DNA-binding protein 2) protein mutations have been identified as a significant cause of early-onset epileptic encephalopathies. A landmark study led by Professor Ingrid Scheffer and colleagues delineated the phenotype of CHD2 myoclonic encephalopathy, highlighting its association with self-induced seizures and exquisite photosensitivity [2]. This research has been pivotal in understanding the clinical spectrum and genetic underpinnings of CHD2-related disorders, paving the way for targeted therapeutic approaches.

In response to the urgent need for novel interventions, we have utilized the Resonance Recognition Model (RRM), a biophysical framework that identifies and targets specific protein resonances associated with pathological conditions. The RRM operates on the principle that protein interactions and functions can be modulated through electromagnetic frequencies corresponding to their unique resonance signatures. By applying this model to CHD2 epileptic encephalopathies, the authors aim to disrupt the pathological resonance patterns implicated in seizure generation and neuronal dysfunction.

* Corresponding author: Irena Cosic

This paper presents the theoretical foundation, computational methodology, and preliminary findings of RRM-based interventions targeting CHD2-related epileptic mechanisms. It explores the potential of resonance-guided modulation as a non-invasive, frequency-specific therapeutic avenue, offering hope for improved outcomes in a condition where conventional pharmacology has often fallen short.

2. Materials

For this research we have used CHD2 protein sequences from healthy subjects as follows: A0A8V0Z847, A0A9L0TTW1, A0A9V1G609, G3MXX3, A0A0B8RW01, A0A096MJY0, O14647 and E9PZM4, from UniProt database. The mutations and deletions related to neurodevelopmental disorders and epileptic seizures are taken from O14647-CHD2_HUMAN from UniProt database, as presented in Table 1.

Table 1 Critical mutations and deletions in human CHD2 protein.

VARIANT ID	POSITION(S)	CHANGE
VAR_078614	112-1828	missing
VAR_078615	121-1828	missing
VAR_070209	548	W>R
VAR_070210	823	L>P
VAR_085039	178-1828	missing

2.1. Methods: Resonant Recognition Model

Here, we utilized the Resonant Recognition Model (RRM), which is innovative approach using knowledge from quantum physics, biochemistry and mathematics to analyze protein biological functions/interactions [3-7]. RRM is based on the findings that certain periodicities within the distribution of energy of delocalized electrons along a protein and DNA/RNA molecules are critical for their biological function and/or interaction with their targets [3-7]. If charge transfer through these macromolecules is introduced, then the charge moving through the macromolecular backbone can produce electromagnetic radiation, absorption and resonance with spectral characteristics corresponding to the energy distribution [3-8].

The RRM model enables calculation of these spectral characteristics, by assigning each amino acid a physical parameter representing the energy of delocalized electrons of each amino acid. In such way the energy distribution along the protein macromolecule is determined. Comparing Fourier spectra for these energy distributions, using cross-spectral function, it has been found that proteins sharing the same biological function/interaction share the same periodicity (frequency) within the energy distribution along the macromolecule [3-9]. Furthermore, it has been shown that interacting proteins and their targets share the same characteristic frequency. Thus, it has been proposed that the RRM frequencies characterize not only a general function, but also recognition and interaction between the macromolecules and their targets, which can then be considered to be resonant recognition. This could be achieved with resonant energy transfer between the interacting macromolecules through oscillations of a physical field, which is electromagnetic in nature. Once when the frequency of certain biological functions and/or interaction is identified it is proposed that by applying this frequency we can either mimic or interfere with the particular biological activity. This idea has been tested on number of proteins and DNA examples [10-15] including activation of L-Lactate Dehydrogenase [10], DNA-protein interaction at distance [11], on photon emission from dying melanoma cells [12], on photon emission from lethal and non-lethal Ebola strains [13], as well as on classic signaling pathway JAK-STAT [14]. Even more, the RRM for the first time explains how and why external blue light can be used in the treatment of Crigler-Najjar syndrome [15].

