BIOGRAPHICAL SKETCH

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NAME: Song, Yuhua

eRA COMMONS USER NAME (credential, e.g., agency login): YHSONG1

POSITION TITLE: Professor of Biomedical Engineering (effective Oct 1, 2022)

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	Completion Date YYYY	FIELD OF STUDY
Jilin University of Technology, Jilin, China	B.S.	1989	Materials Sci. & Eng.
Harbin University of Sci and Tech, Harbin, China	M.S.	1996	Materials Sci. & Eng.
Harbin Institute of Technology, Harbin, China	Ph.D.	1998	Materials Sci. & Eng.
Tsinghua University, Beijing, China	Post-Doc	1999-2001	Computational Mechanics
University of Pittsburgh, Pittsburgh, PA	Post-Doc	2001-2002	Computational Biomechanics
Washington University in St. Louis, St. Louis, MO	Post-Doc	2002-2005	Computational Biology

A. Personal Statement

Dr. Song's research group uses integrated multiscale computational modelling and experimental approaches to investigate the structural, molecular and functional mechanisms of the biomolecular interactions. Her goal is to identify endogenous and exogenous small molecules, including reposition of FDA-approved drugs, to regulate biomolecular interactions underlying important cellular activities in Alzheimer's disease, cancer, cardiovascular disease, dermatopathology, regenerative medicine and precision medicine, with current focus in Alzheimer's disease, for potential therapeutic treatment. Dr. Song is a biomedical researcher and has worked in computational modeling research for near 30 years. Since 2009, with initial support of an NIH K25 "Mentored Quantitative Research Development Award" and Biomedical Engineering Department at University of Alabama at Birmingham, Dr. Song has established biochemical and biological experimental components in her research group that complement Dr. Song's strength in computational modeling. In recent years, in addition to continuing to publish computational studies, Dr Song's lab has published integrated computational and experimental studies with Dr. Song as corresponding author. Dr. Song has published 52 peer-reviewed papers in quality journals including *Int. J. Biol. Macromol., Alzheimer's and Dementia, Frontiers in Neurology, J Biol Chem, Biophysical Journal, J Cell Biochem, Biochemistry, Proteins, Protein Science, and J Am Chem Soc.* Dr. Song has mentored more than 50 trainees with 15 minority and 19 female trainees since she joined UAB in 2006, including postdoctoral associates, graduate, undergraduate and high school students and research assistants. The trainees in her research group have been productive and are recognized by students' awards. Due to her dedication to mentees' training, she was awarded Graduate Dean's Excellence in Mentorship Award. In summary, Dr. Song has a demonstrated record of the accomplished and productive research activities, and her research and mentoring experience have prepared her for accomplishing her research projects and mentoring trainees at different levels.

Ongoing and completed projects that I would like to highlight include:

NIH/NIA R01AG068395 (Role: PI) 09/15/2021 – 05/31/2026
TREM2-endogenous ligand interactions in Alzheimer disease

Alzheimer's Drug Discovery Foundation (Roberson, PI; role: co-Investigator) 04/1/2019 - 04/01/2023
Toward Therapeutic Approaches to TREM2 in Alzheimer's Disease

NSF/MCB MCB2024964 (Zhang, PI; role: collaborator) 08/01/2020 – 07/31/2024
Regulatory functions of intrinsically disordered electronegative clusters (ENC) in RNA-binding proteins

UAB Hugh Kaul Precision Medicine Institute pilot grant (Role: PI) 05/01/2020 – 06/30/2023
Repurposing already-available drugs to target human host proteins and SARS-CoV-2 proteins for COVID-19 prevention and treatment

NIH R01 HL138990-01 (Qin, PI; role: co-Investigator) 07/1/2017 - 03/31/2022
E2F2 and Vascular Function

COVID-19 HPC Consortium spearheaded by White House of Science and Technology Policy, U.S. Department of Energy, NSF and IBM (TG-BIO200084) (Role: PI) 12/03/2020 – 12/03/2021

