

*Curriculum Vitae*

**Dr. Peng Zou**

**Peking University**

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**Education**

Ph.D. in Biological Chemistry, Massachusetts Institute of Technology, 2007-2012

B.S. in Chemistry and in Physics, Peking University, China, 2003-2007

**Appointments**

Assistant Professor, 2015-present

College of Chemistry and Molecular Engineering, Peking University

Principal Investigator, 2015-present

Synthetic and Functional Biomolecules Center, Peking University

PKU-Tsinghua Center for Life Sciences

PKU-IDG/McGovern Institute for Brain Research

Postdoctoral Fellow, 2013-2015

Department of Chemistry and Chemical Biology, Harvard University, Advisor: Professor Adam E. Cohen

Ph.D. Graduate Research Assistant, 2007-2012

Department of Chemistry, Massachusetts Institute of Technology, Advisor: Professor Alice Y. Ting,

Undergraduate Research Assistant, 2005-2007

College of Chemistry and Molecular Engineering, Peking University, Advisor: Professor Bin Xia

**Honors**

2020 O'Keanos-CAPA Young Investigator Award at the Chemical and Biology interface, CAPA

2019 C&EN's Talented 12 Award, Chemical & Engineering News

2019 Oral Presentation Award, Chinese Society of Biochemistry and Molecular Biology

2016 CNHUPO Young Investigator Award, China Human Proteome Organization

2011 CSHA Fellowship, Cold Spring Harbor Laboratory Asia

2008 Lewis Paul Chapin Fellowship, MIT

2008 Department of Chemistry Outstanding Teaching Award, MIT

2005 President's Undergraduate Research Fellowship, Peking University

2005 Wu Si Scholarship, Peking University

2004 Xiang Lu Scholarship, Peking University

- 2003 Freshman Scholarship, Peking University
- 2003 Gold medalist, Chinese Chemistry Olympiad
- 2003 Silver medalist, Chinese Mathematics Olympiad

### Summary of research achievements

Research in my group can be broadly defined as creating novel chemical tools to study cell functions at high spatio-temporal resolution and with high throughput, particularly in neurons. Neural function arises through complex interactions between biological macromolecules, physical forces (e.g. membrane voltage), and chemical signaling (e.g. metabolites). To study cells at these three levels, we develop chemical labeling methods, fluorescent indicators, photoaffinity probes, and integrate these tools with advanced sequencing, proteomics, and imaging techniques.

- **Profiling subcellular transcriptome and proteome with proximity labeling techniques**

In eukaryotic cells, RNAs and proteins are often segregated into subcellular compartments, with their localizations intimately linked to their functions. Yet efforts to investigate the spatial organization of transcriptome and proteome have been hindered by a lack of analytical tools. To address this challenge, my group has developed proximity labeling techniques to conjugate RNAs and proteins with affinity tags in live cells. One of our technique, called CAP-seq, utilizes a genetically-encoded photosensitizer to mediate the proximity-dependent photo-oxidation of RNA molecules, which are subsequently purified and sequenced. Our CAP-seq data have revealed a model of coordinated mitochondrial protein biogenesis via localized translation (*Nat. Chem. Biol.* 2019).

- **Optical recording of neural activity with engineered fluorescent voltage indicators**

Membrane potential is a fundamental biophysical signal that underlies neural activity. Fluorescent neural activity indicators could complement conventional electrode-based recording by offering high spatial resolution, minimal invasiveness, and highly parallel measurement. My group has contributed to this field by designing and developing hybrid voltage indicators that feature protein-dye conjugate structures. Our method is built upon the site-specific modification of voltage-sensing microbial rhodopsin protein with organic dyes, whose fluorescence is tuned by membrane voltage fluctuations via the electrochromic FRET mechanism. By combining the superior photophysics of organic fluorophores with the genetic targeting of protein scaffold, these hybrid voltage indicators offer both an enhanced sensitivity and a red-shifted spectrum over existing fluorescent protein-based indicators, enabling the all-optical investigation of neuronal electrophysiology (*Angew. Chem. Int. Ed.* 2018; *ACS Chem. Neurosci.* 2019).

