Curriculum Vitae for

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A. Education

University of California, Los Angeles, CA	B. S.	1983	Biochemistry
University of California, Los Angeles, CA	Ph.D.	1988	Biochemistry

B. Personal Statement

Research in the Yeates laboratory covers the areas of structural, computational and synthetic biology. Much of our recent efforts focus on very large protein assemblies. These include (1) giant natural protein shells known as bacterial microcompartments (MCPs) that serve as metabolic organelles in many bacteria, and (2) novel proteins that we design in the laboratory to self-assemble into complex architecture such as cubic cages. These systems have attracted attention as new platforms for bioengineering and synthetic biology. We also have long standing research interests in comparative genomics and macromolecular X-ray diffraction.

C. Positions and Honors

Professional Positions

1988-1990	Postdoctoral Researcher, Research Institute of Scripps Clinic
1996-present	Adjunct Asst. Professor; Adjunct Assoc. Professor (1997), The Scripps Research Institute
1990-present	Asst. Professor; Assoc. Prof. (1996); Professor in Chemistry and Biochemistry (2001), Univ. of California, Los Angeles

Awards and Honors

Mathematical Association of America Award (national competition)	1978 & 1979
University of California Regents Scholarship	1979-1983
NIH National Research Service Award (predoctoral trainee)	1984-1987
NSF Presidential Young Investigator	1991-1996
Sidhu Award - Pittsburgh Diffraction Society	1993
McCoy Award for Excellence in Research – UCLA Chem. & Biochem.	1995
Elected Fellow – American Association for the Advancement of Science	2002
Hansen-Dow Award for Excellence in Teaching – UCLA Chem. & Biochem.	2004
Plenary Lecture – German Crystallographic Society	2006
Plenary Lecture – Midwest Quantitative Biology Conference	2006
Keynote Lecture – Biennial Conference of Crystallographers in Australia and New Zealand	2011
Keynote Lecture – Buffalo, Hamilton, Toronto Crystallography Society	2013
Keynote Address – Foundations of Nanoscience, Snowbird, Utah	2013
Plenary Lecture – 11th Workshop on Cyanobacteria, St. Louis, MO	2013
Program Chair – 28th Annual Meeting of the Protein Society	2014
Plenary Lecture – Foldamers Conference, Bordeaux, France	2015

Panels and Professional Service (since 2003)

Cal State LA Bioinformatics Institute – Mentor (2003-2009); DOE Genomes to Life Program, Protein Structure Prediction - panel member (2003); NIH, Physical Biochemistry study section – ad hoc (2003); NSF, Biological Databases and Informatics – program reviewer (2003); DOE-GTL Cellular Interactions - panel chair (2004); Joint Center for Structural Genomics - Scientific Advisory Board (2004-2014); NIH Computational Biophysics Special Emphasis Panel (2004, 2005); Protein Science – Editorial Advisory Board (2006-current); NIH MSFC study section (ad hoc) (2006); NIH Computational Biophysics Special Emphasis Panel, BCMB-Q (2006); Co-

Editor, Acta Crystallographica, sect. D (2006-current); NIH MSFB study section (ad hoc) (2006); Editorial board, Protein Engineering, Design, and Selection (2009-current); NIH MSFD study section (ad hoc) (2007-2009); Director, UCLA X-ray Core Facility (2007-2011); NIH Review Panelist, Eureka Awards (2008); NIH Special Review Panel (TNPC program) (2009); NIH MSFD study section (ad hoc) (2011); NSF MCB panelist (2011); NIH MSFD study section (ad hoc) (2012); NIH Shared Instrumentation (S10) Review Panel (2012); NIH BCMB-A Special Emphasis Review Panel (2013); NSF MCB panel (2014); NIH PCMB study section (2015-)

Executive Positions

Director – UCLA Macromolecular Diffraction Facility (2008-current)
Assoc. Director – UCLA-DOE Institute for Genomics and Proteomics (2014-current)
Graduate Faculty Advisor – Biochemistry and Molecular Biology Program, UCLA (2011-2014)
Graduate Program Executive Committee – Biochemistry, Biophysics, and Structural Biology, UCLA (2015-)

