

CURRICULUM VITAE

Name: Carl O. Pabo

Born: September 1, 1952

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Education: Yale College
New Haven, Connecticut
B.S. (*summa cum laude*)
Molecular Biophysics and Biochemistry 1974

Harvard University
Cambridge, Massachusetts
Ph.D., Biochemistry and Molecular Biology 1980

Positions: Postdoctoral Fellow
Department of Biochemistry and Molecular Biology
Harvard University 1980–1982

Assistant Professor
Department of Biophysics
Johns Hopkins University School of Medicine 1982–1986

Associate Professor
Department of Molecular Biology and Genetics and
Department of Biophysics
Johns Hopkins University School of Medicine 1986–1990

Associate Investigator
Howard Hughes Medical Institute 1986–1991

Professor
Department of Molecular Biology and Genetics and
Department of Biophysics
Johns Hopkins University School of Medicine 1990–1991

Professor
Department of Biology
Massachusetts Institute of Technology 1991–2001

Investigator
Howard Hughes Medical Institute 1991–2001

Investigator
Center for Cancer Research
Massachusetts Institute of Technology 1999–2001

Senior Vice President and Chief Scientific Officer

Sangamo BioSciences, Inc.	2001–2003
Chair, Scientific Advisory Board Sangamo BioSciences, Inc.	1998–2001; 2003–2008
Moore Distinguished Scholar California Institute of Technology	January 2004 – April 2004
Visiting Professor, Bio-X Program Stanford University	September 2004 – April 2005
Visiting Professor, Department of Systems Biology Harvard Medical School	June 2005 – July 2005
Miller Visiting Research Professor University of California at Berkeley	August 2005 – December 2005
Visiting Professor, Department of Systems Biology Harvard Medical School	February 2006 – May 2007
Founder and Research Director Protean Futures LLC	September 2007 – Present
Scientific Advisor NanoDimension	March 2008 – Present
Visiting Professor, Division of Biology and Biological Engineering California Institute of Technology	April 2017– June 2017

Awards:

Elected to Phi Beta Kappa, 1973

NSF Predoctoral Fellowship, 1974–1977

Jane Coffin Childs Memorial Fund
Postdoctoral Fellowship, 1980–1982

American Cancer Society Junior Faculty
Research Award, 1983–1985

Protein Society Young Investigator Award, 1991

Pfizer Award in Enzyme Chemistry, 1992

Elected to American Academy of Arts and Sciences, 1993

Elected to National Academy of Sciences, 1998

Guggenheim Fellowship (“Theories of Thought”), 2005–2006

Teaching:

I have taught courses at Johns Hopkins, MIT, Caltech, and Stanford on biophysical chemistry, X-ray crystallography, protein design and engineering, evolution, theories of thought, and “The World in 2050.”

I have had extensive experience (both in academics and industry) as a mentor and advisor to young scientists.

Book on Thought: In 2001, I decided that the next stages of my work would focus on solving some fundamental problems inherent in existing theories of thought. The questions that concerned me transcended any traditional academic boundaries, and fell outside of areas that my training and my appointment in the Department of Biology at MIT had officially “authorized” me to investigate. I thus made the difficult decision to resign my position as a tenured professor at MIT and as an Investigator with the Howard Hughes Medical Institute, shifting as quickly as possible to focus my work on these studies of thought.

Since that time, I have developed a new way of describing and analyzing thought, using a physical frame of reference that encompasses both words and world. That is: I start by keeping everything grounded with reference to a flow of atomic, molecular events, avoiding any temptation to ever slip and start speaking of symbols, ideas, or thought as if they might exist in some separate, abstract, ethereal realm. [Thought is just one of the many things that complex assemblies of atoms and molecules can do; ideas are just one aspect of the way in which these atomic/molecular systems can be arranged and in which information can move.]

Once I had this clear way of keeping ideas grounded in the physical world, I then developed a set of flow diagrams – using a few, simple symbols to help track the various ways in which information (ideas) can move and change forms. Although my model only needs about a half-dozen such symbols, these can be combined to construct complex flow diagrams, showing the overall flow of information that occurs as we speak; as we think; as we act; as we work with others in a democratic system.

