BIOGRAPHICAL SKETCH

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NAME: QIANG, WEI

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POSITION TITLE: Professor of Chemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Tsinghua University	B.S.	07/2004	Chemistry
Michigan State University	Ph.D.	06/2009	Chemistry
The National Institutes of Health	Postdoctoral	12/2013	Biophysical Chemistry and Solid-State NMR Spectroscopy

A. Personal Statement

My research group at Binghamton University employs solid-state nuclear magnetic resonance (ssNMR) spectroscopy, along with other biochemical, biophysical and cellular biological approaches, to investigate the molecular structures and pathologically relevant influences of β-amyloid (Aβ) aggregates, including fibrils and non-fibrillar oligomers, in Alzheimer's disease (AD). I earned my Ph.D. from Michigan State University in 2009, focusing on the study of HIV fusion peptides and membrane interactions using ssNMR spectroscopy for my doctoral thesis. During my postdoctoral training at the National Institutes of Health (NIH) from 2009 to 2013, I gained experiences in both ssNMR methodology development and biochemical/biophysical studies on Aβ fibrils. I initiated my independent career at Binghamton University in 2014. Over the past decade, I have established a research program with projects aimed at addressing fundamental questions related to the pathology of AD, utilizing a multipronged approach that combines the strengths of ssNMR spectroscopy and fluorescence-based quantitative cell analysis.

We initiated the current project by investigating the structural differences between wild-type $A\beta_{40}$ fibril and several types of post-translationally modified (PTM) Aβ variants' fibrils. These PTM-Aβ variants have long been discovered in senile amyloid plaques extracted from human AD brains. However, their pathological relevance has not been cleared understood and underestimated to some extent. Recently, cumulative evidence from immunohistochemical, biochemical/biophysical and molecular structural studies (including research from my laboratory) has unraveled not only the pathological relevance of several types of PTM-Aβ variants themselves but also their potential triggering effects on the most-abundance wild-type Aβ species, resulting in both enhanced neurotoxicity and the formation of more pathological aggregates. The far-reaching goal of this project is to elucidate how pathological PTM-Aβ variants modulate the structural polymorphisms of fibrillar Aβ aggregates.

I list the selected recent publications related to the current (in chronological order):

1. Hu, Z.W., Vugmeyster, L., Au, D.F., Ostrovsky, D., Sun, Y., and Qiang, W. **(2019)** Molecular structure of an N-terminal phosphorylated β-amyloid fibril. **PNAS**, 116(23), 11253-11258.
2. Hu, Z.W., Au, D.F., Cruceta, L., Vugmeyster, L., and Qiang, W. **(2020)** N-terminal modified Aβ variants enable modulations to the structures and cytotoxicity levels of wild-type Aβ fibrils through cross-seeding. **ACS Chem. Neurosci.**, 11(14), 2058-2065.

3. Hu, Z.W., Cruceta, L., Zhang, S., Sun, Y., and Qiang, W. **(2021)** Cross-seeded fibrillation induced by pyroglutamate-3 and truncated Aβ_{40} variants lead to Aβ_{40} structural polymorphism modulation and elevated toxicity. **ACS Chem. Neurosci.**, 12(19), 3625-3637.
4. Cruceta, L., Sun, Y., Kenyaga, J.M., Ostrovsky, D., Rodgers, A., Vugmeyster, L., Yao, L., Qiang, W. (**2023**) Modulation of aggregation and structural polymorphisms of b-amyloid fibrils in cellular environments by pyroglutamate-3 variants cross-seeding. **J. Biol. Chem.**, 299, 10, 105196.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2025-present Professor, Department of Chemistry, Binghamton University, SUNY, Vestal, NY
2021-present Graduate Program Director/co-Director, Department of Chemistry, Binghamton University
2019-2025 Associate Professor, Department of Chemistry, Binghamton University, SUNY, Vestal, NY
2014-2019 Assistant Professor, Department of Chemistry, Binghamton University, SUNY, Vestal, NY