Computational Investigation of Vitamin D3 and its Hydroxyderivatives as Promising Drugs against COVID-19
NSF-supported Extreme Science and Engineering Discovery Environment (XSEDE) TG-MCB200181 (Role: PI) 06/17/2020 – 06/16/2021
Effects of Self-Oligomerization on Conformation and Ligand Binding in the Alzheimer's Disease Associated Protein TREM2
NSF-supported XSEDE Resource Allocations Committee BIO200050 (Role: PI) 01/01/2021 – 06/30/2021
Integrative computational investigation of already-available drugs to target key human host and SARS-CoV-2 proteins for COVID19 treatment
NSF CBET-1159859 (Role: PI) 10/1/2012 - 09/30/2018
Thrombospondin-1/calreticulin binding in regulating cell intermediate adhesion and collagen expression
AHA 14GRNT2048002 (Bevensee, PI; role: co-Investigator) 07/01/2014 – 06/30/2017
AHA (Southeast Affiliate) Molecular Physiology of Na/Bicarbonate Cotransporters
NIH/NCI 5K25 CA140791 (Role: PI) 08/14/2009 – 06/30/2015
Protein Interactions Underlying Fas-Mediated DISC in Cholangiocarcinoma
NIH R01GM038953 (Falany, PI; role: co-Investigator) 9/30/2010 - 8/31/2014
NIH/NIGMS Human Cytosolic Sulfotransferases
NSF supported XSEDE TG-MCB130026 and **MCB130041** (Role: PI) 11/09/2012 – 11/08/2013
The Interaction of PEG-grafted PLL Copolymers with Biomembrane

a) Yuwei Song, Radomir M. Slominski, Shariq Qayyum, Tae-Kang Kim, Zorica Janjetovic, Chander Raman, Robert C. Tuckey, **Yuhua Song***, Andrzej T. Slominski*. Molecular and structural basis of interactions of vitamin D3 hydroxyderivatives with aryl hydrocarbon receptor (AhR): an integrated experimental and computational study. *International Journal of Biological Macromolecules*, 2022; 209:1111-23. doi: https://doi.org/10.1016/j.ijbiomac.2022.04.048 PMID: 35421413

b) Daniel L. Kober, Melissa Brereton, Colin E. Kluender, Hunter B. Dean, Deborah F. Steinberg, Samantha Nelson, Berevan Baban, Carl Frieden, Jennifer Alexander-Brett, Erik D. Roberson, **Yuhua Song**, and Tom J. Brett. Functional insights from biophysical study of TREM2 interactions with ApoE and $A\beta_{1-42}$. **Featured Article,** *Alzheimer's and Dementia***,** 2021; 17: 475– 488, https://doi.org/10.1002/alz.12194. PMID: 33090700

c) Hunter B Dean, Erik D Roberson*, **Yuhua Song***. Neurodegenerative Disease–Associated Variants in TREM2 Destabilize the Apical Ligand-Binding Region of the Immunoglobulin Domain. *Frontiers in Neurology,* 2019, 10(1252). doi: 10.3389/fneur.2019.01252. PMCID: PMC6985895

d) Romone M. Fancy, Lingyun Wang, Thomas Schmid, Qinghua Zeng, Hong Wang, Tong Zhou, Donald J. Buchsbaum, **Yuhua Song***. Characterization of the Interactions between Calmodulin and Death Receptor 5 in Triple-Negative and Estrogen Receptor Positive Breast Cancer Cells: An Integrated Experimental and Computational Study. *The Journal of Biological Chemistry*, 2016, 291(24):12862-70. PMID: 27129269.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments:

