I dedicate this thesis to my beloved parents (Maa and Deuta), who have been my source of inspiration and my constant pillars of strength. I am forever indebted to them for all their sacrifices in making me what I am today.

To my loving parents………

Declaration

I hereby declare that the thesis entitled *"Inhibition approaches of Amyloid-β and α-Synuclein amyloidogenic aggregation: an In-silico study"* has been submitted to Tezpur University in the Department of Molecular Biology and Biotechnology under the School of Sciences for partial fulfillment for the award of the degree of Doctor of Philosophy in Molecular Biology and Biotechnology.

I am the sole author of this thesis. This is a true copy of an original work carried outby me including any required final revisions, as accepted by my examiners.

Further, I declare that no part of this work has been reproduced elsewhere for award of any other degree.

Date :   **Priyanka Borah**

Place: Tezpur University   **Registration No.: TZ154896 of 2015**

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CERTIFICATE OF THE PRINCIPAL SUPERVISOR

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All helps received by her from various sources have been duly acknowledged. No part of this thesis has been submitted elsewhere for award of any other degree/diploma.

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CERTIFICATE OF THE EXTERNAL EXAMINER AND ODEC

This is to certify that the thesis entitled *"**Inhibition approaches of Amyloid-β and α-Synuclein amyloidogenic aggregation: an In-silico study**"* submitted by Ms. Priyanka Borah to Tezpur University in the Department of Molecular Biology and Biotechnology under the School of Sciences in partial fulfillment of the requirement for the award of the degree of Doctor of Philosophy in Molecular Biology and Biotechnology has been examined by us on ………………………………… and found to be satisfactory

The committee recommends for the award of the degree of Doctor of Philosophy.

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Principal Supervisor   **External Examiner**
Date: **Date:**

Acknowledgements

*First and foremost, I bow down my head to the **almighty God** for good health, wellbeing and for blessing me with immense patience that were necessary to complete this journey of Ph.D. successfully.*

*I would not have been able to complete this degree without the support of numerous people, for which I would like to acknowledge their support. First, I would like to express my sincerest gratitude towards my supervisor **Dr. Venkata Satish Kumar Mattaparthi**, for taking a chance on me and giving me freedom in my research and for his consistent encouragement that I have received throughout the research work. Under his guidance, I successfully overcame many difficulties and learned a lot. He always kept faith in me and guided me through the right direction whenever I needed it the most. At the same time, his constructive criticism and constant vigilance inspired me to perform better. My deep gratitude goes to him for all his dedication and steadiness during the writing of the thesis. I whole-heartedly thank him for everything.*

*I would also like to thank **Prof. Robin Doley**, the Head of the Department of MBBT, Tezpur University, and my Doctoral Committee members – **Prof. S.K. Ray, Dr. R. Mukhopadhyay, and Dr. S. Dasgupta**, Department of MBBT, Tezpur University, for their insight, comments, and valuable suggestions during my Ph.D. tenure.*

*I would like to acknowledge all other **faculty members in the Department of MBBT, Tezpur University** for their help and encouragement and the **technical** and the **non-teaching staffs** of the Department for their technical support. I would like to take this opportunity to thank Tezpur University for*

providing me with the state of the art infrastructure and facilities for advanced research.

*No word would be enough for expressing my gratitude towards lab mates in MOMO Lab: **Mary Ba, Himakshi Ba, Airy Ba, Sushmita Di, P.K. Da, Dorothy and Chainee**, for their immense help and support in the lab works and personal time. Heartfelt thanks to all the project students (**Gariyoshi, Navamallika, Pallav, Krishna, Ambika, Barsha, Hrishikesh and Ayon**) for their help and support.*

*I would like to express my gratitude to my **batchmates and friends** for supporting me in many occasions during this work and for all the time we spent together.*

*I extend my sincere gratitude to the special person of my life, my best friend and my fiancé, **Sidharth**, for being the driving force of this journey with all his unwavering moral and emotional support both professionally and personally. I am deeply thankful to him for helping me in the toughest time of this tenure and for being a source of positivity throughout.*

*Above ground, my biggest thanks of all goes to my **mother** and my **father** for their fulltime support and unconditional love and for giving me a meaningful life. Love you both.*

I thank all those people who have helped me in some way or the other whose names I may have missed out.

Priyanka Borah

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LIST OF ABBREVIATIONS

Å	Angstrom
ACE	Atomic contact Energy
AD	Alzheimer's Disease
ALS	Amyotrophic Lateral Sclerosis
αS	Alpha Synuclein
AMBER	Assisted Model Building with EnergyRefinement
Aβ	Amyloid-Beta
APP	Amyloid Precursor Protein
BBB	Blood brain Barrier
BFE	Binding free energy
CHARMM	Chemistry at HARvard Macromolecular Mechanics
CNS	Central Nervous System
CircRNA	Circular RNA
CoM	Centre of Mass
CPPTRAJ	A rewrite of PTRAJ in C++
CTerm	C-Terminal
3-D	3-Dimensional
DALY	Diability Adjusted Life Years
DBS	Deep Brain Simulation
DNA	Deoxyribonucleic Acid
FAD	Familial Alzheimer's Disease
FF99SB	Force-field 99 Stony Brook
GAFF	General Amber force field
GB	Generalized Born
GBSA	Generalized Born Surface Area
HA	Human Albumin
IAPP	Islet amyloid polypeptide
IDP	Intrinsically Disordered Protein
IDPR	Intrinsically Disordered Protein Region
LB	Lewy Body
MD	Molecular Dynamics