Scientific Appointments

2025 Guest Editor, *Methods in Enzymology*
2024 Ad-hoc Reviewer, NIH Review Panel Molecular Structure and Function B
2023 Reviewer, the Major Research Instrumentation Program, National Science Foundation
2023- Reviewer, the Alzheimer's Association Research Grant (AARG) Program
2022 Ad-hoc Reviewer, NIH Review Panel Molecular Structure and Function B
2021 Ad-hoc Reviewer, NIH Review Panel Biochemistry and Biophysics of Membranes
2019 Reviewer for the American Chemical Society Petroleum Research Fund
2017 Ad-hoc Reviewer, NIH Review Panel Support of Competitive Research program
2017 Ad-hoc Reviewer, NIH Review Panel Molecular Structure and Function B
2016 Chair, Symposium of Biological NMR Spectroscopy, Northeast ACS Meeting, New York
2015- Advisor, the Freshmen Research Immersion Program, Binghamton University, SUNY
2014 Mentor, Summer Research Internship Program, Louis Stokes Alliance for Minority Participation, the National Science Foundation
2010- Scientific Reviewer, for 40+ scientific journals in related fields

Honors

2025 ACS Binghamton Local Section, Distinguished Research Award
2023 the New York State Individual Development Award, SUNY
2022 Founder's Medal Award, International Council on Magnetic Resonance in Biological Systems (ICMRBS)

C. Contributions to Science

1. A substantial segment of my research at Binghamton University, independent from the current project, focuses on unraveling the neurotoxicity mechanisms of β-amyloid aggregates, spanning early-stage aggregates and fibrils. Since 2014, my research group has achieved significant progress in elucidating the potential membrane disruption effects induced by early-stage aggregation of 40-residue β-amyloid peptides. Our exploration led to the reduction of heterogeneity in model Aβ-membrane systems, enabling more in-depth molecular mechanistic studies facilitated by advanced high-resolution techniques. Over the past five years, we have advanced DNP-based ssNMR approaches for investigating high-resolution molecular interactions in Aβ-membrane intermediates. Our goal is to expand these studies from model liposomes to neuronal cells. To this end, we have developed assays to monitor Aβ aggregation, cell membrane disruption and cell death in cellular systems. Additionally, we are developing in-cell ssNMR approaches for in-situ high-resolution characterizations:

a. Qiang, W., Doherty, K.E., Klees, L.M., and Tobin-Miyaji, Y. **(2020)** Time-dependent lipid dynamics, organization and peptide-lipid interaction in phospholipid bilayers with incorporated β-amyloid oligomers. **J. Phys. Chem. Lett.**, 11(19), 8329-8336.
b. Kenyaga, J., Cheng, Q., and Qiang, W. **(2022)** Early-stage β-amyloid-membrane interactions modulate lipid dynamics and influence structural interfaces and fibrillation. **J. Biol. Chem.**, 298(10), 102491.

c. Qiang, W., Kengwerere M.K., Zhao, W., Scott, F.J., Wutoh-Hughes, X., Wang, T., Mentink-Vigier, F. **(2023)** Heterotypic interactions between the 40- and 42-residue isoforms of β-amyloid peptides on lipid bilayer surfaces. **ACS Chem. Neurosci.**, 14, 23, 4153-4162.
d. Kenyaga, J.M., Otieno, S.A., Sun, Y., and Qiang, W. **(2023)** In-cell ^{31}P solid-state NMR measurements of the lipid dynamics and influence of exogenous b-amyloid peptides on live neuroblastoma neuro-2a cells. **Biophys. Chem.**, 297, 107008.

