



Markus Covert

Shriram Chair of the Department of Bioengineering, Professor of Bioengineering and, by courtesy, of Chemical and Systems Biology

CONTACT INFORMATION

- **Chair's Office**

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Bio

BIO

Our focus is on building computational models of complex biological processes, and using these models to guide an experimental program. Such an approach leads to a relatively rapid identification and validation of previously unknown components and interactions. Biological systems of interest include metabolic, regulatory and signaling networks as well as cell-cell interactions. Current research involves the dynamic behavior of NF-kappaB, an important family of transcription factors whose aberrant activity has been linked to oncogenesis, tumor progression, and resistance to chemotherapy.

ACADEMIC APPOINTMENTS

- Professor, Bioengineering
- Professor (By courtesy), Chemical and Systems Biology
- Member, Bio-X
- Member, Cardiovascular Institute
- Faculty Fellow, Sarafan ChEM-H

ADMINISTRATIVE APPOINTMENTS

- Shriram Chair, Stanford Bioengineering, (2023- present)

HONORS AND AWARDS

- Director's Pioneer Award, NIH (2009-2014)
- Allen Distinguished Investigator Award, Paul G. Allen Frontiers Group (2013-2016)

PROFESSIONAL EDUCATION

- Ph.D., UCSD , Bioengineering/ Bioinformatics (2003)
- M.S., UCSD , Bioengineering (2002)
- B.S., Brigham Young University , Chemical Engineering (1997)

LINKS

- Lab Website: <https://www.covert.stanford.edu/>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our focus is on building computational models of complex biological processes, and using these models to guide an experimental program. Such an approach leads to a relatively rapid identification and validation of previously unknown components and interactions. Biological systems of interest include metabolic, regulatory and signaling networks as well as cell-cell interactions. Current research involves the dynamic behavior of NF-kappaB, an important family of transcription factors whose aberrant activity has been linked to oncogenesis, tumor progression, and resistance to chemotherapy.

Teaching

COURSES

2024-25

- Systems Biology: BIOE 101, BIOE 210 (Aut)

2023-24

- Systems Biology: BIOE 101, BIOE 210 (Aut)

2022-23

- Bioengineering Departmental Research Colloquium: BIOE 393 (Aut)
- Systems Biology: BIOE 101, BIOE 210 (Aut)

2021-22

- Bioengineering Departmental Research Colloquium: BIOE 393 (Aut)
- Systems Biology: BIOE 101, BIOE 210 (Aut)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Eliel Akinbami, Meelad Amouzgar, Linus Hein, Yulin Huang, George Walters-Marrah

Postdoctoral Faculty Sponsor

Rong Ma, Nora Vivanco Gonzalez

Doctoral Dissertation Advisor (AC)

Annabelle Fowler, Mia Grahn, Riley Juenemann, Cyrus Knudsen, Heena Saqib, Mica Yang

Doctoral (Program)

Eliel Akinbami, Tyler Cork, Betty Liu, Julia Schaepe

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Bioengineering (Phd Program)
- Biomedical Data Science (Phd Program)
- Chemical and Systems Biology (Phd Program)

