Stanford



Possu Huang

Assistant Professor of Bioengineering

Curriculum Vitae available Online

Bio

BIO

Dr. Possu Huang received his PhD from Caltech with the first demonstration of a computationally designed novel protein-protein interface. He subsequently conducted postdoctoral research at the University of Washington before starting his group at Stanford. His research focuses on advancing the understanding of proteins for the engineering of novel therapeutics and other protein-based nanotechnology. He has contributed to a large number of de novo designed proteins, most notably to the unlocking of the design principles behind the TIM barrel fold and the invention of eOD, an HIV immunogen design. His group uses machine learning, computational modeling, structural biology and experimental library optimization to continue the expansion of protein-based molecular platforms.

ACADEMIC APPOINTMENTS

- Assistant Professor, Bioengineering
- Assistant Professor, Bioengineering
- Member, Bio-X

PROFESSIONAL EDUCATION

- Senior Fellow, University of Washington
- Ph.D., California Institute of Technology , Biochemistry and Molecular Biophysics
- B.A., UC Berkeley , MCB - Biochemistry

LINKS

- Lab Website: http://www.proteindesign.org

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Protein design: molecular engineering, method development and novel therapeutics

PROJECTS

- Structural and mechanistic studies of pore forming toxins by protein design and artificial cells - Stanford University and Osaka University

Teaching

COURSES

2025-26

- Computational Protein Modeling Laboratory: BIOE 301E (Aut)
- Molecular and Cellular Engineering Lab: BIOE 301A, EE 235 (Win)

2024-25

- Molecular and Cellular Engineering Lab: BIOE 301A, EE 235 (Win)
- Protein Design and Modeling using Machine Learning Methods: BIOS 429 (Spr)

2023-24

- Computational Protein Modeling Laboratory: BIOE 301E (Aut)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Nayla Abney, Hajime Fujita, Joshua Sampson, Jason Saunders, Xinyu Xiang, Xiaowei Zhang

Doctoral Dissertation Advisor (AC)

Braxton Bell, Wyatt Blackson, Yilin Chen, Jinho Kim, Hyejin Lee, Jingjia Liu, Tianyu Lu, Richard Shuai

Doctoral (Program)

Hajime Fujita, Thomas Lau, David Li, Lucas Sant'Anna, Magda Zaoralova

Publications

PUBLICATIONS

- **ADAPT-M: a workflow for rapid, quantitative in vitro measurements of enriched protein libraries.** *Nature communications*
  Perez, C. P., DelRosso, N. V., Noland, C. L., Parekh, U., Choe, C. A., Eguchi, R. R., Wen, Q., Fordyce, P. M., Huang, P. S.
  2026

- **De novo design of RNA pseudoknots with deep learning.** *bioRxiv : the preprint server for biology*
  Townley, J., Kladwang, W., Baker, D., Blair, H. M., Choe, C. A., Nesr, G. E., Favor, A., Fisker, E., Haack, D. B., He, S., Hingey, J., Huang, P. S., Huang, et al
  2026

- **A generalizable system for antigenic peptide targeting across HLA-I allotypes.** *bioRxiv : the preprint server for biology*
  Blackson, W., Small, E. L., Sun, S. M., Shinde, O., Pantula, R., Wang, S. J., Rotsides, P., Du, H., Sun, Y., Hwang, D., Wang, C. S., Lu, T., Laskawy, et al
  2026

- **Zero-shot design of a de novo metalloenzyme.** *bioRxiv : the preprint server for biology*
  Nesr, G. E., Dürr, S. L., Mathews, I. I., Wen, Q., Zhao, K., Sarangi, R., Röthlisberger, U., Sunden, F., Huang, P. S.
  2026

- **Structural ontogeny of protein-protein interactions.** *Science (New York, N.Y.)*
  Yang, A., Jiang, H., Jude, K. M., Akpinaroglu, D., Allenspach, S., Li, A. J., Bowden, J., Perez, C. P., Liu, L., Huang, P. S., Kortemme, T., Listgarten, J., Garcia, et al
  2026; 391 (6786): eadx6931