2022 Oct 1 – Professor with Tenure, Department of Biomedical Engineering
2012 - 2022 Associate Professor (with tenure), Department of Biomedical Engineering, UAB
2021 - Scientist, Center for Neurodegeneration and Experimental Therapeutics, UAB
2021 - Graduate Program Director, Department of Biomedical Engineering, UAB
2011 - Faculty of Structural Biology Program, UAB
2011 - 2012 Associate Director, Center for Computational and Structural Dynamics, UAB
2010 - Faculty of Graduate Biomedical Science, UAB
2009 - Associate Scientist, UAB Comprehensive Cancer Center, UAB
2007 - Secondary Faculty, Department of Biochemistry and Molecular Genetics, UAB
2007 - Faculty of Medical Scientist Training Program, UAB
2006 - Associate Scientist, Center for Metabolic Bone Disease, UAB
2006 - Member, Center for Computational and Structural Biology and BioMatrix Engineering and Regenerative Medicine Center, UAB
2006 - 2012 Assistant Professor, Dept of Biomedical Eng, University of Alabama at Birmingham (UAB)
2005 - 2006 Research Instructor, Department of Biochemistry and Molecular Biophysics, Center for Computational Biology, Washington University in St. Louis, School of Medicine
2002 - 2005 Research Associate, Department of Biochemistry and Molecular Biophysics, Center for Computational Biology, Washington University in St. Louis, School of Medicine

Awards and Honors

2021 – 2026 NIH R01 Award from National Institute on Aging
2021 NSF-supported XSEDE XRAC award
2020 - 2021 COVID-19 HPC Consortium Award spearheaded by White House of Sci and Tech Policy, U.S. Dept of Energy, NSF and IBM
2020 – 2021 NSF-supported Extreme Science and Eng Discovery Environment (XSEDE) award
2012 - 2018 NSF award from Biomedical Engineering Program in Division of CBET
2017 Graduate Dean's Excellence in Mentorship Award for 2017
2013 NSF-supported XSEDE award
2012 – 2013 NSF-supported XSEDE award
2009 - 2015 NIH K25 Mentored Quantitative Research Career Development Award, NIH/NCI
2008 - 2009 Startup/Educational Allocation award for computational resources from NSF's Partnerships for Advanced Computational Infrastructure (PACI)
2008 - 2009 The Development Allocation Committee Award from NSF's PACI
2007 - 2008 UAB ADVANCE Faculty Research Awards through the sponsorship of NSF
2006 - 2007 Medium Resource Allocations Committee Award from NSF's PACI
2005 - 2006 Development Allocations Committee Award fom NSF's PACI
2002 Scholarship for the Grace Hopper celebration of women in computing
2000 Postdoctoral Fellowship, China National Science Foundation

Grant review Services

NSF CBET EBMS program, October 2021
UAB Center for Clinical and Translational Science (CCTS), November 2018
NSF CBET EBMS program, September 2018
NIH Membrane Biology and Protein Processing Study Section, October 2017
NSF CBET/CDS&E program, June 2017
Kentucky Science & Engineering Foundation, April 2016
Portuguese Foundation for Science and Technology, Panel Member for the Bioengineering, Biotechnology and Biochemistry Panel, Lisbon, Portugal, October 2012

Editorial Board Services

2007 - MCB: Molecular & Cellular Biomechanics
2011 - Journal of Bioprocessing & Biotechniques
2011 - Journal of Thermodynamics & Catalysis
2018 – Health and Medical Informatics Open Access
2018 – International Journal of Biochemistry & Physiology
2021 – Membranes, Topic Editor in Section "Membranes in Life Science"

Manuscript Review Services

Journal of Chemical Information and Modeling, Computational Biology and Chemistry, Biophysical Journal, Biomechanics and Modeling in Mechanobiology, Journal of Biological Chemistry, ACS Nano, Medicinal Research Reviews, PLoS ONE, Journal of Biomechanics, Computational Science & Discovery, IEEE Transactions on Biomedical Engineering Materials & Design, J Mech Med Biol, Polym. Eng. Sci.