Publications

PUBLICATIONS

- **Cross-evaluation of *E. coli*'s operon structures via a whole-cell model suggests alternative cellular benefits for low- versus high-expressing operons.** *Cell systems*
Sun, G., DeFelice, M. M., Gillies, T. E., Ahn-Horst, T. A., Andrews, C. J., Krummenacker, M., Karp, P. D., Morrison, J. H., Covert, M. W.
2024
- **Whole-cell modeling of *E. coli* colonies enables quantification of single-cell heterogeneity in antibiotic responses.** *PLoS computational biology*
Skalnik, C. J., Cheah, S. Y., Yang, M. Y., Wolff, M. B., Spangler, R. K., Talman, L., Morrison, J. H., Peirce, S. M., Agmon, E., Covert, M. W.
2023; 19 (6): e1011232
- **Whole-cell modeling of *E. coli* confirms that in vitro tRNA aminoacylation measurements are insufficient to support cell growth and predicts a positive feedback mechanism regulating arginine biosynthesis.** *Nucleic acids research*
Choi, H., Covert, M. W.
2023
- **A multiplexed epitope barcoding strategy that enables dynamic cellular phenotypic screens.** *Cell systems*
Kudo, T., Lane, K., Covert, M. W.
2022
- **Simultaneous cross-evaluation of heterogeneous *E. coli* datasets via mechanistic simulation.** *Science (New York, N.Y.)*
Macklin, D. N., Ahn-Horst, T. A., Choi, H., Ruggero, N. A., Carrera, J., Mason, J. C., Sun, G., Agmon, E., DeFelice, M. M., Maayan, I., Lane, K., Spangler, R. K., Gillies, et al
2020; 369 (6502)
- **Engineered Fluorescent *E. coli* Lysogens Allow Live-Cell Imaging of Functional Prophage Induction Triggered inside Macrophages.** *Cell systems*
Bodner, K. n., Melkonian, A. L., Barth, A. I., Kudo, T. n., Tanouchi, Y. n., Covert, M. W.
2020
- **Deep Learning Automates the Quantitative Analysis of Individual Cells in Live-Cell Imaging Experiments.** *PLoS computational biology*
Van Valen, D. A., Kudo, T., Lane, K. M., Macklin, D. N., Quach, N. T., DeFelice, M. M., Maayan, I., Tanouchi, Y., Ashley, E. A., Covert, M. W.
2016; 12 (11)
- **High-sensitivity measurements of multiple kinase activities in live single cells.** *Cell*
Regot, S., Hughey, J. J., Bajar, B. T., Carrasco, S., Covert, M. W.
2014; 157 (7): 1724-1734
- **A Whole-Cell Computational Model Predicts Phenotype from Genotype** *CELL*
Karr, J. R., Sanghvi, J. C., Macklin, D. N., Gutschow, M. V., Jacobs, J. M., Bolival, B., Assad-Garcia, N., Glass, J. I., Covert, M. W.
2012; 150 (2): 389-401
- **The EcoCyc Database (2023).** *EcoSal Plus*
Karp, P. D., Paley, S., Caspi, R., Kothari, A., Krummenacker, M., Midford, P. E., Moore, L. R., Subhraveti, P., Gama-Castro, S., Tierrafria, V. H., Lara, P., Muñoz-Rascado, L., Bonavides-Martinez, et al
2023: eesp00022023
- **An expanded whole-cell model of *E. coli* links cellular physiology with mechanisms of growth rate control.** *NPJ systems biology and applications*
Ahn-Horst, T. A., Mille, L. S., Sun, G., Morrison, J. H., Covert, M. W.
2022; 8 (1): 30
- **Microbial metabolites in the marine carbon cycle.** *Nature microbiology*
Moran, M. A., Kujawinski, E. B., Schroer, W. F., Amin, S. A., Bates, N. R., Bertrand, E. M., Braakman, R., Brown, C. T., Covert, M. W., Doney, S. C., Dyrman, S. T., Edison, A. S., Eren, et al
2022; 7 (4): 508-523

