Stanford

Xiaojing Gao

Assistant Professor of Chemical Engineering

Bio

BIO

How do we design biological systems as “smart medicine” that sense patients’ states, process the information, and respond accordingly? To realize this vision, we engineer towards a “simple” goal: producing specific proteins in the right cells at the right time. There is an inspiring history of such methods transforming basic research (e.g., dissecting neural circuits) and biomedicine (e.g., ablating cancer), yet they remain inadequate in many scenarios, especially in organisms (including human patients) where it is possible but nontrivial to introduce polynucleotides.

We envision pushing the envelope by focusing on a hitherto under-explored aspect: controllers compatible with RNA delivery. We expect such controllers to leverage the safety features of mRNA vectors and the post-pandemic burst of research activities, offer additional benefits such as robust performance and compact delivery, and synergize with conventional DNA-level control to further enhance the precision of payload production. Knowing that the controllers are fundamentally confined by the cells they operate in, rather than dealing with the impossible task of completely insulating the controllers from the biological contexts, our philosophy is to incorporate biology as design features (e.g., endogenous retention mechanism in the protein secretory pathway and housekeeping RNA-editing enzymes), leading to innovation in three areas. First, we are developing a plug-and-play platform based on engineered viral proteases to process signals and control intercellular communications. Second, we are co-opting RNA editing to create programmable modular sensors for transcript markers that represent cell types/states and ligands that represent extracellular environments. Third, considering the immunogenic risk of components sourced from non-human organisms, we are “humanizing” the controllers by using human domains and then further computationally reducing their potential immunogenicity. We identified two proof-of-principle applications, non-invasive early disease detection and mRNA-mediated engineering of therapeutic cells, and are dedicating our efforts to applying our controllers to them.

ACADEMIC APPOINTMENTS

- Assistant Professor, Chemical Engineering
- Member, Bio-X
- Member, Wu Tsai Human Performance Alliance
- Faculty Fellow, Sarafan ChEM-H
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Rising Star Award, BMES CMBE (2024)
- New Innovator Award (DP2), National Institutes of Health/NIBIB (2023-2028)
- Finalist, Freeman Hrabowski Scholars, HHMI (2023)

- Trailblazer Award (R21), National Institutes of Health/NIBIB (2022-2025)
- NARSAD Young Investigator Grant, Brain & Behavior Research Foundation (2022-2024)
- 35 under 35, China, MIT Tech Review (2021)
- Terman Faculty Fellow, Stanford University (2020-2023)
- Pathway to Independence Award (K99/R00), National Institutes of Health (2019-2023)
- DARPA Riser, DARPA's 60th Anniversary Symposium (2018)
- HHWF Postdoctoral Fellowship, Helen Hay Whitney Foundation-HHMI (2016-2019)
- Enlight Foundation/Bio-X Interdisciplinary Fellowship, Stanford University (2012-2015)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Early Career Board, ACS Synthetic biology (2024 - present)
- Member, Engineering Biology Research Consortium (2021 - present)

PROFESSIONAL EDUCATION

- Postdoctoral Fellow, California Institute of Technology , Biology and Biological Engineering (2020)
- Ph.D., Stanford University , Biology (2015)
- B.S., Peking University , Biology (2009)

LINKS

- Gao Lab: https://gaolab.blog/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

How do we design biological systems as "smart medicine" that sense patients' states, process the information, and respond accordingly? To realize this vision, we will tackle fundamental challenges across different levels of complexity, such as (1) protein components that minimize their crosstalk with human cells and immunogenicity, (2) biomolecular circuits that function robustly in different cells and are easy to deliver, (3) multicellular consortia that communicate through scalable channels, and (4) therapeutic modules that interface with physiological inputs/outputs. Our engineering targets include biomolecules, molecular circuits, viruses, and cells, and our approach combines quantitative experimental analysis with computational simulation. The molecular tools we build will be applied to diverse fields such as neurobiology and cancer therapy.

Teaching

COURSES

2023-24

- Chemical Kinetics and Reaction Engineering: CHEMENG 320 (Win)
- Colloquium: CHEMENG 699 (Aut, Win, Spr)
- Introduction to kinetics and reactor design: CHEMENG 130B (Aut)

2022-23

- Chemical Kinetics and Reaction Engineering: CHEMENG 320 (Spr)
- Colloquium: CHEMENG 699 (Aut, Win, Spr)
- Introduction to kinetics and reactor design: CHEMENG 130B (Aut)

2021-22

- Colloquium: CHEMENG 699 (Aut, Win, Spr)
- Introduction to kinetics and reactor design: CHEMENG 130B (Aut)

2020-21

- Colloquium: CHEMENG 699 (Aut, Win, Spr)
- Graduate Practical Training: CHEMENG 299 (Sum)
- Introduction to kinetics and reactor design: CHEMENG 130B (Aut)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Jeremy Bjelajac, Matt DeJong, Zhuoran Li, John Shin, Brendan Wirtz, Spencer Zhao