2. A second collaborative project in my group studied the membrane interaction of pH-low insertion peptides (pHLIPs). These short peptides possess inherent properties for sensing local environmental pH variations. pHLIP undergoes conformational changes and inserts into the membrane bilayer by adopting an α-helix structure below a critical pH value. Over the past decade, pHLIPs have played important roles as diagnostic agents for tumors and as drug delivery platforms in the development of anti-cancer therapeutics. This is attributed to the lower micro-environmental pH around tumors compared to the physiological pH. I am the PI on the listed publications on this subject:

   a. Shu, N.S., Chung, M.S., Yao, L., An, M., and Qiang, W. **(2015)** Residue-specific structures and membrane locations of pH-low insertion peptide by solid-state nuclear magnetic resonance. **Nature Communications** 6, 7787.
   b. Hanz, S.Z., Shu, N.S., Qian, J., Christman, N., Kranz, P., An, M., Grewer, C., and Qiang, W. **(2016)** Protonation-driven membrane insertion of the pH-low insertion peptide. **Angew. Chem. Int. Ed.** 55(40), 12376-12381.
   c. Otieno S.A., Hanz, S.Z., Chakravorty, B., Zhang, A., Klees, L.M., An, M., and Qiang, W. **(2018)** pH-dependent thermodynamic intermediates of pHLIP membrane insertion determined by solid-state NMR spectroscopy. **PNAS**, 115(48), 12194-12199.
   d. Otieno S.A., and Qiang, W. (**2021**) Roles of key residues and lipid dynamics reveal pHLIP-membrane interactions at intermediate pH. **Biophys. J.**, 120(11), 4649-4662.

3. I have obtained extensive experiences and trainings on the biophysical approaches for the characterizations of amyloid fibrils during my postdoctoral research at NIH. These techniques, including a variety of fluorescence assays, TEM, AFM, and most importantly, the solid-state NMR spectroscopy, will be utilized in this proposal. In addition, I have worked with human brain tissue samples to extract amyloid plaques. Results from my postdoctoral research solved the high-resolution structures of the anti-parallel β sheet amyloid fibrils formed by the Iowa mutant of Aβ. Such amyloid depositions were mainly discovered in the main blood vessels and were known to related to the Cerebral Amyloid Angiopathy. I have also studied the structural changes and kinetics of amyloid fibrils during the seeding process. In addition, I participated in the work of solving the first high-resolution structural model for the amyloid fibrils from human brain. Recently, my postdoctoral work resulted in the very first solid-state NMR screening of β-amyloid fibril structures in brain-seeded fibrils from different clinical subtypes. I have also worked on the method development in solid-state NMR spectroscopy and the NMR-based structural determination of proteins and protein assemblies. This experience started from my postdoctoral research and continued in my independent career. I have developed novel NMR acquisition approaches to enhance the spectral sensitivity, and stochastic dipolar recoupling method to achieve quantitative distance measurements in uniformly isotope-labeled proteins. I have also developed computational modeling protocols to obtain high-resolution amyloid fibril structures using limited solid-state NMR constraints. In addition, I participated in the development of automatic NMR resonance assignment software.

   a. Qiang, W., Yau, W.M., Luo, Y., Mattson, M.P. and Tycko, R. **(2012)** Antiparallel β-sheet architecture in Iowa-mutant β-amyloid fibrils. **PNAS** 109(12), 4443-4448.
   b. Qiang, W., Kelley, K., and Tycko, R. **(2013)** Polymorph-specific kinetics and thermodynamics of β-amyloid fibril growth. **JACS** 135(18), 6860-6871.
   c. Lu, J.X., Qiang, W., Yau, W.M., Schwieters, C.D., Meredith, S.C., and Tycko, R. **(2013)** Molecular structure of β-amyloid fibrils in Alzheimer's disease brain tissue. **Cell** 154(6), 1257-1268.
   d. Qiang, W., Yau, W.M., Lu, J.X., Collinge, J., and Tycko, R. **(2017)** Structural variation in amyloid-β fibrils from Alzheimer's disease clinical subtypes. **Nature**, 541, 217-221.