C. Contribution to Science

1. My early research was to use the combined computational and experimental approaches to study the materials processing procedure, especially for rapid prototyping & rapid tooling, plastic sheet thermoforming and solidification process. The experimental results were used to validate the computational model, the results from computational model had been used to help optimize the parameters for the materials processing procedure to obtain the quality products with low cost and short production period.

a . **Yuhua Song**, Kaifing Zhang, Zongren Wang, Faxi Diao. 3-dimensional finite element analysis of temperature field and thermal stress for plastics thermoforming. *Journal of Materials Processing Technology*, 2000, 97(1):35-43.
b. **Yuhua Song**, Kaifing Zhang, Zongren Wang, Faxi Dao, Yongnian Yan, Renji Zhang. Coupled thermo-mechanical analysis of plastics thermoforming. *Polymer Engineering and Science*, 2000, 40(8):1736-46.
c. **Yuhua Song**, Yongnian Yan, Renji Zhang Qingping Lu, Da Xu. 3-D nonlinear coupled thermomechanical finite element analysis of the dimensional accuracy for casting dies in rapid tooling. *Finite Elements in Analysis and Design*, 2001, 38 (1):79-91.
d. **Yuhua Song**, Yongnian Yan, Renji Zhang. Manufacture of the die of auto-mobile deck part based on rapid prototyping and rapid tooling technology. *J. of Materials Processing Tech*, 2002, 20(1-3):237-242

2. My postdoctoral research has been in three areas of multiscale computational modeling of biological systems. **(1)** I used combined experimental and computational approach to develop the subject specific finite element model of the anterior cruciate ligament (ACL) (kinematics driven model) to more accurately to calculate the force and stress distribution in the ACL, and the finite element model of the knee joint (force driven model) to calculate both the knee kinematics and force, stress distribution in the ACL. The developed model can help design improved surgical procedures following ACL injuries. **(2)** I developed a 3-D adaptive finite element solver (SMOL) of solving Smoluchowski equation for substrate-biological macromolecular diffusion. The developed SMOL software has been successfully for the study of both wild type and mutant mouse acetylcholinesterase, and has been successfully used by Dr. J. Andrew McCammon's group at the University of California, San Diego for tetrameric acetylcholinesterase diffusion distribution and diffusion rate constant calculation. These studies laid the groundwork for the integration of molecule-scale information into cellular-scale systems, such as the neuromuscular junction. **(3)** I investigated salicylate effects on the micro- and mesoscopic properties of a dipalmitoylphosphatidylcholine bilayer with molecular dynamics simulations. Results are validated with experimental data and support the conclusion that salicylate influences the electrical but not the mechanical properties of DPPC membranes, providing molecular insights for the influence of salicylate on hearing through affecting of the electromechanical coupling in the outer hair cells of the ear and laying the basis for the multiscale research to understand the macroscopic effects of ligand-induced changes in membrane properties.

a. **Yuhua Song**, Richard E. Debski, Volker Musahl, Maribeth Thomas, Savio L-Y. Woo. A three dimensional finite element model of the human anterior cruciate ligament – a computational analysis with experimental validation. *J Biomech*. 2004, 37(3):383-390. PMID: 14757458
b. **Yuhua Song ,** Yongjie Zhang , Tongye Shen , Chandrajit L. Bajaj , J. Andrew McCammon and Nathan A. Baker. Finite element solution of the steady-state Smoluchowski equation for rate constant calculations. *Biophys J.* 2004, 86(4):2017-2029. PMCID: PMC1304055
c. **Yuhua Song**, Yongjie Zhang, Chandrajit L. Bajaj, Nathan A. Baker. Continuum diffusion reaction rate calculations of wild type and mutant mouse acetylcholinesterase: adaptive finite element analysis. *Biophys J.* 2004, 87(3):1558-1566. PMCID: PMC1304562
d. **Yuhua Song**, Victor Guallar, Nathan A. Baker. Molecular dynamics simulation of salicylate effects on the micro- and mesoscopic properties of a dipalmitoylphosphatidylcholine bilayer. *Biochemistry,*2005, 44(41), 13425-13438. PMCID: PMC2435121