- **High throughput mutational characterization of the GPCR ligand C5a using yeast display and deep sequencing.** *Structure (London, England : 1993)*
  Xu, Y., Thakkar, K., Guan, L., Miao, Y., Mehibel, M., Lee, R. B., Marciano, D., Viswanathan, V., Wang, Z., Wang, J., Ji, L., Cao, H., Petrakian, et al
  2025

- **ADAPT-M: A workflow for rapid, quantitative in vitro measurements of enriched protein libraries.** *bioRxiv : the preprint server for biology*
  Perez, C. P., DelRosso, N. V., Noland, C. L., Parekh, U., Choe, C. A., Eguchi, R. R., Wen, Q., Fordyce, P. M., Huang, P. S.
  2025

- **Ensemble-conditioned protein sequence design with Caliby.** *bioRxiv : the preprint server for biology*
  Shuai, R. W., Lu, T., Bhatti, S., Kouba, P., Huang, P. S.
  2025
- **SLAE: Strictly Local All-atom Environment for Protein Representation.** *bioRxiv : the preprint server for biology*
  Chen, Y., Zhao, C., Huang, P. S., Lu, T., Wayment-Steele, H. K.
  2025
- **Conditional Protein Structure Generation with Protpardelle-1c.** *bioRxiv : the preprint server for biology*
  Lu, T., Shuai, R., Kouba, P., Li, Z., Chen, Y., Shirali, A., Kim, J., Huang, P. S.
  2025
- **Assessing generative model coverage of protein structures with SHAPES.** *Cell systems*
  Lu, T., Liu, M., Chen, Y., Kim, J., Huang, P. S.
  2025: 101347
- **Sidechain conditioning and modeling for full-atom protein sequence design with FAMPNN.** *Proceedings of machine learning research*
  Widatalla, T., Shuai, R. W., Hie, B. L., Huang, P. S.
  2025; 267: 66746-66771
- **Sidechain conditioning and modeling for full-atom protein sequence design with FAMPNN.** *Proceedings of machine learning research*
  Widatalla, T., Shuai, R. W., Hie, B. L., Huang, P.
  2025; 267: 66746-66771
- **SHAPES of protein generative models**
  Huang, P.
  SPRINGER.2025: S44
- **Assessing Generative Model Coverage of Protein Structures with SHAPES.** *bioRxiv : the preprint server for biology*
  Lu, T., Liu, M., Chen, Y., Kim, J., Huang, P. S.
  2025
- **Sidechain conditioning and modeling for full-atom protein sequence design with FAMPNN**
  Widatalla, T., Shuai, R. W., Hie, B. L., Huang, P.
  edited by Singh, A., Fazel, M., Hsu, D., Lacoste-Julien, S., Berkenkamp, F., Maharaj, T., Wagstaff, K., Zhu, J.
  JMLR-JOURNAL MACHINE LEARNING RESEARCH.2025: 66746-66771
- **Targeting peptide antigens using a multiallelic MHC I-binding system.** *Nature biotechnology*
  Du, H., Mallik, L., Hwang, D., Sun, Y., Kaku, C., Hoces, D., Sun, S. M., Ghinnagow, R., Carro, S. D., Phan, H. A., Gupta, S., Blackson, W., Lee, et al
  2024
- **A general system for targeting MHC class II-antigen complex via a single adaptable loop.** *Nature biotechnology*
  Du, H., Liu, J., Jude, K. M., Yang, X., Li, Y., Bell, B., Yang, H., Kassardjian, A., Blackson, W., Mobedi, A., Parekh, U., Parra Sperberg, R. A., Julien, et al
  2024
- **A General Platform for Targeting MHC-II Antigens via a Single Loop**
  Huang, P.
  WILEY.2024: 55
- **An all-atom protein generative model.** *Proceedings of the National Academy of Sciences of the United States of America*
  Chu, A. E., Kim, J., Cheng, L., El Nesr, G., Xu, M., Shuai, R. W., Huang, P. S.
  2024; 121 (27): e2311500121
- **A cysteine-specific solubilizing tag strategy enables efficient chemical protein synthesis of difficult targets.** *Chemical science*
  Li, W., Jacobsen, M. T., Park, C., Jung, J. U., Lin, N. P., Huang, P. S., Lal, R. A., Chou, D. H.
  2024; 15 (9): 3214-3222
- **Sparks of function by de novo protein design.** *Nature biotechnology*
  Chu, A. E., Lu, T., Huang, P. S.