4. My Ph.D. work focused on the molecular mechanistic and structural studies of membrane fusion. I have learned quantitative NMR approaches such as the REDOR techniques, which will be utilized extensively in this proposal. I have also obtained experiences with biochemistry of liposomes and fluorescence assays to characterize the membrane leakage and fusion. I developed an efficient chemical synthesis protocols for the HIV fusion peptide oligomers, and characterizes their relative fusion activities in lipid vesicles using stopped-flow fluorescence and solid-state NMR. I discovered the correlation between the fusion activity and their membrane insertion depths for different HIV fusion peptide oligomers.

    a. Qiang, W., Yang, J., and Weliky, D.P. **(2007)** Solid-state nuclear magnetic resonance meaurements of HIV fusion peptide to lipid distances reveal the intimate contact of β strand peptide with membranes and the proximity of the Ala-14-Gly-16 region with lipid headgroups. **Biochemistry** 46(17), 4997-5008.
    b. Qiang, W., Bodner, M.L., and Weliky, D.P. **(2008)** Solid-state NMR spectroscopy of human immunodeficiency virus fusion peptides associated with host-cell-like membranes: 2D correlation spectra and distance measurements support a fully extended conformation and models for specific antiparallel strand registries. **JACS** 130(16), 5459-5471.
    c. Qiang, W., Weliky, D.P. **(2008)** HIV fusion peptide and its cross-linked oligomers: efficient syntheses, significance of trimer in fusion activity, correlation of β strand conformation with membrane cholesterol, and proximity to lipid headgroups. **Biochemistry** 48(2), 289-301.
    d. Qiang, W., Sun, Y., and Weliky, D.P. **(2009)** A strong correlation between fusogenicity and membrane insertion depth of the HIV fusion peptide. **PNAS** 106(36), 15314-15319.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1X1L5BTIIATQE/bibliography/public/

BIOGRAPHICAL SKETCH

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NAME: Minfei Su

eRA COMMONS USER NAME (credential, e.g., agency login): MINFEISU

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Nanjing Agricultural University, China	BS	06/2007	Biotechnology
Nanjing University, China	MS	06/2010	Botany
North Dakota State University	PhD	08/2016	Biochemistry
Weill Cornell Medical College of Cornell University	Postdoctoral Associate	07/2021	Physiology and Biophysics
Weill Cornell Medical College of Cornell University	Instructor	08/2023	Physiology and Biophysics

A. Personal Statement

My research group at Binghamton University focuses on employing cryo-electron microscopy (cryo-EM) combined with biochemical, cellular, and molecular dynamics simulation studies, to provide structural and biochemical insights into important proteins, including G protein-coupled receptors (GPCRs) and β-amyloid fibrils. I have fourteen years of experience in structural biology studies. I received my PhD degree from North Dakota State University in 2016, working on determining structures of critical autophagy-related proteins using X-ray crystallography and small-angle X-ray scattering. During my postdoctoral training at Weill Cornell Medical College of Cornell University, my research focused on elucidating the fundamental mechanisms of activation of G-proteins by adrenergic receptors using cryo-EM. Now collaborating with Dr. Wei Qiang at Binghamton University, we are also interested in depicting the structural details of wild-type $A\beta_{40}$ fibril and post-translationally modified Aβ variants' fibrils. Using the state-of-the-art cryo-electron microscopies at New York Structural Biology Center, we have made significant progress in structural studies of $A\beta_{40}$ fibril.

Publications most relevant to this proposal (employing cryo-EM to solve protein structures at atomic resolution).
(*, These authors contributed equally; §, Corresponding author)

1. **Minfei Su***, Jinan Wang*, Guoqing Xiang, Hung Nguyen Do, Joshua Levitz, Yinglong Miao§ and Xin-Yun Huang§ **(2023)**. Structural basis of agonist specificity of α_{1A}-adrenergic receptor. ***Nature Communications*** 14, 4819.
2. **Minfei Su***, Navid Paknejad*, Lan Zhu, Jinan Wang, Hung Nguyen Do, Yinglong Miao, Wei Liu, Richard K. Hite§ and Xin-Yun Huang§ **(2022)**. Structures of β_1-adrenergic receptor in complex with Gs and ligands of different efficacies. ***Nature Communications*** 13(1), 4095.
3. Kamela O. Alegre*, Navid Paknejad*, **Minfei Su***, Jian-Shu Lou, Jianyun Huang, Kelsey D. Jordan, Edward T. Eng, Joel R. Meyerson, Richard K. Hite§ and Xin-Yun Huang§ **(2021)**. Structural basis and mechanism of activation of two different families of G proteins by the same GPCR. ***Nature Structural & Molecular Biology*** 28, 936–944.