In addition, once when characteristic frequency of certain biological functions is identified the RRM is capable to design *de novo* bioactive peptides with desired biological function [3-7,16-20]. This design of *de novo* peptides with desired biological function could be used for design of novel peptidic drugs with targeted biological function. This concept has been already successfully applied in a number of examples for design of: peptide that can prevent resistant bacteria [16], peptide that can prevent SARS-CoV-2 virus entry into the host cells via ACE2 receptor [17], peptide to mimic myxoma virus oncolytic function [18], HIV envelope protein analogue [19], FGF analogue [20].

All these findings could be used, not only to understand biological processes and resonances in biomolecules, but also to influence these biological processes using either radiation or design of related molecules and conductive particles.

We have here applied the RRM model to CHD2 proteins from healthy subjects and to their mutations/deletions that are primarily responsible for mild to severe neurodevelopmental disorders and often accompanied by epileptic seizures [1,2]. The aim of this study is to find out if there is RRM frequency characterizing CHD2 biological function in DNA repair and transcriptional control and consequently to propose possible treatments.

3. Results

When all available CHD2 proteins from healthy subjects have been analyzed, it has been found indeed that they all have only one common RRM frequency of $f=0.0005$, as presented in Figure 1. According to the RRM this frequency is characterizing CHD2 biological function in DNA repair and transcriptional control.

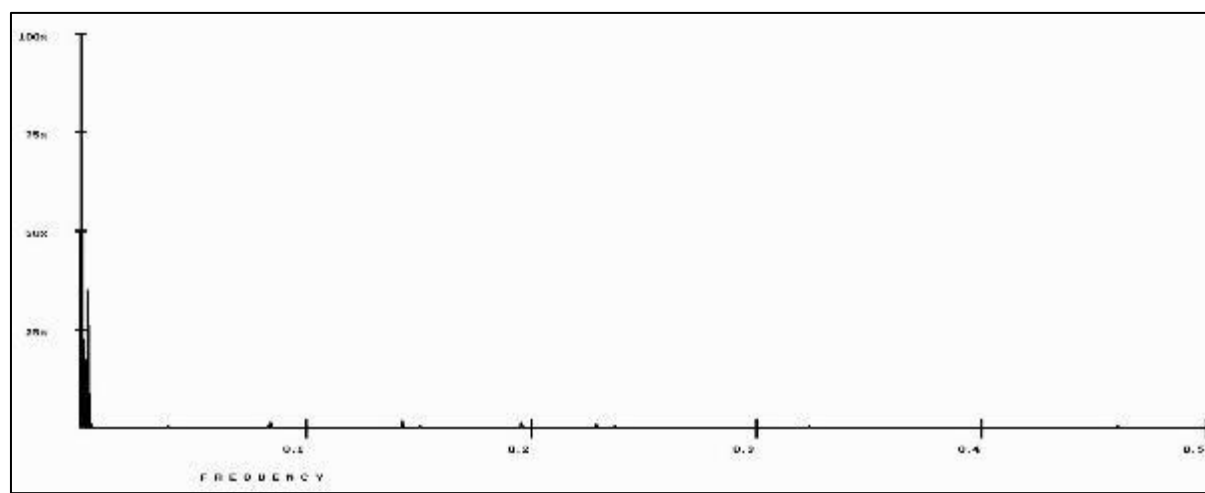


Figure 1 Cross spectrum of all CHD2 proteins from healthy subjects showing the characteristic common RRM frequency at $f=0.0005$.

This CHD2 RRM characteristic frequency represent electromagnetic frequency in the range of 0.2 to 0.4mm in wavelength [3-5]. This frequency is in a very far infrared spectrum. According to RRM principles, it can be proposed that this frequency is characterizing the normal function of CHD2 proteins in DNA repair and transcriptional control.