- **Vivarium: an interface and engine for integrative multiscale modeling in computational biology.** *Bioinformatics (Oxford, England)*
Agmon, E., Spangler, R. K., Skalnik, C. J., Poole, W., Peirce, S. M., Morrison, J. H., Covert, M. W.
2022
- **The E. coli Whole-Cell Modeling Project.** *EcoSal Plus*
Sun, G., Ahn-Horst, T. A., Covert, M. W.
2021: eESP00012020
- **A forecast for large-scale, predictive biology: Lessons from meteorology.** *Cell systems*
Covert, M. W., Gillies, T. E., Kudo, T., Agmon, E.
2021; 12 (6): 488-496
- **Building Structural Models of a Whole Mycoplasma Cell.** *Journal of molecular biology*
Maritan, M., Autin, L., Karr, J., Covert, M. W., Olson, A. J., Goodsell, D. S.
2021: 167351
- **A Protocol to Engineer Bacteriophages for Live-Cell Imaging of Bacterial Prophage Induction Inside Mammalian Cells.** *STAR protocols*
Bodner, K., Melkonian, A. L., Covert, M. W.
2020; 1 (2): 100084
- **Stress-mediated exit to quiescence restricted by increasing persistence in CDK4/6 activation.** *eLife*
Yang, H. W., Cappell, S. D., Jaimovich, A., Liu, C., Chung, M., Daigh, L. H., Pack, L. R., Fan, Y., Regot, S., Covert, M., Meyer, T.
2020; 9
- **A Protocol to Engineer Bacteriophages for Live-Cell Imaging of Bacterial Prophage Induction Inside Mammalian Cells** *STAR Protocols*
Bodner, K., Melkonian, A. L., Covert, M. W.
2020
- **The Enemy of My Enemy: New Insights Regarding Bacteriophage-Mammalian Cell Interactions.** *Trends in microbiology*
Bodner, K. n., Melkonian, A. L., Covert, M. W.
2020
- **Deep learning for cellular image analysis.** *Nature methods*
Moen, E., Bannon, D., Kudo, T., Graf, W., Covert, M., Van Valen, D.
2019
- **NF-kappaB signaling dynamics is controlled by a dose-sensing autoregulatory loop.** *Science signaling*
DeFelice, M. M., Clark, H. R., Hughey, J. J., Maayan, I., Kudo, T., Gutschow, M. V., Covert, M. W., Regot, S.
2019; 12 (579)
- **Techniques for Studying Decoding of Single Cell Dynamics.** *Frontiers in immunology*
Jeknić, S., Kudo, T., Covert, M. W.
2019; 10: 755
- **Escalating Threat Levels of Bacterial Infection Can Be Discriminated by Distinct MAPK and NF-kappaB Signaling Dynamics in Single Host Cells.** *Cell systems*
Lane, K., Andres-Terre, M., Kudo, T., Monack, D. M., Covert, M. W.
2019
- **Simultaneous Cross-Evaluation of Heterogeneous E. coli Datasets via Mechanistic Simulation**
Covert, M.
CELL PRESS.2019: 451A
- **Combinatorial processing of bacterial and host-derived innate immune stimuli at the single-cell level.** *Molecular biology of the cell*
Gutschow, M. V., Mason, J. C., Lane, K. M., Maayan, I., Hughey, J. J., Bajar, B. T., Amatya, D. N., Valle, S. D., Covert, M. W.
2018: mbcE18070423
- **Live-cell measurements of kinase activity in single cells using translocation reporters** *NATURE PROTOCOLS*
Kudo, T., Jeknic, S., Macklin, D. N., Akhter, S., Hughey, J. J., Regot, S., Covert, M. W.
2018; 13 (1): 155–69