- **Profiling genomic targets of ROS signaling**

Reactive oxygen species (ROS) have recently emerged as signaling molecules in mammalian cells, including neurons. ROS reacts with DNA to form 8-oxoG as the major product, which is closely associated with neurodegeneration. Genomic profiling of 8-oxoG could help elucidate its function in ROS signaling, but unfortunately, commercially available antibodies towards 8-oxoG are plagued with poor specificity and low binding affinity. My group addressed this challenge by engineering DNA repair enzymes. Through structure-guided mutagenesis, the lyase activity of glycosylase OGG1 is blocked while retaining its ability to recognize 8-oxoG. Its high affinity and target specificity have enabled the identification of >1000 8-oxoG-rich “hot zones” in mouse embryonic fibroblast genome, particularly in CpG islands and in regulatory elements, revealing that guanine oxidation is more likely to accumulate in accessible and transcriptionally

active chromatin regions (*Biochemistry* 2020).

### Professional affiliations

Members, Chinese Chemical Society, American Chemical Society, Chinese-American Chemistry and Chemical Biology Professors Association (CAPA)

### Teaching activities

#### Undergraduate courses

Fundamentals of Life Chemistry, 48 credit hours / semester, organizer

Chemistry Today, 16 credit hours / semester, participant

Chemical Biology Labs, 32 credit hours / semester, participant

Integrated Science Laboratory III, 24 credit hours / semester, participant

#### Graduate courses

PTN Chemical Biology Module, 24 credit hours / semester, organizer

PTN Neurobiology Module, 4 credit hours / semester, participant

PTN Synthetic Biology Module, 4 credit hours / semester, participant

### Grants

1. Chemical labeling and functional manipulations of protein glycosylation, Ministry of Science and Technology of China (2018YFA0507600), RMB 2,400,000, co-PI (2018-2023)
2. Protein labeling technique for profiling nascent synaptic proteome, Beijing Municipal Natural Science Foundation (5182011), RMB 200,000, PI (2018-2020)
3. Spatiotemporally-resolved detection of protein lipidation, National Natural Science Foundation of China (91753131), RMB 800,000, PI (2018-2020)
4. Study of centromere protein machinery and the molecular mechanism of cell fate determination, Ministry of Science and Technology of China (2017YFA0503600), RMB 2,400,000, co-PI (2017-2022)
5. An optical-electrical integrated bioimaging system with ultrahigh spatial and temporal resolutions, National Natural Science Foundation of China (21727806), RMB 900,000, co-PI (2018-2022)
6. Development of fluorescent voltage sensors and their application in the mechanistic study of neuronal signaling, National Natural Science Foundation of China (21673009), RMB 680,000, PI (2017-2020)

### Publications (\*denotes the corresponding author)

1. Li, Y., Tian, C., Liu, K., Zhou, Y., Yang, J.\* and **Zou, P.\*** (2020). A clickable APEX probe for proximity-dependent proteomic profiling in yeast. *Cell Chem. Biol.* **accepted**.