Mutations and deletions in the CHD2 gene are primarily responsible for mild to severe neurodevelopmental disorders and often accompanied by epileptic seizures. To check if calculated RRM frequency of $f=0.0005$ is related to CHD2 biological function, we have analyzed proteins with mutations and deletions from individuals with related health problems, as presented in Table 1. When CHD2 proteins with mutations and deletions from individuals with related health problems have been analyzed, it has been shown that CHD2 RRM characteristic frequency disappear from the spectrum, as presented in Figure 2. This result can explain the possible reason for elimination of CHD2 biological function in proteins with mutations and deletions, causing the related disorders.

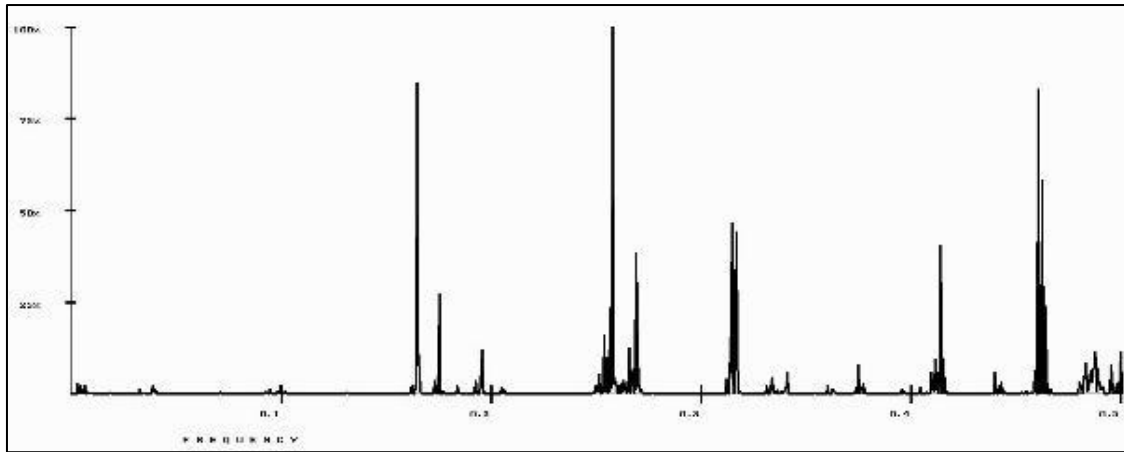


Figure 2 Cross spectrum of CHD2 proteins with mutations and deletions showing lack of characteristic RRM frequency at $f=0.0005$.

On the other hand, the analysis of large segments of CHD2 protein that are missing in affected individuals have shown that the previously identified characteristic RRM frequency of $f=0.0005$ for normal functioning is preserved, as presented in Figure 3.

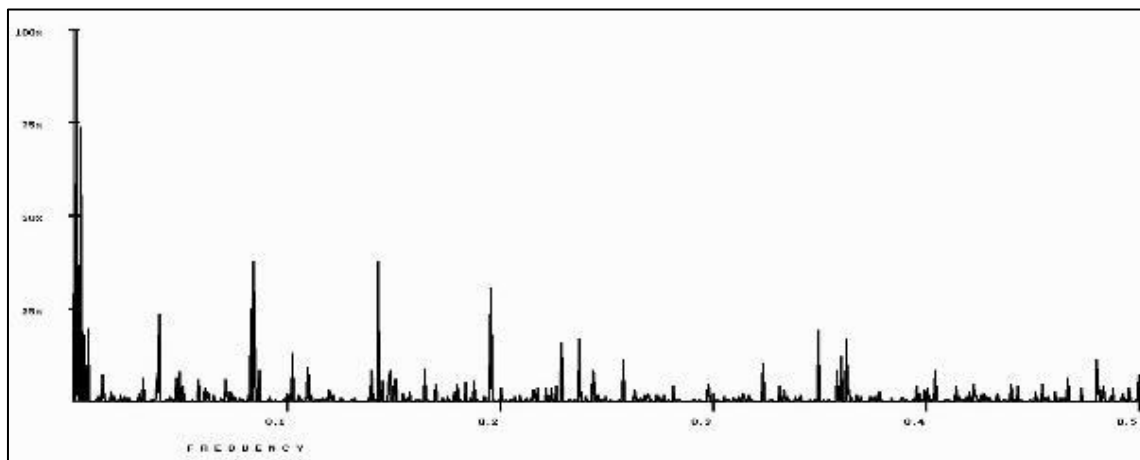


Figure 3 Cross spectrum of large segments of CHD2 proteins that are missing in affected individuals showing preservation of characteristic RRM frequency at $f=0.0005$.