My model is not intended to compete with or to replace any existing model in psychology or the cognitive neurosciences. Rather, it addresses a critical problem that’s been ignored in previous work. A “blind spot” arises since 1) Thought (when problem-solving) typically proceeds with attention focused like a flashlight. The brain typically looks out at some aspect of the surrounding world (as I did in my studies of protein-DNA interactions). 2) Much of the actual work of the brain proceeds in the background (at a level that Steven Pinker had referred to as that of the “computational unconscious”). That is, much of the underlying process of thought remains out of sight, as if hidden behind a curtain, as if in this blind spot of thought.

My model – unlike any existing model in psychology – is designed to help illuminate this blind spot (step #2 above) while still allowing most of the person’s attention to remain focused as in step #1 above. Thus, my model allows the thinker to proceed with ANY problem of interest in ANY domain of inquiry. I provide a simple, qualitative way of tracking the flow of information, thus helping to make thought as effective as possible.

Having these new ways to think about the flow of thought thus lets me pinpoint some existing limitations in our current patterns of thought and – simultaneously – lets me point out alternative strategies that will help society better address some of the critical challenges now facing the planet. [I.e., once I had a model that worked at the appropriate scale, the whole problem of information flow became one of “circuit design”: In the

same way that adjustments in the layout of an electronic circuit can improve signal processing capacity, so I find that shifts in the flow of thought – involving relatively modest changes in the way that “cognitive agents” develop and share ideas – should allow society to solve significantly more complex problems.]

I’m now finishing my book, *Thought++*, with publication expected in fall 2017. The ideas offered here (also introduced now via my blog at carlpabo.com) give profound new insights about the best ways to approach some of the most critical challenges of the modern world. As with our understanding of any other natural phenomenon, a better understanding of the physical nature and meaning of thought helps us learn how to use it more effectively.

The Institute:

These new methods of thought can help with a wide range of problems – with issues arising in our personal lives, in education, academics, business, and government. But they are especially important when trying to address the hyper-complex challenges of the modern age – global warming, environmental degradation, risks to the stability of our social and financial systems, risks posed by artificial intelligence, etc. *Thought++* offers some fresh ways of addressing these global challenges, and I’m now setting up an institute – the Better World Institute for Thought & Policy – so as to expand my work in this area. [Everything is moving very rapidly, and I’m delighted to provide current details upon request. I have started fundraising so as to move quickly to help ensure a livable human future.]

Patents:

Listed on last two pages of CV (after publications).

PUBLICATIONS

1. Pabo, C.O., Sauer, R.T., Sturtevant, J.M. & Ptashne, M. (1979) The λ Repressor Contains Two Domains. **Proc. Natl. Acad. Sci., USA** **76**, 1608-1612.
2. Sauer, R.T., Pabo, C.O., Meyer, B.J., Ptashne, M. & Backman, K.C. (1979) The Regulatory Functions of the λ Repressor Reside in the Amino-Terminal Domain. **Nature** **279**, 396-400.
3. Johnson, A.D., Pabo, C.O. & Sauer, R. T. (1980) Bacteriophage λ Repressor and Cro Protein: Interactions with Operator DNA. **Meth. Enz.** **65**, 839-856.
4. Ptashne, M., Jeffrey, A., Johnson, A.D., Mauer, R., Meyer, B.J., Pabo, C.O., Roberts, T.M. & Sauer, R.T. (1980) How the λ Repressor and Cro Work. **Cell** **19**, 1-11.
5. Pabo, C.O., Krovatin, W., Jeffrey, A. & Sauer, R.T. (1982) The N-Terminal Arms of λ Repressor Wrap Around the Operator DNA. **Nature** **298**, 441-443.
6. Pabo, C.O. & Lewis, M. (1982) The Operator-Binding Domain of λ Repressor: Structure and DNA Recognition. **Nature** **298**, 443-447.
7. Sauer, R.T., Yocum, R.R., Doolittle, R.F., Lewis, M. & Pabo, C.O. (1982) Homology Among DNA-Binding Proteins Suggests Use of a Conserved Super-Secondary Structure. **Nature** **298**, 447-451.
8. Ptashne, M., Johnson, A.D. & Pabo, C.O. (1982) A Genetic Switch in a Bacterial Virus. **Scientific American** **247**, 128-140.
9. Lewis, M., Jeffrey, A., Wang, J-H., Ladner, R.C., Ptashne, M. & Pabo, C.O. (1983) Structure of the Operator-Binding Domain of λ Repressor: Implications for DNA Recognition and Gene Regulation. **Cold Spring Harbor Symp. Quant. Biol.** **47**, 435-440.
10. Gussin, G., Johnson, A.D., Pabo, C.O. & Sauer, R.T. (1983) Repressor and Cro. **Lambda II** (J. Roberts, ed.) Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 93-121.
11. Ohlendorf, D.H., Anderson, W.F., Lewis, M., Pabo, C.O. & Matthews, B.W. (1983) Comparison of the Structures of Cro and λ Repressor Proteins from Bacteriophage λ . **J. Mol. Biol.** **169**, 757-769.
12. Sauer, R.T. & Pabo, C.O. (1983) Protein-DNA Recognition: The λ Repressor-Operator Complex. **American Society for Microbiology News** **49**, 131-136.
13. Pabo, C.O. (1983) Designing Proteins and Peptides. **Nature** **301**, 200.
14. Pabo, C.O., Jordan, S.R. & Frankel, A.D. (1983) Systematic Analysis of Possible Hydrogen Bonds Between Amino Acid Side Chains and B-Form DNA. **J. Biomolecular Structure and Dynamics** **1**, 1039-1049.
15. Sauer, R.T. & Pabo, C.O. (1984) How λ Repressor Binds Operator DNA. **Microbiology** **1984**.