2024; 42 (2): 203-215

- **A general platform for targeting MHC-II antigens via a single loop.** *bioRxiv : the preprint server for biology*
  Du, H., Liu, J., Jude, K. M., Yang, X., Li, Y., Bell, B., Yang, H., Kassardjian, A., Mobedi, A., Parekh, U., Sperberg, R. A., Julien, J. P., Mellins, et al
  2024

- **A cysteine-specific solubilizing tag strategy enables efficient chemical protein synthesis of difficult targets** *CHEMICAL SCIENCE*
  Li, W., Jacobsen, M. T., Park, C., Jung, J., Lin, N., Huang, P., Lal, R. A., Chou, D.
  2024

- **How can the protein design community best support biologists who want to harness AI tools for protein structure prediction and design?** *CELL SYSTEMS*
  Hoecker, B., Lu, P., Glasgow, A., Marks, D. S., Chatterjee, P., Slusky, J. S. G., Schueler-Furman, O., Huang, P.
  2023; 14 (8): 629-632

- **Fully synthetic platform to rapidly generate tetravalent bispecific nanobody-based immunoglobulins.** *Proceedings of the National Academy of Sciences of the United States of America*
  Misson Mindrebo, L., Liu, H., Ozorowski, G., Tran, Q., Woehl, J., Khalek, I., Smith, J. M., Barman, S., Zhao, F., Keating, C., Limbo, O., Verma, M., Liu, et al
  2023; 120 (24): e2216612120

- **An all-atom protein generative model.** *bioRxiv : the preprint server for biology*
  Chu, A. E., Cheng, L., Nesr, G. E., Xu, M., Huang, P. S.
  2023

- **Rational Design of Improved and Novel Photodissociable GFPs and RFPs**
  Westberg, M., Trigo, M. L., Devenish, S., Huang, P., Lin, M. Z.
  WILEY.2023

- **De Novo Design of a Highly Stable Ovoid TIM Barrel: Unlocking Pocket Shape towards Functional Design.** *Biodesign research*
  Chu, A. E., Fernandez, D., Liu, J., Eguchi, R. R., Huang, P. S.
  2022; 2022: 9842315

- **Ig-VAE: Generative modeling of protein structure by direct 3D coordinate generation.** *PLoS computational biology*
  Eguchi, R. R., Choe, C. A., Huang, P. S.
  2022; 18 (6): e1010271

- **Protein sequence design with a learned potential.** *Nature communications*
  Anand, N., Eguchi, R., Mathews, I. I., Perez, C. P., Derry, A., Altman, R. B., Huang, P.
  2022; 13 (1): 746

- **Chimeric mutants of staphylococcal hemolysin, which act as both one-component and two-component hemolysin, created by grafting the stem domain.** *The FEBS journal*
  Ghanem, N., Kanagami, N., Matsui, T., Takeda, K., Kaneko, J., Shiraishi, Y., Choe, C. A., Uchikubo-Kamo, T., Shirouzu, M., Hashimoto, T., Ogawa, T., Matsuura, T., Huang, et al
  2022

- **Interleukin-2 superkines by computational design.** *Proceedings of the National Academy of Sciences of the United States of America*
  Ren, J., Chu, A. E., Jude, K. M., Picton, L. K., Kare, A. J., Su, L., Montano Romero, A., Huang, P. S., Garcia, K. C.
  2022; 119 (12): e2117401119

- **Structure-based protein design with deep learning.** *Current opinion in chemical biology*
  Ovchinnikov, S., Huang, P.
  2021; 65: 136-144

- **Theoretical basis for stabilizing messenger RNA through secondary structure design.** *Nucleic acids research*
  Wayment-Steele, H. K., Kim, D. S., Choe, C. A., Nicol, J. J., Wellington-Oguri, R., Watkins, A. M., Parra Sperberg, R. A., Huang, P., Participants, E., Das, R.
  2021

- **Optical control of fast and processive engineered myosins in vitro and in living cells.** *Nature chemical biology*