All results above are confirming that RRM frequency of $f=0.0005$ is characterizing the normal function of CHD2 protein. In addition, it could be postulated that this function is predominantly in the second part of the CHD2 protein, after amino acid at position 178, which is missing in affected individuals.

4. Discussion

The Resonance Recognition Model (RRM), pioneered by I. Cosic, offers a compelling framework for understanding protein interactions through electromagnetic resonance frequencies. In this study, we applied RRM model to the CHD2 protein, which is chromodomain helicase DNA-binding protein 2, that is critical regulator of chromatin remodeling and neuronal gene expression. Mutations and deletions in CHD2 are strongly associated with developmental and epileptic encephalopathy (DEE), characterized by early-onset, drug-resistant seizures and neurodevelopmental impairments.

Our analysis revealed a consistent association between CHD2 protein activity and a specific far-infrared resonance RRM frequency of 0.0005 corresponding to wavelength of 0.2 to 0.4mm, suggesting that lack of this frequency (wavelength) may represent a biophysical signature of the dysfunctional protein. This finding aligns with RRM's premise that functional proteins exhibit unique electromagnetic frequencies, and that disruptions in these frequencies may correlate with disease states.

We hypothesize here two potential therapeutic strategies based on this resonance signature:

- **Infrared Frequency Modulation:** Delivering targeted far-infrared radiation at 0.2 to 0.4mm wavelength, which corresponds to RRM frequency of 0.0005 may restore resonance balance in DNA repair and transcriptional control. However, engineering a device capable of emitting such far infra-red frequency presents significant technical challenges.
- **Resonance-Matched Protein Therapy:** Alternatively, synthesizing a protein with a matching resonance profile could offer a biologically integrated solution. By delivering this engineered protein to individuals with CHD2 mutations and deletions, it would be possible to compensate for the dysfunctional native protein, potentially reducing seizure frequency and improving neurodevelopmental outcomes.

These approaches represent a paradigm shift in treating genetic epilepsies, not by targeting symptoms or conventional molecular pathways, but by restoring resonance coherence at the quantum-biological level. Further research is needed to validate the therapeutic efficacy of resonance-matched interventions, including *in vitro* and *in vivo* models, safety profiling, and delivery mechanisms.

Our findings open new avenues for precision bioelectromagnetic therapy in neurogenetic disorders and underscore the potential of RRM model as a diagnostic and therapeutic tool in personalized medicine.

5. Conclusion

In conclusion, our study has demonstrated the potential of the Resonance Recognition Model (RRM) in understanding and addressing the pathological mechanisms underlying CHD2-related developmental and epileptic encephalopathies (DEE). By identifying a specific far-infrared resonance RRM frequency of 0.0005, we have uncovered a biophysical signature associated with the normal function of CHD2 proteins in DNA repair and transcriptional control.

Our findings suggest that disruptions in this resonance frequency due to CHD2 mutations and deletions may contribute to the severe neurodevelopmental and epileptic manifestations observed in affected individuals. This insight opens up new avenues for therapeutic interventions, including the potential use of targeted far-infrared radiation and resonance-matched protein therapies to restore normal CHD2 function.

The application of RRM in this context represents a paradigm shift in the treatment of genetic epilepsies, moving beyond conventional pharmacological approaches to explore the quantum-biological level of protein interactions. Further research is needed to validate these therapeutic strategies and to develop practical methods for their implementation in clinical settings.