Postdoctoral Faculty Sponsor

Noa Katz, Alex Vlahos, Meng Zhang

Doctoral Dissertation Advisor (AC)

Carlos Aldrete, Connie An, Connor Call, Jeewoo Kang, Natalie Kolber, Santiago Mille Fragoso, Eric Wolfsberg, Xiaowei Zhang

Doctoral Dissertation Co-Advisor (AC)

Wyatt Blackson, Yixin Hu, Phil Kim, Christian Otero, Jocelyn Padilla, Duo Sun, Pengli Wang

Postdoctoral Research Mentor

Noa Katz, Alex Vlahos

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biophysics (Phd Program)
- Cancer Biology (Phd Program)
- Neurosciences (Phd Program)

Publications

PUBLICATIONS

- **Post-Transcriptional Modular Synthetic Receptors.** *bioRxiv : the preprint server for biology*
  Zhang, X., Mille-Fragoso, L. S., Kaseniit, K. E., Call, C. C., Zhang, M., Hu, Y., Xie, Y., Gao, X. J.
  2024
- **Compact Programmable Control of Protein Secretion in Mammalian Cells.** *bioRxiv : the preprint server for biology*
  Vlahos, A. E., Call, C. C., Kadaba, S. E., Guo, S., Gao, X. J.
  2023
- **Modular, programmable RNA sensing using ADAR editing in living cells.** *Nature biotechnology*
  Kaseniit, K. E., Katz, N., Kolber, N. S., Call, C. C., Wengier, D. L., Cody, W. B., Sattely, E. S., Gao, X. J.
  2022
- **Protease-controlled secretion and display of intercellular signals.** *Nature communications*
  Vlahos, A. E., Kang, J., Aldrete, C. A., Zhu, R., Chong, L. S., Elowitz, M. B., Gao, X. J.
  2022; 13 (1): 912
- **Engineering multiple levels of specificity in an RNA viral vector** *BioRxiv*
  Gao, X. J., Chong, L. S., Ince, M. H., Kim, M. S., Elowitz, M. B.
  2020

- **Programmable protein circuits in living cells.** *Science (New York, N.Y.)*
  Gao, X. J., Chong, L. S., Kim, M. S., Elowitz, M. B.
  2018; 361 (6408): 1252-1258
- **Protease-Driven Phase Separation of Elastin-Like Polypeptides.** *Biomacromolecules*
  Wirtz, B. M., Yun, A. G., Wick, C., Gao, X. J., Mai, D. J.
  2024
- **Topological Organization of Ventral Tegmental Area Connectivity Revealed by Viral-Genetic Dissection of Input-Output Relations.** *Cell reports*
  Beier, K. T., Gao, X. J., Xie, S., DeLoach, K. E., Malenka, R. C., Luo, L.
  2019; 26 (1): 159
- **Synthetic biology: Precision timing in a cell.** *Nature*
  Gao, X. J., Elowitz, M. B.
  2016; 538 (7626): 462-463
- **Cas9-triggered chain ablation of cas9 as a gene drive brake.** *Nature biotechnology*
  Wu, B. n., Luo, L. n., Gao, X. J.
  2016; 34 (2): 137–38
- **Viral-genetic tracing of the input-output organization of a central noradrenaline circuit.** *Nature*
  Schwarz, L. A., Miyamichi, K., Gao, X. J., Beier, K. T., Weissbourd, B., DeLoach, K. E., Ren, J., Ibanes, S., Malenka, R. C., Kremer, E. J., Luo, L.
  2015; 524 (7563): 88-92
- **Circuit Architecture of VTA Dopamine Neurons Revealed by Systematic Input-Output Mapping** *CELL*
  Beier, K. T., Steinberg, E. E., DeLoach, K. E., Xie, S., Miyamichi, K., Schwarz, L., Gao, X. J., Kremer, E. J., Malenka, R. C., Luo, L.
  2015; 162 (3): 622-634
- **A transcriptional reporter of intracellular Ca(2+) in Drosophila.** *Nature neuroscience*
  Gao, X. J., Riabinina, O., Li, J., Potter, C. J., Clandinin, T. R., Luo, L.
  2015; 18 (6): 917-925
- **Extremely sparse olfactory inputs are sufficient to mediate innate aversion in Drosophila.** *PloS one*
  Gao, X. J., Clandinin, T. R., Luo, L.
  2015; 10 (4)
- **Drosophila chemotaxis** *FLY*
  Gao, X. J.
  2014; 8 (1): 3-6
- **Specific Kinematics and Motor-Related Neurons for Aversive Chemotaxis in Drosophila** *CURRENT BIOLOGY*
  Gao, X. J., Potter, C. J., Gohl, D. M., Silies, M., Katsov, A. Y., Clandinin, T. R., Luo, L.
  2013; 23 (13): 1163-1172
- **A versatile in vivo system for directed dissection of gene expression patterns** *NATURE METHODS*
  Gohl, D. M., Silies, M. A., Gao, X. J., Bhalerao, S., Luongo, F. J., Lin, C., Potter, C. J., Clandinin, T. R.
  2011; 8 (3): 231-U71