Ruijgrok, P. V., Ghosh, R. P., Zemsky, S. n., Nakamura, M. n., Gong, R. n., Ning, L. n., Chen, R. n., Vachharajani, V. T., Chu, A. E., Anand, N. n., Eguchi, R. R., Huang, P. S., Lin, et al
2021

- **Correction to 'Theoretical basis for stabilizing messenger RNA through secondary structure design'.** *Nucleic acids research*
  Wayment-Steele, H. K., Kim, D. S., Choe, C. A., Nicol, J. J., Wellington-Oguri, R., Watkins, A. M., Parra Sperberg, R. A., Huang, P. S., Participants, E., Das, R.
  2021
- **Identification of N-Terminally Diversified GLP-1R Agonists Using Saturation Mutagenesis and Chemical Design.** *ACS chemical biology*
  Longwell, C. K., Hanna, S., Hartrampf, N., Sperberg, R. A., Huang, P., Pentelute, B. L., Cochran, J. R.
  2020
- **Tight and specific lanthanide binding in a de novo TIM barrel with a large internal cavity designed by symmetric domain fusion.** *Proceedings of the National Academy of Sciences of the United States of America*
  Caldwell, S. J., Haydon, I. C., Piperidou, N., Huang, P., Bick, M. J., Sjostrom, H. S., Hilvert, D., Baker, D., Zeymer, C.
  2020
- **HIV-1 VRC01 Germline-Targeting Immunogens Select Distinct Epitope-Specific B Cell Receptors.** *Immunity*
  Lin, Y., Parks, K. R., Weidle, C., Naidu, A. S., Khechaduri, A., Riker, A. O., Takushi, B., Chun, J., Borst, A. J., Veesler, D., Stuart, A., Agrawal, P., Gray, et al
  2020; 53 (4): 840
- **Computational design of transmembrane pores.** *Nature*
  Xu, C., Lu, P., Gamal El-Din, T. M., Pei, X. Y., Johnson, M. C., Uyeda, A., Bick, M. J., Xu, Q., Jiang, D., Bai, H., Reggiano, G., Hsia, Y., Brunette, et al
  2020
- **Theoretical basis for stabilizing messenger RNA through secondary structure design.** *bioRxiv : the preprint server for biology*
  Wayment-Steele, H. K., Kim, D. S., Choe, C. A., Nicol, J. J., Wellington-Oguri, R., Watkins, A. M., Sperberg, R. A., Huang, P. S., Participants, E., Das, R.
  2020
- **Engineering a potent receptor superagonist or antagonist from a novel IL-6 family cytokine ligand.** *Proceedings of the National Academy of Sciences of the United States of America*
  Kim, J. W., Marquez, C. P., Sperberg, R. A., Wu, J., Bae, W. G., Huang, P., Sweet-Cordero, E. A., Cochran, J. R.
  2020
- **Macromolecular modeling and design in Rosetta: recent methods and frameworks.** *Nature methods*
  Leman, J. K., Weitzner, B. D., Lewis, S. M., Adolf-Bryfogle, J., Alam, N., Alford, R. F., Aprahamian, M., Baker, D., Barlow, K. A., Barth, P., Basanta, B., Bender, B. J., Blacklock, et al
  2020
- **Computational design of closely related proteins that adopt two well-defined but structurally divergent folds.** *Proceedings of the National Academy of Sciences of the United States of America*
  Wei, K. Y., Moschidi, D., Bick, M. J., Nerli, S., McShan, A. C., Carter, L. P., Huang, P., Fletcher, D. A., Sgourakis, N. G., Boyken, S. E., Baker, D.
  2020
- **Harnessing Human Neural Networks for Protein Design.** *Biochemistry*
  Huang, P., Thompson, K. A.
  2019
- **Heterodimer assembly from de novo repeat protein structures**
  Huang, P.
  AMER CHEMICAL SOC.2019
- **Multi-Scale Structural Analysis of Proteins by Deep Semantic Segmentation.** *Bioinformatics (Oxford, England)*
  Eguchi, R. R., Huang, P.
  2019
- **The molecular basis of chaperone-mediated interleukin 23 assembly control.** *Nature communications*