3. After I became an independent investigator, in addition to my continued effort in multiscale computational modeling of biological systems, I have established biochemical and biological experimental components in my research group with the support of a "Mentored Quantitative Research Development Award" (NIH K25 award) and Biomedical Engineering Department at The University of Alabama at Birmingham. One focus area in my group using integrated computational modeling and experimental approaches is to determine new protein target that could regulate the death-receptor mediated apoptosis and identify key molecular markers for the regulation of cell apoptosis and cell survival pathways in breast cancer. Computational modelling have helped to predict protein binding site, key residues for protein function, help to generate the hypothesis and interpret the molecular and structural mechanisms for protein interactions for its molecular and cellular signaling activities; and the experimental results are used to validate the computational results and test the hypothesis to implement the project objective. The results of this study could unveil the potential target(s) to regulate death-receptor-mediated apoptosis and aid in the development of strategies to increase chemotherapeutic drug efficacy and overcome the drug resistance in breast cancer treatments.

a. Hongyi Yang, **Yuhua Song***. Structural insight for roles of DR5 death domain mutations on oligomerization of DR5 death domain – FADD complex in the death-inducing signaling complex formation: a computational study. *Journal of Molecular Modeling*, 2016, 22 (4): 89, page 1-12. PMID: 26995783
b. Romone M. Fancy, Lingyun Wang, Thomas Schmid, Qinghua Zeng, Hong Wang, Tong Zhou, Donald J. Buchsbaum, **Yuhua Song***. Characterization of the Interactions between Calmodulin and Death Receptor 5 in Triple-Negative and Estrogen Receptor Positive Breast Cancer Cells: An Integrated Experimental and Computational Study. *The Journal of Biological Chemistry*, 2016, 291(24):12862-70. PMID: 27129269
c. Romone M. Fancy, Harrison Kim, Tong Zhou, Kurt R. Zinn, Donald J. Buchsbaum, **Yuhua Song***. Calmodulin Binding to Death Receptor 5-mediated Death-inducing Signaling Complex in Breast Cancer Cells. *J Cell Biochem.* 2017 Aug;118(8):2285-2294. PMID: 28092099, PMCID: PMC5462859.
d. Romone M. Fancy, Harrison Kim, Tiara Napier, Donald J. Buchsbaum, Kurt R. Zinn. **Yuhua Song***. Calmodulin antagonist enhances DR5-mediated apoptotic signaling in TRA-8 resistant triple negative breast cancer cells. *J Cell Biochem*. 2018, *119(7):6216-6230*. PMID: 29663486 PMCID: PMC5993614

4. With the support from a NSF grant, we have been investigating the molecular regulatory mechanisms for thrombospondin (TSP1)/calreticulin (CRT) binding modulated cellular signaling in focal adhesion disassembly, resistance to anoikis and collagen production with integrated computational modeling and experimental approaches. The goal of this project is to further elucidate the molecular events at the level of protein-protein interactions involved in the formation of the TSP1-CRT-LRP1 ternary complex induced by TSP1-CRT binding that signals intermediate adhesion, resistance to anoikis, and collagen production. Computational modeling predicts that direct interaction between TSP1 and cell surface CRT induces an altered conformation of CRT which exposes otherwise cryptic sites for CRT binding to LRP1 to trigger intracellular signaling for intermediate adhesion and collagen production, which will be validated with experimental studies. Knowledge from this project could lead to identification of novel strategies and drug
targets for modifying aberrant tissue repair responses that occur in scarring, the foreign body response, or conversely in wound healing deficiencies through the regulation of TSP1-CRT-LRP1 ternary complex formation.