Overall, our study highlights the importance of interdisciplinary approaches in tackling complex genetic disorders and underscores the potential of RRM as a diagnostic and therapeutic tool in personalized medicine. By continuing to explore the resonance properties of proteins, we can pave the way for innovative treatments that improve the lives of individuals with CHD2-related DEE and other neurogenetic disorders.

Compliance with ethical standards

Disclosure of conflict of interest

Authors declare they have no competing interests.

Authors Contributions

Conceptualization, I.C., D.C. and C.H.; Methodology, I.C. and D.C.; Writing—Original Draft Preparation—Review and Editing, I.C., D.C. and C.H.

Funding

This research received no external funding.

References

- [1] Thomas RH, Zhang LM, Carvill GL, Archer JS, Heavin SB, Mandelstam SA, Craiu D et al.: CHD2 Myoclonic Encephalopathy Is Frequently Associated with Self-Induced Seizures. *Neurology*, 2015; 84(9), doi: 10.1212/WNL.0000000000001305.
- [2] Wilson MM, Henshall DC, Byrne SM, Brennan GP: CHD2-Related CNS Pathologies. *Int J Mol Sci.*, 2021; 8, 22(2), 588, doi: 10.3390/ijms22020588.
- [3] Cosic I: Macromolecular Bioactivity: Is it Resonant Interaction between Macromolecules? -Theory and Applications. *IEEE Trans on Biomedical Engineering*, 1994; 41, 1101-1114.
- [4] Cosic I: Virtual spectroscopy for fun and profit. *Biotechnology*, 1995; 13, 236-238.
- [5] Cosic I: The Resonant Recognition Model of Macromolecular Bioactivity: Theory and Applications. Basel: Birkhauser Verlag, 1997.
- [6] Cosic I: Resonant Recognition Model of Protein Protein and Protein DNA Recognition in Bioinstrumentation and Biosensors. ed by Wise D. Marcel Dekker Inc., New York, 1990; 475-510.
- [7] Cosic I, Cosic D: Macromolecular Resonances. In: Bandyopadhyay A., Ray K. (eds) *Rhythmic Oscillations in Proteins to Human Cognition. Studies in Rhythm Engineering*. Springer, Singapore, 2021; 1, 11-45, doi: 10.1007/978-981-15-7253-1_1.
- [8] 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.
- [9] Cosic I, Paspaliaris V, Cosic D: Analysis of Protein-Receptor on an Example of Leptin-Leptin Receptor Interaction Using the Resonant Recognition Model. *MDPI Appl. Sci.*, 2019; 9, 5169, doi:10.3390/app9235169.
- [10] Vojisavljevic V, Pirogova E, Cosic I: The Effect of Electromagnetic Radiation (550nm-850nm) on I-Lactate Dehydrogenase Kinetics. *Internat J Radiat Biol*, 2007; 83, 221-230.
- [11] Cosic I, Cosic D: DNA-Protein Interactions at Distance Explained by the Resonant Recognition Model. *International Journal of Sciences*, 2024; 13(11), 1-5, doi: 10.18483/ijSci.2805.
- [12] 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.
- [13] 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.
- [14] 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.
- [15] 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.
- [16] Mishra A, Cosic I, Loncarevic I, Cosic D, Fletcher HM. Inhibition of β -lactamase function by de novo designed peptide. *PLoS ONE*, 2023; 18(9), 1-15, doi: 10.1371/journal.pone.0290845.
- [17] Cosic I, Kuhar U, Krapez U, Slavec B, Cosic D, Loncarevic I: De Novo Designed Peptide to Prevent SARS-CoV-2 Interaction with ACE2 Receptor on Host Cells. *International Journal of Sciences*, 2022; 11(2), 1-8, doi: 10.18483/ijSci.2558.
- [18] 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.
- [19] Krsmanovic V, Biquard JM, Sikorska-Walker M, Cosic I, Desgranges C, Traubaud 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.
- [20] 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.