Meier, S. n., Bohnacker, S. n., Klose, C. J., Lopez, A. n., Choe, C. A., Schmid, P. W., Bloemeke, N. n., Rührnößl, F. n., Haslbeck, M. n., Bieren, J. E., Sattler, M. n., Huang, P. S., Feige, et al
2019; 10 (1): 4121

- **Structure and Functional Binding Epitope of V-domain Ig Suppressor of T Cell Activation.** *Cell reports*
  Mehta, N. n., Maddineni, S. n., Mathews, I. I., Andres Parra Sperberg, R. n., Huang, P. S., Cochran, J. R.
  2019; 28 (10): 2509–16.e5

- **De novo design of a fluorescence-activating beta-barrel.** *Nature*
  Dou, J., Vorobieva, A. A., Sheffler, W., Doyle, L. A., Park, H., Bick, M. J., Mao, B., Foight, G. W., Lee, M. Y., Gagnon, L. A., Carter, L., Sankaran, B., Ovchinnikov, et al
  2018

- **Generative Modeling for Protein Structures**
  Anand, N., Huang, P.
  edited by Bengio, S., Wallach, H., Larochelle, H., Grauman, K., CesaBianchi, N., Garnett, R.
  NEURAL INFORMATION PROCESSING SYSTEMS (NIPS).2018

- **Designing repeat proteins: a modular approach to protein design.** *Current opinion in structural biology*
  Parmeggiani, F., Huang, P.
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- **Protein structure determination using metagenome sequence data** *SCIENCE*
  Ovchinnikov, S., Park, H., Varghese, N., Huang, P., Pavlopoulos, G. A., Kim, D. E., Kamisetty, H., Kyrpides, N. C., Baker, D.
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- **A computationally engineered RAS rheostat reveals RAS-ERK signaling dynamics** *NATURE CHEMICAL BIOLOGY*
  Rose, J. C., Huang, P., Camp, N. D., Ye, J., Leidal, A. M., Goreshnik, I., Trevillian, B. M., Dickinson, M. S., Cunningham-Bryant, D., Debnath, J., Baker, D., Wolf-Yadlin, A., Maly, et al
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- **Accurate de novo design of hyperstable constrained peptides** *NATURE*
  Bhardwaj, G., Mulligan, V. K., Bahl, C. D., Gilmore, J. M., Harvey, P. J., Cheneval, O., Buchko, G. W., Pulavarti, S. V., Kaas, Q., Eletsky, A., Huang, P., Johnsen, W. A., Greisen, et al
  2016; 538 (7625): 329-?

- **The coming of age of de novo protein design** *NATURE*
  Huang, P., Boyken, S. E., Baker, D.
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- **Design of a hyperstable 60-subunit protein icosahedron** *NATURE*
  Hsia, Y., Bale, J. B., Gonen, S., Shi, D., Sheffler, W., Fong, K. K., Nattermann, U., Xu, C., Huang, P., Ravichandran, R., Yi, S., Davis, T. N., Gonen, et al
  2016; 535 (7610): 136-?

- **De novo design of a four-fold symmetric TIM-barrel protein with atomic-level accuracy.** *Nature chemical biology*
  Huang, P., Feldmeier, K., Parmeggiani, F., Fernandez Velasco, D. A., Höcker, B., Baker, D.
  2016; 12 (1): 29-34

- **Exploring the repeat protein universe through computational protein design** *NATURE*
  Brunette, T. J., Parmeggiani, F., Huang, P., Bhabha, G., Ekiert, D. C., Tsutakawa, S. E., Hura, G. L., Tainer, J. A., Baker, D.
  2015; 528 (7583): 580-?

- **Computational design and experimental verification of a symmetric protein homodimer** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Mou, Y., Huang, P., Hsu, F., Huang, S., Mayo, S. L.
  2015; 112 (34): 10714-10719

- **Using Molecular Dynamics Simulations as an Aid in the Prediction of Domain Swapping of Computationally Designed Protein Variants** *JOURNAL OF MOLECULAR BIOLOGY*
  Mou, Y., Huang, P., Thomas, L. M., Mayo, S. L.