4. **Minfei Su**[*], Lan Zhu[*], Yixiao Zhang[*], Navid Paknejad[*], Raja Dey, Jianyun Huang, Ming-Yue Lee, Dewight Williams, Kelsey D. Jordan, Edward T. Eng, Oliver P. Ernst, Joel R. Meyerson, Richard K. Hite, Thomas Walz, Wei Liu[§] and Xin-Yun Huang[§] **(2020)**. Structural basis of the activation of heterotrimeric Gs-protein by isoproterenol-bound β_1-adrenergic receptor. ***Molecular Cell*** 80(1), 59-71.

B. Positions, Scientific Appointments, and Honors

Positions

2023 - present	Assistant Professor, Department of Chemistry, Binghamton University, SUNY, Vestal, NY
2021 - 2023	Instructor, Department of Physiology and Biophysics, Weill Cornell Medical College of Cornell University, New York, NY

Honors

2023	American Heart Association Career Development Award
2018	Protein Society's Year 2017 “Best Paper” Award
2015	The American Society for Biochemistry and Molecular Biology Best Thematic Poster Award
2014	North Dakota Established Program to Stimulate Competitive Research Doctoral Dissertation Assistantship

C. Contributions to Science

([*], These authors contributed equally; [§], Corresponding author)

1. β_1-adrenergic receptor (β_1-AR) is the predominantly expressed β-AR isoform in the adult human heart. Downregulation of β_1-ARs has been described in most cases of heart failure. We solved the first cryo-EM structure of β_1-AR in complex with heterotrimeric Gs protein to elucidate the molecular mechanism of activation of heterotrimeric Gs protein by β_1-AR. β_1-AR is known to primarily couple to Gs and secondarily to Gi, which lead to opposite effects on downstream cAMP signaling. The molecular basis for this dual G-protein signaling ability is profoundly important for understanding β_1-AR physiology, and GPCR/G-protein physiology more broadly. We determined and compared the cryo-EM structures of β_1-AR in complex with Gi, Gs or a chimeric Gi protein, and demonstrated the structural differences between the interactions of β_1-ARs with Gs and Gi. To investigate the activation of G-proteins by GPCRs bound with ligands of different efficacies, we also solved and compared the cryo-EM structures of β_1-AR–Gs complex bound with a full agonist, a partial agonist, or a weak partial agonist. We discovered that efficacy of the ligand-bound GPCR in catalyzing G-protein activation is correlated with the stability of the intermediate state of the ligand–GPCR–G-protein complex.

    a. **Minfei Su**[*], Navid Paknejad[*], Lan Zhu, Jinan Wang, Hung Nguyen Do, Yinglong Miao, Wei Liu, Richard K. Hite[§] and Xin-Yun Huang[§] **(2022)**. Structures of β_1-adrenergic receptor in complex with Gs and ligands of different efficacies. ***Nature Communications*** 13(1), 4095.
    b. Kamela O. Alegre[*], Navid Paknejad[*], **Minfei Su**[*], Jian-Shu Lou, Jianyun Huang, Kelsey D. Jordan, Edward T. Eng, Joel R. Meyerson, Richard K. Hite[§] and Xin-Yun Huang[§] **(2021)**. Structural basis and mechanism of activation of two different families of G proteins by the same GPCR. ***Nature Structural & Molecular Biology*** 28, 936–944.
    c. **Minfei Su**[*], Lan Zhu[*], Yixiao Zhang[*], Navid Paknejad[*], Raja Dey, Jianyun Huang, Ming-Yue Lee, Dewight Williams, Kelsey D. Jordan, Edward T. Eng, Oliver P. Ernst, Joel R. Meyerson, Richard K. Hite, Thomas Walz, Wei Liu[§] and Xin-Yun Huang[§] **(2020)**. Structural basis of the activation of heterotrimeric Gs-protein by isoproterenol-bound β_1-adrenergic receptor. ***Molecular Cell*** 80(1), 59-71.