a. Qi Yan, Joanne E. Murphy-Ullrich, **Yuhua Song**. Structural Insight for the Role of Thrombospondin-1 Binding to Calreticulin in Calreticulin-Induced Focal Adhesion Disassembly. *Biochemistry,* 2010, 49(17): 3685-3694. PMCID: PMC2943676
b. Qi Yan, Joanne E. Murphy-Ullrich, **Yuhua Song**. Molecular and Structural Insight for the Role of Key Residues of Thrombospondin-1 and Calreticulin in Thrombospondin-1- Calreticulin Binding. *Biochemistry,* 2011, 50(4): 566-573. PMCID: PMC3037594
c. Lingyun Wang, Joanne E, Murphy-Ullrich, **Yuhua Song**. Molecular insight for the effect of lipid bilayer environments on thrombospondin-1 and calreticulin interactions. *Biochemistry*, 2014, 53 (40), pp 6309–6322. PMID: 25260145
d. Lingyun Wang, Joanne E, Murphy-Ullrich, **Yuhua Song***. Multiscale Simulation of the Interaction of Calreticulin-Thrombospondin-1 Complex with a Model Membrane Microdomain. *J Biomol Struct Dyn.* 2019, 37(3):811-822. doi: 10.1080/07391102.2018.1433065. PMID: 29380675

5. With the support from Alzheimer's Drug Discovery Foundation and an NIH R01 grant, another research focus in my research group is the investigation of transmembrane protein TREM2 structure and function mechanism in Alzheimer's disease with integrated computational modeling and experimental approaches. Both Alzheimer's disease (AD) and frontotemporal dementia (FTD) - associated variants cause localized instability in three loops adjacent to the region that correspond to the complementarity-determining regions (CDRs) of antibodies. This instability ultimately disrupts tethering between these CDRs and the core of the immunoglobulin domain of TREM2. Thus, our results provide further evidence that the proposed loss-of-function caused by neurodegenerative disease–associated variants may be driven by altered conformational stability of the ligand-interacting CDR and, ultimately, loss of affinity or specificity for TREM2 ligands. Biological membranes play an important role in cellular function. Knowledge regarding biomembrane structure, mechanics, and electrostatics is crucial to understanding the function of membrane-bound proteins, including transmembrane protein TREM2. Results from these studies will provide molecular insight into TREM2 immune activation by endogenous ligand and available drug binding, offering a molecular basis for therapeutic strategy development to better target TREM2 for AD treatment.

a. Daniel L. Kober, Melissa Brereton, Colin E. Kluender, Hunter B. Dean, Deborah F. Steinberg, Samantha Nelson, Berevan Baban, Carl Frieden, Jennifer Alexander-Brett, Erik D. Roberson, **Yuhua Song**, and Tom J. Brett. Functional insights from biophysical study of TREM2 interactions with ApoE and $A\beta_{1\text{-}42}$. *Alzheimer's & Dementia*. **Featured Article,** 2021;17(3):475-88. PMID: 33090700 PMCID: PMC8026773 https://doi.org/10.1002/alz.12194
b. Hunter B Dean, Erik D Roberson*, **Yuhua Song***. Neurodegenerative Disease–Associated Variants in TREM2 Destabilize the Apical Ligand-Binding Region of the Immunoglobulin Domain. *Frontiers in Neurology,* 2019, 10(1252). PMID: 32021611 PMCID: PMC6985895 doi: 10.3389/fneur.2019.01252
c. Lingyun Wang, **Yuhua Song***. Molecular insights into the effect of an apoptotic raft-like bilayer on the conformation and dynamics of calreticulin. *Biochimica et Biophysica Acta (BBA) – Biomembranes.* 2020,1862(2): p. 183146 https://doi.org/10.1016/j.bbamem.2019.183146. PMID: 31816323.
d**. Yuhua Song**, Victor Guallar, Nathan A. Baker. Molecular dynamics simulation of salicylate effects on the micro- and mesoscopic properties of a dipalmitoylphosphatidylcholine bilayer. *Biochemistry,* 2005, 44(41), 13425-13438. PMCID: PMC2435121

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