2. Yuan, Y.<sup>#</sup>, Li, Z.<sup>#</sup>, Yang, N.<sup>#</sup>, Han, Y., Ji, X., Han, D., Wang, X., Li, Y., Liu, T., Yuan, F., He, J., Liu, Y., Ni, C., **Zou, P.**, Wang, G.\*<sup>#</sup>, Guo, X.\* and Zhou, Y.\* (2020). Exosome alpha-synuclein release in plasma may be associated with postoperative delirium in hip fracture patients. *Front Aging Neurosci.* **12**, 67.
3. Fang, Y. and **Zou, P.**\* (2020). Genome-wide mapping of oxidative DNA damage via engineering of 8-oxoguanine DNA glycosylase. *Biochemistry* **59**, 85-89.
4. Xu, Y.<sup>#</sup>, Deng, M.<sup>#</sup>, Zhang, S.<sup>#</sup>, Yang, J.<sup>#</sup>, Peng, L., Chu, J.\* and **Zou, P.**\* (2019). Imaging neuronal activity with fast and sensitive red-shifted electrochromic FRET indicators. *ACS Chem. Neurosci.* **10**, 4768-4775.
5. Wang, C., **Zou, P.**, Yang, C., Liu, L., Cheng, L., He, X., Zhang, L., Zhang, Y., Jiang, H.\* and Chen, P.R.\* (2019). Dynamic modifications of biomacromolecules: mechanism and chemical interventions. *Sci. China Life Sci.* **62**, 1459-1471.
6. Wang, P.<sup>#</sup>, Tang, W.<sup>#</sup>, Li, Z.<sup>#</sup>, Zou, Z., Zhou, Y., Li, R., Xiong, T., Wang, J.\* and **Zou, P.**\* (2019). Mapping spatial transcriptome with light-activated proximity-dependent RNA labeling. *Nat. Chem. Biol.* **15**, 1110-1119.
7. Yu, H., Zhao, T., Liu, S., Wu, Q., Johnson, O., Wu, Z., Zhuang, Z., Shi, Y., Peng, L., He, R., Yang, Y., Sun, J., Wang, X., Xu, H., Zeng, Z., **Zou, P.**, Lei, X., Luo, W.\* and Li, Y.\* (2019). MRGPRX4 is a bile acid receptor for human cholestatic itch. *Elife* **8**, e48431.
8. Zhou, Y.<sup>#</sup>, Wang, G.<sup>#</sup>, Wang, P., Li, Z., Yue, T., Wang, J. and **Zou, P.**\* (2019). Expanding APEX2 substrates for proximity-dependent labeling of nucleic acids and proteins in living cells. *Angew. Chem. Int. Ed. Engl.* **58**, 11763-11767.
9. Zhou, Y.<sup>#</sup>, Zhu, L.<sup>#</sup> and **Zou P.**\* (2019). A brief introduction to Nobel Prize in Chemistry 2018: harnessing the power of evolution. *Univ. Chem.* **34**, 1-6.
10. Kiskinis, E.<sup>#</sup>, Kralj, J. M.<sup>#</sup>, **Zou, P.**<sup>#</sup>, Weinstein, E. N.<sup>#</sup>, Zhang, H., Tsioras, K., Wiskow, O., Ortega, J. A., Eggan, K.\* and Cohen, A. E.\* (2018). All-optical electrophysiology for high-throughput functional characterization of a human iPSC-derived motor neuron model of ALS. *Stem Cell Reports* **10**, 1991-2004.
11. Wang, A.<sup>#</sup>, Feng, J.<sup>#</sup>, Li, Y.\* and **Zou, P.**\* (2018). Beyond fluorescent proteins: hybrid and bioluminescent indicators for imaging neural activities. *ACS Chem. Neurosci.* **9**, 639-650.
12. Xu, Y.<sup>#</sup>, Peng, L.<sup>#</sup>, Wang, S.<sup>#</sup>, Wang, A.<sup>#</sup>, Ma, R., Zhou, Y., Yang, J., Sun, D. E., Lin, W., Chen, X. and **Zou, P.**\* (2018). Hybrid indicators for fast and sensitive voltage imaging. *Angew. Chem. Int. Ed. Engl.* **57**, 3949-3953.
13. Park, K., Kuo, Y., Shvadchak, V., Ingargiola, A., Dai, X., Hsiung, L., Kim, W., Zhou, H., **Zou, P.**, Levine, A. J., Li, J. and Weiss, S.\* (2018). Membrane insertion of- and membrane potential sensing by-semiconductor voltage nanosensors: Feasibility demonstration. *Sci. Adv.* **4**, e1601453.
14. Peng, L.<sup>#</sup>, Xu, Y.<sup>#</sup> and **Zou, P.**\* (2017). Genetically-encoded voltage indicators. *Chin. Chem. Lett.* **28**, 1925-1928.
15. Xu, Y., **Zou, P.**\* and Cohen, A. E.\* (2017). Voltage imaging with genetically encoded indicators. *Curr. Opin. Chem. Biol.* **39**, 1-10.
16. Abdelfattah, A. S., Farhi, S. L., Zhao, Y. X., Brinks, D., **Zou, P.**, Ruangkittisakul, A., Platasa, J., Pieribone, V. A., Ballanyi, K., Cohen, A. E. and Campbell, R. E.\* (2016). A bright and fast red