- **Combining Comprehensive Analysis of Off-Site Lambda Phage Integration with a CRISPR-Based Means of Characterizing Downstream Physiology** *MBIO*
Tanouchi, Y., Covert, M. W.
2017; 8 (5)
- **Measuring Signaling and RNA-Seq in the Same Cell Links Gene Expression to Dynamic Patterns of NF- κ B Activation.** *Cell systems*
Lane, K., Van Valen, D., DeFelice, M. M., Macklin, D. N., Kudo, T., Jaimovich, A., Carr, A., Meyer, T., Pe'er, D., Boutet, S. C., Covert, M. W.
2017; 4 (4): 458-469 e5
- **High-resolution imaging and computational analysis of haematopoietic cell dynamics in vivo.** *Nature communications*
Koechlein, C. S., Harris, J. R., Lee, T. K., Weeks, J., Fox, R. G., Zimdahl, B., Ito, T., Blevins, A., Jung, S., Chute, J. P., Chourasia, A., Covert, M. W., Reya, et al
2016; 7: 12169-?
- **Why Build Whole-Cell Models?** *Trends in cell biology*
Carrera, J., Covert, M. W.
2015; 25 (12): 719-722
- **NetworkPainter: dynamic intracellular pathway animation in Cytobank** *BMC BIOINFORMATICS*
Karr, J. R., Guturu, H., Chen, E. Y., Blair, S. L., Irish, J. M., Kotecha, N., Covert, M. W.
2015; 16
- **Summary of the DREAM8 Parameter Estimation Challenge: Toward Parameter Identification for Whole-Cell Models.** *PLoS computational biology*
Karr, J. R., Williams, A. H., Zucker, J. D., Raue, A., Steiert, B., Timmer, J., Kreutz, C., Wilkinson, S., Allgood, B. A., Bot, B. M., Hoff, B. R., Kellen, M. R., Covert, et al
2015; 11 (5)
- **Summary of the DREAM8 Parameter Estimation Challenge: Toward Parameter Identification for Whole-Cell Models.** *PLoS computational biology*
Karr, J. R., Williams, A. H., Zucker, J. D., Raue, A., Steiert, B., Timmer, J., Kreutz, C., Wilkinson, S., Allgood, B. A., Bot, B. M., Hoff, B. R., Kellen, M. R., Covert, et al
2015; 11 (5): e1004096
- **Single-cell variation leads to population invariance in NF- κ B signaling dynamics.** *Molecular biology of the cell*
Hughey, J. J., Gutschow, M. V., Bajar, B. T., Covert, M. W.
2015; 26 (3): 583-590
- **NetworkPainter: dynamic intracellular pathway animation in Cytobank.** *BMC bioinformatics*
Karr, J. R., Guturu, H., Chen, E. Y., Blair, S. L., Irish, J. M., Kotecha, N., Covert, M. W.
2015; 16: 172-?
- **WholeCellSimDB: a hybrid relational/HDF database for whole-cell model predictions** *DATABASE-THE JOURNAL OF BIOLOGICAL DATABASES AND CURATION*
Karr, J. R., Phillips, N. C., Covert, M. W.
2014
- **Nonlytic viral spread enhanced by autophagy components** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Bird, S. W., Maynard, N. D., Covert, M. W., Kirkegaard, K.
2014; 111 (36): 13081-13086
- **Nonlytic viral spread enhanced by autophagy components.** *Proceedings of the National Academy of Sciences of the United States of America*
Bird, S. W., Maynard, N. D., Covert, M. W., Kirkegaard, K.
2014; 111 (36): 13081-13086
- **The future of whole-cell modeling** *CURRENT OPINION IN BIOTECHNOLOGY*
Macklin, D. N., Ruggero, N. A., Covert, M. W.
2014; 28: 111-115
- **Incorporation of flexible objectives and time-linked simulation with flux balance analysis.** *Journal of theoretical biology*