16. Pabo, C.O. & Sauer, R.T. (1984) Protein-DNA Recognition. **Ann. Rev. Biochem.** **53**, 293-321.
17. Pabo, C.O. (1984) DNA-Protein Interactions. **Proceedings of the Robert A. Welch Foundation Conferences on Chemical Research XXVII Stereospecificity in Chemistry and Biochemistry** Robert A. Welch Foundation, Houston, TX, 222-255.
18. Lewis, M., Wang, J. & Pabo, C.O. (1985) Structure of the Operator Binding Domain of λ Repressor. **Biological Macromolecules and Assemblies, Volume 2** (Drs. Jurnak & McPherson, eds.) John Wiley and Sons, Inc., New York, 266-287.
19. Jordan, S.R., Pabo, C.O., Vershon, A.K. & Sauer, R.T. (1985) Crystallization of the Arc Repressor. **J. Mol. Biol.** **185**, 445-446.
20. Jordan, S.R., Whitcombe, T.V., Berg, J.M. & Pabo, C.O. (1985) Systematic Variation in DNA Length Yields Highly Ordered Repressor-Operator Co-Crystals. **Science** **230**, 1383-1385.
21. Pabo, C.O. & Suchanek, E.G. (1986) Computer-Aided Model-Building Strategies for Protein Design. **Biochemistry** **25**, 5987-5991.
22. Sauer, R.T., Hehir, K., Stearman, R.S., Weiss, M.A., Jeitler-Nilsson, A., Suchanek, E.G. & Pabo, C.O. (1986) An Engineered Intersubunit Disulfide Enhances the Stability and DNA Binding of the N-Terminal Domain of λ Repressor. **Biochemistry** **25**, 5992-5998.
23. Weiss, M.A., Pabo, C.O., Karplus, M. & Sauer, R.T. (1986) Dimerization of the Operator-Binding Domain of Phage λ Repressor. **Biochemistry** **26**, 897-904.
24. Pabo, C.O. (1987) Introductory chapter for **Protein Engineering** (D. L. Oxender & C. F. Fox, eds.) Alan R. Liss, Inc., New York, xv-xvii.
25. Berg, J.M., Jordan, S.R. & Pabo, C.O. (1987) The Structure and Function of Bacteriophage λ Repressor. **DNA: Protein Interactions and Gene Regulation** (E.B. Thompson & J. Papaconstantinou, eds.) University of Texas Press, Austin, 1-12.
26. Pabo, C.O. (1987) New Generation Databases for Molecular Biology. **Nature** **327**, 467.
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29. Frankel, A.D. & Pabo, C.O. (1988) Fingering Too Many Proteins. **Cell** **53**, 675.
30. Frankel, A.D., Chen, L., Cotter, R.J. & Pabo C.O. (1988) Dimerization of the Tat Protein from HIV: A Cysteine-Rich Peptide Mimics the Normal Metal-Linked Dimer Interface. **Proc. Natl. Acad. Sci., USA** **85**, 6297-6300.

