CURRICULUM VITAE

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| Name: | Carl O. Pabo | |
| Born: | September 1, 1952 | |
| Address: | Protean Futures LLC<br>475 Gate Five Road, Suite 210A<br>Sausalito, CA 94965 | |
| Email: | carl@carlpabo.com | |
| Education: | Yale College<br>New Haven, Connecticut<br>B.S. (*summa cum laude*)<br>Molecular Biophysics and Biochemistry | 1974 |
| | Harvard University<br>Cambridge, Massachusetts<br>Ph.D., Biochemistry and Molecular Biology | 1980 |
| Positions: | Postdoctoral Fellow<br>Department of Biochemistry and Molecular Biology<br>Harvard University | 1980–1982 |
| | Assistant Professor<br>Department of Biophysics<br>Johns Hopkins University School of Medicine | 1982–1986 |
| | Associate Professor<br>Department of Molecular Biology and Genetics and<br>Department of Biophysics<br>Johns Hopkins University School of Medicine | 1986–1990 |
| | Associate Investigator<br>Howard Hughes Medical Institute | 1986–1991 |
| | Professor<br>Department of Molecular Biology and Genetics and<br>Department of Biophysics<br>Johns Hopkins University School of Medicine | 1990–1991 |
| | Professor<br>Department of Biology<br>Massachusetts Institute of Technology | 1991–2001 |
| | Investigator<br>Howard Hughes Medical Institute | 1991–2001 |

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| Investigator<br>Center for Cancer Research<br>Massachusetts Institute of Technology | 1999–2001 |
| Senior Vice President and Chief Scientific Officer<br>Sangamo BioSciences, Inc. | 2001–2003 |
| Chair, Scientific Advisory Board<br>Sangamo BioSciences, Inc. | 1998–2001;<br>2003–2008 |
| Moore Distinguished Scholar<br>California Institute of Technology | January 2004 –<br>April 2004 |
| Visiting Professor, Bio-X Program<br>Stanford University | September 2004 –<br>April 2005 |
| Visiting Professor, Department of Systems Biology<br>Harvard Medical School | June 2005 –<br>July 2005 |
| Miller Visiting Research Professor<br>University of California at Berkeley | August 2005 –<br>December 2005 |
| Visiting Professor, Department of Systems Biology<br>Harvard Medical School | February 2006 –<br>May 2007 |
| Founder and Research Director<br>Protean Futures LLC | September 2007 –<br>Present |
| Scientific Advisor<br>NanoDimension | March 2008 –<br>Present |
| Visiting Professor, Division of Biology<br>and Biological Engineering<br>California Institute of Technology | April 2017 –<br>June 2017 |
| Founder and President<br>Humanity 2050, Inc. (humanity2050.org) | August 2017 –<br>June 2023 |

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.

Research:

I was born and have lived as an explorer: trying to understand everything I can about life, the world, the human condition, and prospects for the human future.

I started my career — building a solid foundation for all later work — by taking a strictly scientific stance, working on the structure and design of DNA-binding proteins, using X-ray crystallography to determine the atomic details of protein-DNA interactions, and then learning how to design novel DNA-binding proteins that bound so tightly and specifically that they were used (even before CRISPR) as tools for genome editing.

However, in much the way that Columbus and Magellan always wondered about the “world beyond the horizon,” I kept wondering about atomic/molecular systems (as with the human brain, and as with human societies) that were too complicated to usefully be described at an atomic/molecular level.

Seeing the chaos that filled the newspapers, seeing that scientific knowledge (by itself) cannot solve the fundamental problems facing the modern world, I felt impelled to see if I could find some better way to think about human thought and the human future, some better way to help address the most fundamental challenges now facing society. I thus resigned my tenured faculty position as a full professor at MIT and resigned my appointment as an Investigator with the Howard Hughes Medical Institute. I sailed on.

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.)

With my new model of thought as a foundation, I began to see how my concerns about cognition were connected with the most critical challenges of the modern world. It became clear that all these different challenges stem from a single root problem: Society’s challenges are so complex that the cognitive capacity of the human mind is easily overwhelmed in the search for solutions.

This "crisis of complexity" has become the central theme of my current work, as I develop a set of new tools to help minds work amidst this complexity and as I share ideas about how to limit the growth of complexity.

My hope is that these ideas offer both leaders and citizens new ways to address the pressing challenges of the modern age and improve prospects for a flourishing human future.

Humanity 2050: I founded an institute — Humanity 2050 — that focused on testing these new tools of thought on some of the hyper-complex challenges of the modern age. Though we were unable to secure long-term funding, I am continuing this work as an independent researcher/scholar.

The strategies that we developed at Humanity 2050 build on my model of thought. The use of 1) "special focus teams" and 2) a new "algorithm for thought" offer novel methods for crafting effective, actionable plans amidst the complexity of the modern world. As society prepares to face a new set of challenges – as with the impacts of artificial intelligence and with the development of new realms of neurotechnology – I now extend the work of Humanity 2050 as I devise strategies for reining in complexity.

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

Consulting: Given the pan-disciplinary range of interests and experiences summarized above, my background also has allowed me to play an important role as an advisor in venture capital, working with ND Capital (aka NanoDimension) from 2008 onwards.

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 $\lambda$ 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 $\lambda$ 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 $\lambda$ 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 $\lambda$ 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.