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- **Control of repeat-protein curvature by computational protein design** *NATURE STRUCTURAL & MOLECULAR BIOLOGY*
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- **A General Computational Approach for Repeat Protein Design** *JOURNAL OF MOLECULAR BIOLOGY*
  Parmeggiani, F., Huang, P., Vorobiev, S., Xiao, R., Park, K., Caprari, S., Su, M., Seetharaman, J., Mao, L., Janjua, H., Montelione, G. T., Hunt, J., Baker, et al
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- **Computational De Novo Design of a Self-Assembling Peptide with Predefined Structure** *JOURNAL OF MOLECULAR BIOLOGY*
  Kaltofen, S., Li, C., Huang, P., Serpell, L. C., Barth, A., Andre, I.
  2015; 427 (2): 550-562
- **High thermodynamic stability of parametrically designed helical bundles** *SCIENCE*
  Huang, P., Oberdorfer, G., Xu, C., Pei, X. Y., Nannenga, B. L., Rogers, J. M., DiMaio, F., Gonen, T., Luisi, B., Baker, D.
  2014; 346 (6208): 481-485
- **Immune Focusing and Enhanced Neutralization Induced by HIV-1 gp140 Chemical Cross-Linking** *JOURNAL OF VIROLOGY*
  Schiffner, T., Kong, L., Duncan, C. J., Back, J. W., Benschop, J. J., Shen, X., Huang, P. S., Stewart-Jones, G. B., DeStefano, J., Seaman, M. S., Tomaras, G. D., Montefiori, D. C., Schief, et al
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- **Rational HIV Immunogen Design to Target Specific Germline B Cell Receptors** *SCIENCE*
  Jardine, J., Julien, J., Menis, S., Ota, T., Kalyuzhniy, O., McGuire, A., Sok, D., Huang, P., MacPherson, S., Jones, M., Nieusma, T., Mathison, J., Baker, et al
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- **Domain 1 of Mucosal Addressin Cell Adhesion Molecule Has an I1-set Fold and a Flexible Integrin-binding Loop** *JOURNAL OF BIOLOGICAL CHEMISTRY*
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  Pejchal, R., Doores, K. J., Walker, L. M., Khayat, R., Huang, P., Wang, S., Stanfield, R. L., Julien, J., Ramos, A., Crispin, M., Depetris, R., Katpally, U., Marozsan, et al
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- **High-resolution structure prediction of a circular permutation loop** *PROTEIN SCIENCE*
  Correia, B. E., Holmes, M. A., Huang, P., Strong, R. K., Schief, W. R.
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- **Computation-Guided Backbone Grafting of a Discontinuous Motif onto a Protein Scaffold** *SCIENCE*
  Azoitei, M. L., Correia, B. E., Ban, Y. A., Carrico, C., Kalyuzhniy, O., Chen, L., Schroeter, A., Huang, P., McLellan, J. S., Kwong, P. D., Baker, D., Strong, R. K., Schief, et al
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- **RosettaRemodel: A Generalized Framework for Flexible Backbone Protein Design** *PLOS ONE*
  Huang, P., Ban, Y. A., Richter, F., Andre, I., Vernon, R., Schief, W. R., Baker, D.
  2011; 6 (8)
- **A Chimeric HIV-1 Envelope Glycoprotein Trimer with an Embedded Granulocyte-Macrophage Colony-stimulating Factor (GM-CSF) Domain Induces Enhanced Antibody and T Cell Responses** *JOURNAL OF BIOLOGICAL CHEMISTRY*
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- **Modulation of Integrin Activation by an Entropic Spring in the beta-Knee** *JOURNAL OF BIOLOGICAL CHEMISTRY*
  Smagghe, B. J., Huang, P., Ban, Y. A., Baker, D., Springer, T. A.
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- **A de novo designed protein-protein interface** *PROTEIN SCIENCE*
  Huang, P., Love, J. J., Mayo, S. L.
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- **Adaptation of a fast Fourier transform-based docking algorithm for protein design** *JOURNAL OF COMPUTATIONAL CHEMISTRY*
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- **A designed protein interface that blocks fibril formation** *JOURNAL OF THE AMERICAN CHEMICAL SOCIETY*
  Shukla, U. J., Marino, H., Huang, P. S., Mayo, S. L., Love, J. J.
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