- Birch, E. W., Udell, M., Covert, M. W.
2014; 345: 12-21
- **WholeCellSimDB: a hybrid relational/HDF database for whole-cell model predictions.** *Database : the journal of biological databases and curation*
Karr, J. R., Phillips, N. C., Covert, M. W.
2014; 2014
 - **Accelerated discovery via a whole-cell model.** *Nature methods*
Sanghvi, J. C., Regot, S., Carrasco, S., Karr, J. R., Gutschow, M. V., Bolival, B., Covert, M. W.
2013; 10 (12): 1192-1195
 - **Accelerated discovery via a whole-cell model** *NATURE METHODS*
Sanghvi, J. C., Regot, S., Carrasco, S., Karr, J. R., Gutschow, M. V., Bolival, B., Covert, M. W.
2013; 10 (12): 1192-?
 - **Towards a whole-cell modeling approach for synthetic biology** *CHAOS*
Purcell, O., Jain, B., Karr, J. R., Covert, M. W., Lu, T. K.
2013; 23 (2)
 - **Single-Cell and Population NF-kappa B Dynamic Responses Depend on Lipopolysaccharide Preparation** *PLOS ONE*
Gutschow, M. V., Hughey, J. J., Ruggero, N. A., Bajar, B. T., Valle, S. D., Covert, M. W.
2013; 8 (1)
 - **WholeCellKB: model organism databases for comprehensive whole-cell models.** *Nucleic acids research*
Karr, J. R., Sanghvi, J. C., Macklin, D. N., Arora, A., Covert, M. W.
2013; 41 (Database issue): D787-92
 - **Accelerated discovery via a whole-cell model** *Nature Methods.*
Sanghvi, J. C., Regot, S., Carrasco, G. S., Karr, J. R., Gutschow, M. V., Bolival, B., Covert, M.
2013
 - **WholeCellViz: data visualization for whole-cell models.** *BMC bioinformatics*
Lee, R., Karr, J. R., Covert, M. W.
2013; 14 (1): 253-?
 - **WholeCellKB: model organism databases for comprehensive whole-cell models** *NUCLEIC ACIDS RESEARCH*
Karr, J. R., Sanghvi, J. C., Macklin, D. N., Arora, A., Covert, M. W.
2013; 41 (D1): D787-D792
 - **Single-cell and population NF- κ B dynamic responses depend on lipopolysaccharide preparation.** *PLoS one*
Gutschow, M. V., Hughey, J. J., Ruggero, N. A., Bajar, B. T., Valle, S. D., Covert, M. W.
2013; 8 (1)
 - **Determining Host Metabolic Limitations on Viral Replication via Integrated Modeling and Experimental Perturbation** *PLOS COMPUTATIONAL BIOLOGY*
Birch, E. W., Ruggero, N. A., Covert, M. W.
2012; 8 (10)
 - **Neuron-to-neuron transmission of alpha-synuclein fibrils through axonal transport** *ANNALS OF NEUROLOGY*
Freundt, E. C., Maynard, N., Clancy, E. K., Roy, S., Bousset, L., Sourigues, Y., Covert, M., Melki, R., Kirkegaard, K., Brahic, M.
2012; 72 (4): 517-524
 - **Competing pathways control host resistance to virus via tRNA modification and programmed ribosomal frameshifting** *MOLECULAR SYSTEMS BIOLOGY*
Maynard, N. D., Macklin, D. N., Kirkegaard, K., Covert, M. W.
2012; 8
 - **High-throughput, single-cell NF-kappa B dynamics** *CURRENT OPINION IN GENETICS & DEVELOPMENT*
Lee, T. K., Covert, M. W.
2010; 20 (6): 677-683