2. α_1-adrenergic receptors (α_1-ARs) play critical roles in the cardiovascular and nervous systems. However, due to the lack of selective agonists for α_1-AR subtypes, their therapeutic potential has been largely unexplored. We employed cryo-EM to study the structures of α_{1A}-AR in complex with heterotrimeric Gq-proteins and either the endogenous common agonist epinephrine or the α_{1A}-AR-specific synthetic agonist A61603. Our results provide structural insights into the design of selective agonists targeting individual α_1-AR subtypes.

a. **Minfei Su**[*], Jinan Wang[*], Guoqing Xiang, Hung Nguyen Do, Joshua Levitz, Yinglong Miao[§] and Xin-Yun Huang[§] **(2023)**. Structural basis of agonist specificity of α_{1A}-adrenergic receptor. ***Nature Communications*** 14, 4819.

3. ATG14 binding to BECN homologs is essential for autophagy, a catabolic pathway essential for organismal homeostasis in all eukaryotes. We elucidated BECN1:ATG14 and BECN2:ATG14 coiled-coil domain heterodimer structures in the context of autophagy. The studies identified structure-based mechanistic differences in BECN1 and BECN2 homodimerization and heterodimerization which likely dictate competitive ATG14 recruitment.

   a. **Minfei Su**, Yue Li, Shane Wyborny, David Neau, Srinivas Chakravarthy, Beth Levine, Christopher L. Colbert and Sangita Sinha[§] **(2017)**. BECN2 interacts with ATG14 through a metastable coiled-coil to mediate autophagy. ***Protein Science*** 26(5), 972-984.
   b. Yang Mei, **Minfei Su**, Ruslan Sanishvili, Srinivas Chakravarthy, Christopher L. Colbert and Sangita Sinha[§] **(2016)**. Identification of BECN1 and ATG14 coiled-coil interface residues that are important for starvation-induced autophagy. ***Biochemistry*** 55(30), 4239–4253.
   c. Yang Mei, Karen Glover, **Minfei Su**, Sangita Sinha[§] **(2016)**. Conformational flexibility of BECN1: Essential to its key role in autophagy and beyond. ***Protein Science*** 25(10), 1767-1785.

4. γ-herpesviruses (γHVs) encode homologs of cellular Bcl-2 proteins, which are critical to their viral reactivation and oncogenic transformation. These γHV Bcl-2 homologs bind to the autophagy effector BECN1 to down-regulate autophagy. We determined the molecular mechanism of γHV68 Bcl-2 mediated down-regulation of autophagy and developed a cell-permeable peptide inhibitor selectively inhibits γHV68 Bcl-2-mediated down-regulation of autophagy.

   a. **Minfei Su**, Yang Mei, Ruslan Sanishvili, Beth Levine Christopher Colbert, Sangita Sinha[§] **(2014)**. Targeting γ-herpesvirus 68 Bcl-2 mediated down-regulation of autophagy. ***The Journal of Biological Chemistry*** 289(12), 8029-8040.
   b. **Minfei Su**, Yang Mei, Sangita Sinha[§] **(2013)**. Role of the crosstalk between autophagy and apoptosis in cancer. ***Journal of Oncology*** 2013, 102735.
   c. Yang Mei, **Minfei Su**, Gaurav Soni, Saeed Salem, Christopher Colbert, Sangita Sinha[§] **(2013)**. Intrinsically disordered regions in autophagy proteins. ***Proteins: Structure, Function, and Bioinformatics*** 82(4), 565-578.