- fluorescent protein voltage indicator that reports neuronal activity in organotypic brain slices. *J. Neurosci.* **36**, 2458-2472.
17. Hochbaum, D. R.<sup>#</sup>, Zhao, Y.<sup>#</sup>, Farhi, S. L., Klapoetke, N., Werley, C. A., Kapoor, V., **Zou, P.**, Kralj, J. M., Maclaurin, D., Smedemark-Margulies, N., Saulnier, J. L., Boulting, G. L., Straub, C., Cho, Y. K., Melkonian, M., Wong, G. K. S., Harrison, D. J., Murthy, V. N., Sabatini, B. L., Boyden, E. S., Campbell, R. E. and Cohen, A. E.\* (2014). All-optical electrophysiology in mammalian neurons using engineered microbial rhodopsins. *Nat. Methods* **11**, 825-833.
  18. **Zou, P.**<sup>#</sup>, Zhao, Y.<sup>#</sup>, Douglass, A. D., Hochbaum, D. R., Brinks, D., Werley, C. A., Harrison, D. J., Campbell, R. E.\* and Cohen, A. E.\* (2014). Bright and fast multicoloured voltage reporters via electrochromic FRET. *Nat. Commun.* **5**, 4625.
  19. Hung, V., **Zou, P.**, Rhee, H. W., Udeshi, N. D., Cracan, V., Svinkina, T., Carr, S. A., Mootha, V. K. and Ting, A. Y.\* (2014). Proteomic mapping of the human mitochondrial intermembrane space in live cells via ratiometric APEX tagging. *Mol. Cell* **55**, 332-341.
  20. Scotti, E., Calamai, M., Goulbourne, C. N., Zhang, L., Hong, C., Lin, R. R., Choi, J., Pilch, P. F., Fong, L. G., **Zou, P.**, Ting, A. Y., Pavone, F. S., Young, S. G. and Tontonoz, P.\* (2013). IDOL stimulates clathrin-independent endocytosis and multivesicular body-mediated lysosomal degradation of the low-density lipoprotein receptor. *Mol. Cell Biol.* **33**, 1503-1514.
  21. Rhee, H. W.<sup>#</sup>, **Zou, P.**<sup>#</sup>, Udeshi, N. D., Martell, J. D., Mootha, V. K., Carr, S. A. and Ting, A. Y.\* (2013). Proteomic mapping of mitochondria in living cells via spatially restricted enzymatic tagging. *Science* **339**, 1328-1331.
  22. Kang, X., Zhong, N., **Zou, P.**, Zhang, S. N., Jin, C. W. and Xia, B.\* (2012). Foldon unfolding mediates the interconversion between M-pro-C monomer and 3D domain-swapped dimer. *Proc. Natl. Acad. Sci. U. S. A.* **109**, 14900-14905.
  23. Cohen, J. D., **Zou, P.** and Ting, A. Y.\* (2012). Site-specific protein modification using lipoic acid ligase and bis-aryl hydrazone formation. *Chembiochem* **13**, 888-894.
  24. **Zou, P.** and Ting, A. Y.\* (2011). Imaging LDL receptor oligomerization during endocytosis using a co-internalization assay. *ACS Chem. Biol.* **6**, 308-313.
  25. Prince, R. N., Schreiter, E. R., **Zou, P.**, Wiley, H. S., Ting, A. Y., Lee, R. T. and Lauffenburger, D. A.\* (2010). The heparin-binding domain of HB-EGF mediates localization to sites of cell-cell contact and prevents HB-EGF proteolytic release. *J. Cell Sci.* **123**, 2308-2318.
  26. Zhong, N.<sup>#</sup>, Zhang, S. N.<sup>#</sup>, Xue, F.<sup>#</sup>, Kang, X., **Zou, P.**, Chen, J. X., Liang, C., Rao, Z. H., Jin, C. W., Lou, Z. Y.\* and Xia, B.\* (2009). C-terminal domain of SARS-CoV main protease can form a 3D domain-swapped dimer. *Protein Sci.* **18**, 839-844.
  27. Zhong, N., Zhang, S. N., **Zou, P.**, Chen, J. X., Kang, X., Li, Z., Liang, C., Jin, C. W. and Xia, B.\* (2008). Without its N-finger, the main protease of severe acute respiratory syndrome coronavirus can form a novel dimer through its C-terminal domain. *J. Virol.* **82**, 4227-4234.