27. Frankel, A.D., Berg, J.M. & Pabo, C.O. (1987) Metal-Dependent Folding of a Single Zinc Finger from Transcription Factor IIIA. **Proc. Natl. Acad. Sci., USA 84**, 4841-4845.

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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.

31. Stearman, R.S., Frankel, A.D., Freire, E., Liu, B. & Pabo, C.O. (1988) Combining Thermostable Mutations Increases the Stability of $\lambda$ Repressor. **Biochemistry 27**, 7571-7574.

32. Jordan, S.R. & Pabo, C.O. (1988) Structure of the $\lambda$ 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) $\lambda$ Repressor: A Model System for Understanding Protein-DNA Interactions and Protein Stability. **Adv. Prot. Chem. 40**, 1-61.

35. Bowie, J.U., Clarke, N.D., Pabo, C.O. & Sauer, R.T. (1990) Identification of Protein Folds: Matching Hydrophobicity Patterns of Sequence Sets with Solvent Accessibility Patterns of Known Structures. **Proteins 7**, 257-264.

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37. Liu, B., Kissinger, C.R., Pabo, C.O., Martin-Blanco, E. & Kornberg, T.B (1990) Crystallization and Preliminary X-ray Diffraction Studies of the Engrailed Homeodomain and of an Engrailed Homeodomain/DNA Complex. **Biochem. and Biophys. Res. Comm. 171**, 257-259.

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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.

41. Wolberger, C. Vershon, A.K., Liu, B., Johnson, A.D. & Pabo, C.O. (1991) Crystal Structure of a MAT$\alpha$2 Homeodomain-Operator Complex Suggests a General Model for Homeodomain-DNA Interactions. **Cell 67**, 517-528.

42. Clarke, N.D., Beamer, L.J., Goldberg, H.R., Berkower, C. & Pabo, C.O. (1991) The DNA Binding Arm of $\lambda$ Repressor: Critical Contacts from a Flexible Region. **Science 254**, 267-270.

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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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51. Ma, P.C.M., Rould, M.A., Weintraub, H. & Pabo, C.O. (1994) Crystal Structure of MyoD bHLH Domain-DNA Complex: Perspectives on DNA Recognition and Implications for Transcriptional Activation. **Cell 77**, 451-459.

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.

60. Greisman, H.A. & Pabo, C.O. (1997) A General Strategy for Selecting High-Affinity Zinc Finger Proteins for Diverse DNA Target Sites. **Science 275**, 657-661.

61. Kim, J.-S., Kim, J., Cepek, K.L., Sharp, P.A., & Pabo, C.O. (1997) Design of TATA Box-Binding Protein/Zinc Finger Fusions for Targeted Regulation of Gene Expression. **Proc. Natl. Acad. Sci., USA 94**, 3616-3620.

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63. Kim, J.-S. & Pabo, C.O. (1997) Transcriptional Repression by Zinc Finger Peptides. **J. Biol. Chem. 272**, 29795-29800.

64. Pomerantz, J.L., Wolfe, S.A., & Pabo, C.O. (1998) Structure-Based Design of a Dimeric Zinc Finger Protein. **Biochemistry 37**, 965-970.

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66. Elrod-Erickson, M., Benson, T.E., & Pabo, C.O. (1998) High-Resolution Structures of Variant Zif268-DNA Complexes: Implications for Understanding Zinc Finger-DNA Recognition. **Structure 6**, 451-464.

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71. Xu, H.E., Rould, M.A., Xu, W., Epstein, J.A., Maas, R.L., & Pabo, C.O. (1999) Crystal Structure of the Human Pax6 Paired Domain-DNA Complex Reveals Specific Roles for the Linker Region and Carboxy-terminal Subdomain in DNA Binding. **Genes & Development 13**, 1263-1275.

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73. Elrod-Erickson, M., & Pabo, C.O. (1999) Binding Studies with Mutants of Zif268: Contribution of Individual Side Chains to Binding Affinity and Specificity in the Zif268 Zinc Finger-DNA Complex. **J. Biol. Chem. 274**, 19281-19285.

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Vascular Endothelial Growth Factor A in Glioblastoma Cells Using Engineered Zinc Finger Transcription Factors. **Cancer Res. 63**, 8968-8976.

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## PATENTS

### Protein Translocation

Frankel, A., Pabo, C.O., Barsoum, J.G., Fawell, S.E., Pepinsky, and Blake, R. (inventors for the first six patents listed below):

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

**Nucleic Acid Conjugates of Tat-derived Transport Polypeptides** (US patent #5,670,617; issued in 1997)

**Fusion Protein Comprising Tat-derived Transport Moiety** (US patent #5,674,980; issued in 1997)

**Tat-derived Transport Polypeptide Conjugates** (US patent #5,747,641; issued in 1998)

**Tat-derived Transport Polypeptides and Fusion Proteins** (US patent #5,804,604; issued in 1998)

**Tat-derived Transport Polypeptides** (US patent #6,316,003; issued in 2001)

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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Miller, J., Guofu, L., Pabo, C.0., and Collingwood, T. --- **Simultaneous Modulation of Multiple Genes** (US patent # 7,361,635; issued in 2008 and US patent #7,939,327; issued in 2011)

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Wang, B.S. and Pabo, C.O. --- **Dimerizing Peptides** (US patent #7,943,731; issued in 2011)