- **Single-cell NF-kappa B dynamics reveal digital activation and analogue information processing** *NATURE*
Tay, S., Hughey, J. J., Lee, T. K., Lipniacki, T., Quake, S. R., Covert, M. W.
2010; 466 (7303): 267-U149
- **A Forward-Genetic Screen and Dynamic Analysis of Lambda Phage Host-Dependencies Reveals an Extensive Interaction Network and a New Anti-Viral Strategy** *PLOS GENETICS*
Maynard, N. D., Birch, E. W., Sanghvi, J. C., Chen, L., Gutschow, M. V., Covert, M. W.
2010; 6 (7)
- **The virus as metabolic engineer** *BIOTECHNOLOGY JOURNAL*
Maynard, N. D., Gutschow, M. V., Birch, E. W., Covert, M. W.
2010; 5 (7): 686-694
- **Computational modeling of mammalian signaling networks** *WILEY INTERDISCIPLINARY REVIEWS-SYSTEMS BIOLOGY AND MEDICINE*
Hughey, J. J., Lee, T. K., Covert, M. W.
2010; 2 (2): 194-209
- **Genome-scale metabolic networks** *WILEY INTERDISCIPLINARY REVIEWS-SYSTEMS BIOLOGY AND MEDICINE*
Terzer, M., Maynard, N. D., Covert, M. W., Stelling, J.
2009; 1 (3): 285-297
- **A Noisy Paracrine Signal Determines the Cellular NF-kappa B Response to Lipopolysaccharide** *SCIENCE SIGNALING*
Lee, T. K., Denny, E. M., Sanghvi, J. C., Gaston, J. E., Maynard, N. D., Hughey, J. J., Covert, M. W.
2009; 2 (93)
- **A dynamic network of transcription in LPS-treated human subjects** *BMC SYSTEMS BIOLOGY*
Seok, J., Xiao, W., Moldawer, L. L., Davis, R. W., Covert, M. W.
2009; 3
- **Integrating metabolic, transcriptional regulatory and signal transduction models in Escherichia coli** *BIOINFORMATICS*
Covert, M. W., Xiao, N., Chen, T. J., Karr, J. R.
2008; 24 (18): 2044-2050
- **Integrated Flux Balance Analysis Model of Escherichia coli** *Bioinformatics*.
Covert, M. W., Xiao, N., Chen, T. J., Karr, J. R.
2008; 18 (24): 2044-2050
- **Achieving stability of lipopolysaccharide-induced NF-kappa B activation** *SCIENCE*
Covert, M. W., Leung, T. H., Gaston, J. E., Baltimore, D.
2005; 309 (5742): 1854-1857
- **Integrated regulatory and metabolic models** *Computational Systems Biology, Academic Press, New York*
Covert, M.W.
2005
- **Computational Systems Biology. Integrated regulatory and metabolic models**
Covert, M. W.
Academic Press.2005
- **Integrating high-throughput and computational data elucidates bacterial networks** *NATURE*
Covert, M. W., Knight, E. M., Reed, J. L., Herrgard, M. J., Palsson, B. O.
2004; 429 (6987): 92-96
- **Reconstruction of microbial transcriptional regulatory networks** *CURRENT OPINION IN BIOTECHNOLOGY*
Herrgard, M. J., Covert, M. W., Palsson, B. O.
2004; 15 (1): 70-77
- **Identifying constraints that govern cell behavior: A key to converting conceptual to computational models in biology?** *BIOTECHNOLOGY AND BIOENGINEERING*
Covert, M. W., Famili, I., Palsson, B. O.

2003; 84 (7): 763-772

- **Reconciling gene expression data with known genome-scale regulatory network structures** *3rd International Conference on Systems Biology 2002*
Herrgard, M. J., Covert, M. W., Palsson, B. O.
COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT.2003: 2423-34
- **Constraints-based models: Regulation of gene expression reduces the steady-state solution space** *JOURNAL OF THEORETICAL BIOLOGY*
Covert, M. W., Palsson, B. O.
2003; 221 (3): 309-325
- **Transcriptional regulation in constraints-based metabolic models of Escherichia coli** *JOURNAL OF BIOLOGICAL CHEMISTRY*
Covert, M. W., Palsson, B. O.
2002; 277 (31): 28058-28064
- **Genome-scale metabolic model of Helicobacter pylori 26695** *9th International Conference on Microbial Genomes*
Schilling, C. H., Covert, M. W., Famili, I., Church, G. M., Edwards, J. S., Palsson, B. O.
AMER SOC MICROBIOLOGY.2002: 4582-93
- **Metabolic modelling of microbes: the flux-balance approach** *Environ Microbiol.*
Edwards, J. S., Covert, M. W., Palsson, B. Ø.
2002; 3 (4): 133-40
- **Regulation of gene expression in flux balance models of metabolism** *JOURNAL OF THEORETICAL BIOLOGY*
Covert, M. W., Schilling, C. H., Palsson, B.
2001; 213 (1): 73-88
- **Metabolic modeling of microbial strains in silico** *TRENDS IN BIOCHEMICAL SCIENCES*
Covert, M. W., Schilling, C. H., Famili, I., Edwards, J. S., Goryanin, I. I., Selkov, E., Palsson, B. O.
2001; 26 (3): 179-186
- **Encyclopedia of Microbiology. Genomic Engineering of Bacterial Metabolism**
Edwards, J. S., Schilling, C. H., Covert, M. W., Smith, S. J., Palsson, B. Ø.
Academic Press.2000