D. Contributions to Science (out of approx. 150 publications)

1. Structural Biology of Bacterial Metabolic Organelles – Carboxysomes and Other Bacterial Microcompartments

- Kerfeld, C. A., Sawaya, M.R., Tanaka, S., Nguyen, C.V., Phillips, M., Beeby, M., and Yeates, T.O. 2005. Protein structures forming the shell of primitive bacterial organelles. *Science* **309**, 936-8.
- Tanaka, S., Kerfeld, C. A., Sawaya, M. R., Cai, F., Heinhorst, S., Cannon, G. C. & Yeates, T. O. (2008). Atomic-level models of the bacterial carboxysome shell. *Science* **319**, 1083-6.
- Tanaka, S., Sawaya, M.R., and Yeates, T.O. 2010. Structure and mechanisms of a protein-based organelle in *Escherichia coli*. *Science* **327**, 81-4.
- Thompson, M.C., Cascio, D., Leibly, D.J., Yeates, T.O. 2015. An allosteric model for control of pore opening by substrate binding in the EutL microcompartment shell protein. *Protein Sci*. doi: 10.1002/pro.2672.

The first three papers listed above describe the first crystal structures of proteins that self-assemble to form protein-based organelles in diverse bacteria. These intracellular microcompartments enhance specific metabolic processes by encapsulating sequentially-acting enzymes in order to sequester toxic or volatile intermediates, but their mechanisms of action and their relatively widespread occurrence in nature are not yet well appreciated. These initial papers opened up a new area of structural and synthetic biology. Our subsequent studies have illuminated a number of key mechanisms underlying assembly, selective molecular transport, and enzyme targeting in these extraordinary systems. The fourth paper above is an example of a recent finding related to allosteric control of molecular transport in these systems.

2. Designing Self-Assembling Protein Materials

- Padilla, J.E., Colovos, C., and Yeates, T.O. 2001. Nanohedra: using symmetry to design self assembling protein cages, layers, crystals, and filaments. *PNAS* **98**, 2217-21.

The paper above introduced for the first time a broadly applicable strategy, based on principle of symmetry, for designing novel proteins that would self-assemble to form elaborate structures such as cages, molecular layers, and three-dimensional crystals with atomic level precision.

- Lai, Y.-T., Cascio, D., Yeates, T.O. 2012. Structure of a 16-nm cage designed by using protein oligomers. *Science* **336**, 1129.

This paper confirmed the strategy we first proposed by elucidating the crystal structure of a designed 12-subunit, half-megadalton protein assembly resembling a tetrahedral cage. Subsequent studies have illuminated the flexibility and polymorphic behavior of this system.

- Lai, Y.-T., Reading, E., Hura, G.L., Tsai, K.L., Laganowsky, A., Asturias, F.J., Tainer, J.A., Robinson, C.V., Yeates, T.O. 2014. Structure of a designed protein cage that self-assembles into a highly porous cube. *Nat Chem*. **6**, 1065-71.

  This recent paper extended the oligomer-fusion method to create the largest designed protein assembly to date: a 24-subunit cage in the shape of a cube, 225Å in diameter. The crystal structure matches the design within about 1Å over the protein backbone. A hybrid combination of various biophysical methods was used to characterize the flexibility and heterogeneity.

  In conjunction with our own achievements in designing self-assembling protein materials, we have been collaborating with David Baker's group on a powerful variation on the symmetry-based ideas we laid out in Padilla et al. (2001). We have done the crystallographic work to validate the success of those new interface-design approaches.

3. Computational Genomics / Bioinformatics

- Pellegrini, M., Marcotte, E.M., Thompson, M.J., Eisenberg, D., and Yeates, T.O. 1999. Assigning protein functions by comparative genome analysis: Protein phylogenetic profiles. *PNAS*, **96**, 4285-4288
- Bowers, P.M., Cokus, S.J., Eisenberg, D., Yeates, T.O. 2004. Use of logic relationships to decipher protein network organization. *Science* **306**, 2246-9.