### Invited talks

2020/01 University of California, San Diego, La Jolla, CA, USA, Invited Speaker

2020/01 The Scripps Research Institute, La Jolla, CA, USA, Invited Speaker

- 2019/12 The IUPAC International Symposium on Bioorganic Chemistry (ISBOC-12), Shenzhen, Invited Speaker
- 2019/11 The 11<sup>th</sup> Chinese National Conference on Chemical Biology, Guangzhou, Invited Speaker
- 2019/11 The 4<sup>th</sup> A3 Roundtable Meeting on Chemical Probe Research Hub, Sendai, Japan, Invited Speaker
- 2019/11 School of Pharmacy, PKU Medical School, Beijing, Invited Speaker
- 2019/10 The Chinese Society of Biochemistry and Molecular Biology Annual Meeting, Taiyuan, Oral Presentation
- 2019/10 2019 PKU-SFBC Symposium, Beijing, Invited Speaker
- 2019/08 Korea Institute of Science and Technology, Seoul, Korea, Invited Speaker
- 2019/08 Seoul National University, Seoul, Korea, Invited Speaker
- 2019/08 Ajou University, Suwon, Korea, Invited Speaker
- 2019/05 The 1<sup>st</sup> National RNA Research Conference (Junior), Beijing, Oral Presentation
- 2019/05 Dalian Institute of Chemical Physics, CAS, Dalian, Invited Speaker
- 2019/04 POSTECH-IBS-PKU Conference for Chemical Biology and Biomaterial, Pohang, Korea, Invited Speaker
- 2019/04 The 3<sup>rd</sup> Fluorescent Probe and Imaging Symposium, Xi'an, Invited Speaker
- 2019/01 Hokkaido University & Peking University Joint Symposium, Sapporo, Japan, Invited Speaker
- 2018/12 HKU Chemical Biology Symposium 2018, Hong Kong, China, Invited Speaker
- 2018/12 National Institute of Biological Sciences, Beijing, Invited Speaker
- 2018/12 ACS Publication Symposium, Beijing, Oral Presentation
- 2018/11 The 3<sup>rd</sup> A3 Roundtable Meeting on Chemical Probe Research Hub, Jeju, Korea, Invited Speaker
- 2018/08 The 5<sup>th</sup> Asian Chemical Biology Conference, Xi'an, Oral Presentation
- 2018/07 The 5<sup>th</sup> National Conference of Biophysical Chemistry, Taiyuan, Oral Presentation
- 2018/05 The 31<sup>st</sup> Chinese Chemical Society Conference, Hangzhou, Oral Presentation
- 2018/05 PKU-UC Davis Bilateral Symposium, Beijing, Invited Speaker
- 2018/01 Academy of Military Medical Sciences, Beijing, Invited Speaker
- 2017/11 The 15<sup>th</sup> Chinese Biophysics Congress, Shanghai, Invited Speaker
- 2017/11 The 2<sup>nd</sup> A3 Roundtable Meeting on Chemical Probe Research Hub, Hangzhou, Invited Speaker
- 2017/09 The 10<sup>th</sup> Chinese National Conference on Chemical Biology, Wuhan, Invited Speaker
- 2017/08 The 2<sup>nd</sup> Biomedical Imaging Method Symposium, Xi'an, Invited Speaker
- 2017/05 Institute of Microbiology, CAS, Beijing, Invited Speaker
- 2017/05 The 1<sup>st</sup> Peking University-Boehringer Ingelheim Joint Symposium on Biomedical Research, Beijing, Invited Speaker
- 2017/04 The 1<sup>st</sup> Fluorescent Probe and Imaging Symposium, Dalian, Invited Speaker
- 2017/02 HOPE meeting, Tokyo, Japan, Oral Presentation
- 2016/11 Symposium at Institute of Biological Chemistry, Academia Sinica, Taiwan, Invited Speaker
- 2016/10 Chinese Society of Biochemistry and Molecular Biology Conference, Hangzhou, Oral Presentation
- 2016/07 Chinese Chemical Society Conference, Dalian, Oral Presentation
- 2016/06 National Conference of Biophysical Chemistry, Hefei, Invited Speaker

- 2016/05 CNHUPO Conference, Xiamen, Oral Presentation
- 2016/04 Frontiers in Proteomics (National Center for Protein Sciences), Beijing, Invited Speaker
- 2016/04 PKU-HKU Joint Symposium on Chemical Biology, Hongkong, Invited Speaker
- 2016/03 Health Science Forum (Shanghai Institutes for Biological Sciences), Shanghai, Invited Speaker
- 2016/02 The 2015 Annual Symposium for the Undergraduate Students of Bio-Liyun (ASUSBioLY), Beijing, Invited Speaker
- 2015/12 National Institute of Biological Sciences, Beijing, Invited Speaker
- 2015/12 Cold Spring Harbor Asia Conference, Suzhou, Oral Presentation
- 2015/10 The 5<sup>th</sup> Symposium of the Chinese Protein Society, Jining, Invited Speaker
- 2015/10 PKU-Sun Yat-sen University Joint Symposium on Chemical Biology, Guangzhou, Invited Speaker
- 2015/08 The 9<sup>th</sup> Chinese National Conference on Chemical Biology, Tianjin, Invited Speaker
- 2014/09 Janelia Farm Research Campus, Howard Hughes Medical Institute, Virginia, USA, Oral Presentation
- 2014/02 BIOPIC, Peking University, Beijing, Invited Speaker
- 2013/07 Bioimaging Club, University of Michigan, Ann Arbor, MI, USA, Invited Speaker