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32. Jordan, S.R. & Pabo, C.O. (1988) Structure of the λ Complex at 2.5 Å Resolution: Detailed View of the Repressor-Operator Interactions. **Science** **242**, 893-899.
33. Frankel, A.D. & Pabo, C.O. (1988) Cellular Uptake of the Tat Protein from Human Immunodeficiency Virus. **Cell** **55**, 1189-1193.
34. Sauer, R.T., Jordan, S.R. & Pabo, C.O. (1990) λ Repressor: A Model System for Understanding Protein-DNA Interactions and Protein Stability. **Adv. Prot. Chem.** **40**, 1-61.
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40. Pavletich, N.P. & Pabo, C.O. (1991) Zinc Finger-DNA Recognition: Crystal Structure of a Zif268-DNA Complex at 2.1 Å. **Science** **252**, 809-817.
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45. Beamer, L.J. & Pabo, C.O. (1992) Refined 1.8 Å Crystal Structure of the λ Repressor-Operator Complex. **J. Mol. Biol.** **227**, 177-196.
46. Pavletich, N.P. & Pabo, C.O. (1993) Crystal Structure of a Five Finger GLI-DNA Complex: New Perspectives on Zinc Fingers. **Science** **261**, 1701-1707.
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49. Raumann, B.E., Rould, M.A., Pabo, C.O. & Sauer, R.T. (1994) DNA Recognition by β -sheets in the Arc Repressor-Operator Crystal Structure. **Nature** **367**, 754-757.
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52. Nekludova, L. & Pabo, C.O. (1994) Distinctive DNA Conformation with Enlarged Major Groove Is Found in Zn Finger-DNA and Other Protein-DNA Complexes. **Proc. Natl. Acad. Sci., USA**, **91**, 6948-6952.
53. Clarke, N.D., Kissinger, C.R., Desjarlais, J., Gilliland, G.L., & Pabo, C.O. (1994) Structural Studies of the Engrailed Homeodomain. **Prot. Sci.** **3**, 1779-1787.
54. Pomerantz, J.L., Sharp, P.A., & Pabo, C.O. (1995) Structure-Based Design of Transcription Factors. **Science** **267**, 93-96.
55. Xu, W., Rould, M.A., Jun, S., Desplan, C., & Pabo, C.O. (1995) Crystal Structure of a Paired Domain-DNA Complex at 2.5 Å Resolution Reveals Structural Basis for Pax Developmental Mutations. **Cell** **80**, 639-650.
56. Pomerantz, J.L., Pabo, C.O., & Sharp, P.A. (1995) Analysis of Homeodomain Function by Structure-Based Design of a Transcription Factor. **Proc. Natl. Acad. Sci., USA** **92**, 9752-9756.
57. Klemm, J.D. & Pabo, C.O. (1996) Oct-1 POU Domain-DNA Interactions: Cooperative Binding of Isolated Subdomains and Effects of Covalent Linkage. **Genes & Development** **10**, 27-36.
58. Rebar, E.J., Greisman, H.A., & Pabo, C.O. (1996) Phage Display Methods for Selecting Zinc Finger Proteins with Novel DNA-Binding Specificities. **Methods In Enzymology** **267**, 129-149.
59. Elrod-Erickson, M., Rould, M.A., Nekludova, L., & Pabo, C.O. (1996) Zif268 Protein-DNA Complex Refined at 1.6 Å: A Model System for Understanding Zinc Finger-DNA Interactions. **Structure** **4**, 1171-1180.

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64. Pomerantz, J.L., Wolfe, S.A., & Pabo, C.O. (1998) Structure-Based Design of a Dimeric Zinc Finger Protein. **Biochemistry** **37**, 965-970.
65. Kim, J.-S. & Pabo, C.O. (1998) Getting a Handhold on DNA: Design of Poly-Zinc Finger Proteins with Femtomolar Dissociation Constants. **Proc. Natl. Acad. Sci. USA** **95**, 2812-2817.
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Protein Translocation

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Nucleic Acids Encoding and Methods of Making Tat-derived Transport Polypeptides (US patent #5,652,122; issued in 1997)

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Design of DNA-Binding Proteins

Rebar, E.J. and Pabo, C.O. --- **Zinc Finger Proteins with High Affinity New DNA Binding Specificities** (US patent #5,789,538; issued in 1998)

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