  The first paper above is one in a series from our laboratory and David Eisenberg's at UCLA that opened up the area of comparative genomics at a time when the number of completely sequences genomes was beginning to explode. The ideas were instrumental in promoting the now popular notion of protein interaction networks. The methods have spawned numerous extensions (as in the second paper listed above by Bowers, et al.) and similar applications by other research groups. Taken together, our papers on this topic have been cited by others about 3000 times.

- Mallick, P., Eisenberg, D., and Yeates, T.O. 2002. Genomic evidence that the intracellular proteins of archaeal microbes contain disulfide bonds. *PNAS* **99**, 9679-9684.
- Beeby, M., O'connor, B.D., Ryttersgaard, C., Boutz, D.R., Perry, L.J., and Yeates, T.O. 2005. The Genomics of disulfide bonding and protein stabilization in thermophiles. *PLoS Biol.* **3**, 1549-58.

  The comparative structural genomics studies above led to the surprising conclusion that thermophilic archaea use disulfide bonding as a key mechanism for protein stability. This unexpected result challenged the textbook view that the typically reducing environment in the cytosol would prevent disulfide bonding from being used as a general stabilizing mechanism. This represents a novel discovery in the area of archaeal microbiology. Subsequent studies provided further confirmation, while detailed investigations revealed cases of stabilization involving highly unusual protein topologies.

4. Knotting and Topological Complexity in Proteins

- King, N. P., Yeates, E. O., Yeates, T. O. 2007. Identification of rare slipknots in proteins and their implications for stability and folding. *J Mol Biol* **373**, 153-66.

- Yeates, T. O., T. S. Norcross, King, N.P. 2007. Knotted and topologically complex proteins as models for studying folding and stability. *Curr. Opin. Chem. Biol.* **11**, 595-603.
- King, N.P., Jacobitz, A.W., Sawaya, M.R., Goldschmidt, L., Yeates, T.O. 2010. Structure and folding of a designed knotted protein. *PNAS* **107**, 20732-20737.

The papers above include computational discoveries of new kinds of topological complexity in protein structures, along with experimental studies to test their effects and design studies to create complex proteins. A key finding was that a number of proteins contain knotted substructures (which we coined 'slipknots') that had been overlooked by previous computational studies of protein knotting. Complex topologies of this type present challenges for understanding the routes by which proteins reach their folded configurations. Our findings and ideas on this topic have motivated ongoing work in a number of laboratories on simulating protein folding pathways.

5. Protein Crystallography

- Padilla, J.E., and Yeates, T.O. 2003. A statistic for local intensity differences: robustness to anisotropy and pseudo-centering and utility for detecting twinning. *Acta Cryst. D* **59**, 1124-30.

The paper above is one in a series in which we introduced new equations for analyzing diffraction data from macromolecular crystals. These equations have been incorporated into the most widely used programs for analyzing macromolecular X-ray diffraction data and are evaluated during the course of practically every macromolecular diffraction experiment world-wide. The equations and associated variables have been absorbed into the crystallography vernacular.

- Yeates, T.O. and Kent, S.B.H. (2012). Racemic protein crystallography. *Annu. Rev. Biophys*. **41**.

This paper is a current review related to the idea of dramatically improving the success rate of protein crystallization by a racemic (synthetic) approach. In a paper on crystal space group symmetries in 1995 (Wukovitz and Yeates, 1995. *Nature Structural Biology*) where we answered the long-standing puzzle regarding why protein crystals prefer a few dominant space groups, we predicted that racemic crystallization could eventually lead to a much higher success rate for obtaining protein crystals. Very specific predictions were also made about what racemic space groups would provide this profound advantage. The accuracy of those predictions has been proven by recent experimental work (principally by Stephen Kent along with our group and other collaborators).

- Banatao, D.R., Cascio, D., Crowley, C.S., Fleissner, M.R., Tienson, H.L., and Yeates, T.O. 2006. An approach to crystallizing proteins by synthetic symmetrization. *PNAS* **103**, 16230-5.

This paper introduced the idea of "synthetic symmetrization" for improving the success rate of protein crystallization, which remains the key bottleneck in structural biology. The original work utilized genetic engineering and disulfide cross-linking, while subsequent studies have highlighted potentially more powerful approaches based on metal binding site design.