ABBREVIATIONS

miRNA	MicroRNA
MM	Molecular Mechanics
ns	nanosecond
NMR	Nuclear Magnetic Resonance Spectroscopy
OleA	Oleuropein Aglycone
ps	picosecond
PB	Poisson-Boltzmann
PBC	Periodic boundary conditions
PBSA	Poisson-Boltzmann Surface Area
PD	Parkinson's Disease
PDB	Protein Data Bank
PEG	Polyethylene Gycol
PME	Particle Mesh Ewald
PMF	Potential of Mean Force
PPI	Protein-protein interaction
PRED	Per-residue energy decomposition
PRR	Proline-Rich Region
PSEN	Presenilin
PTM	Post Translational Modification
PME	Particle Mesh Ewald
PTRAJ	Short for Process TRAJectory
RCSB	Research Collaboratory for StructuralBioinformatics
REMD	Replica Exchange Molecular Dynamics
Rg	Radius of Gyration
RMSD	Root Mean Square Deviation
RMSF	Root Mean Square Fluctuation
RNA	Ribonucleic Acid
ROS	Reactive Oxygen Species
RSV	Resveratrol
SASA	Solvent-accessible surface area
TABFO	Toxic Amyloid Beta Fibrillar Oligomer
TIP3P	Transferable Intermolecular Potential Three-point

ABBREVIATIONS

UCSF	University of California, San Francisco
UniProt	Universal Protein Resource
US	Umbrella Sampling
VMD	Visual Molecular Dynamics
WHAM	Weighted Histogram Analysis Method
WHO	World Health Organization
WT	Wild Type

LIST OF PUBLICATIONS

This thesis is partly based on the following original communications:

1. **Borah, P.** and Mattaparthi, V. S. K. Insights Into Resveratrol as an Inhibitor Against Aβ1-42 Peptide Aggregation: A Molecular Dynamics Simulation Study*, Current Chemical Biology,*2022.DOI: *http://dx.doi.org/10.2174/2212796817666221221141713*

2. **Borah,P.,** Sanjeev, A., and Mattaparthi, V.S.K. Computational investigation on the effect of Oleuropein aglycone on the α-Synuclein aggregation. *Journal of Biomolecular Structure and Dynamics,* 39*(4),* 1249-1270, 2020. DOI: https://doi.org/10.1080/07391102.2020.1728384

3. Dutta, N., **Borah, P**., and Mattaparthi, V. S. K. Effect of CTerm of Human albumin on the aggregation propensity of Aβ$_{1-42}$ peptide: A Potential of mean force study. *Journal of Biomolecular Structure and Dynamics,* 39*(4),*1-18, 2020. DOI: https://doi.org/10.1080/07391102.2020.1730970

4. **Borah, P.** and Mattaparthi, V. S. K. Computational investigation on the role of C-Terminal of human albumin on the dimerization of Aβ$_{1-42}$ peptide. *Biointerface Research in Applied Chemistry,* 10*(1),* 4944-4944, 2020*.* DOI: *https://doi.org/10.33263/BRIAC101.94494*

5. **Borah, P.** and Mattaparthi, V. S. K. Effect of ionic strength on the aggregation propensity of Aβ$_{1-42}$ peptide: an *In-silico* study*, Current Chemical Biology,* 14, 216-226, 2020*.* DOI: http://dx.doi.org/10.2174/2212796814999200818103147

6. **Borah, P.** and Mattaparthi, V. S. K. Computational Investigation on the Interaction Sites of the K84s and K102s Peptides with α-Synuclein for Understanding the Anti-Aggregation Mechanism . Current Biotechnology, 2023. DOI: http://dx.doi.org/10.2174/2211440112666230331104839

In addition, this thesis also contains unpublished data.

CONFERENCE PROCEEDINGS

[1]   **Borah, P** and Mattaparthi, V.S.K. "An *In-silico* study of the role of Resveratrol on $A\beta_{1-42}$ peptide aggregation" National Seminar on "Excitements in Biological Research" held at Department of MBBT, Tezpur University on 6th March, 2023. (Oral Presentation, 3rd Prize).

[2]   **Borah, P** and Mattaparthi, V.S.K. "Computational Investigation on the effect of Polyethyene Glycol as crowding agent on the conformational dynamics of α-Synuclein" National Seminar on "Research at the Interface of Chemical, Biological and Material Sciences", Held at Department of Chemical Sciences, Tezpur University on 10th March, 2023. (Oral Presentation).

[3]   **Borah, P** and Mattaparthi, V.S.K. "An in-silico investigation on the role of oleuropein aglycone on the   aggregation propensity of α-synuclein" the India-12th India-Japan Science and Technology Conclave: International Conference on Frontier Areas of Science and Technology (ICFAST-2022) held at the University of Hyderabad on September 09-10, 2022. (Poster Presentation).

[4]   **Borah, P**. "Awareness and Sensitization" Programme on "Good Academic Research Practices" held at the Dept. of MBBT, Tezpur University in association with UGC on 11 Dec, 2021.