



## Warren L. DeLano 21 June 1972–3 November 2009

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On 3 November our community lost a young, extremely talented scientist under tragic circumstances when Warren DeLano died suddenly. To the readers of *Nature Structural & Molecular Biology* and to the larger biochemical and computer science communities, Warren is best known for his computer system PyMOL, an Open Source program for visualization of complex macromolecular systems. Chances are that in this issue, most of the illustrations of biomolecules were created with PyMOL.

Warren grew up in Palo Alto, California, at a time and with a loving family that greatly valued the development of computer technology and science. Warren's life-long commitment to computational biosciences began when he was an undergraduate research student (majoring in molecular biophysics and biochemistry (MB&B) and computer science at Yale University) and asked one of us (A.T.B.) to supervise his MB&B senior thesis research. At the time, MB&B and the Center of Structural Biology had become a powerhouse of what we now know call "structural biology." Warren was attracted to solving the complexities of macromolecular systems using computational tools.

I (A.T.B.) still remember when Warren showed up in my office one day. He was clearly very special, full of energy, and eager to become involved in computational research in my lab. I first suggested that he work on structure prediction of helical bundles. Then, after graduating, he continued in the lab for two years as "Scientific Programmer," working on a second project involving molecular replacement. Two first-author papers quickly resulted. But, in my memory, the most remarkable thing happened after a lab discussion about my general idea of creating a universal computing language for X-ray crystallography (what would eventually become the Crystallography and NMR System, CNS). Warren recognized the importance of implementing powerful scripting capabilities for the new system. Within days he had created very complex code in CNS (see subroutines `parser.f` and `define.f`), which implemented hierarchical data structures, scope and subroutines, all written in FORTRAN. It is an example of what the Stanford University computer scientist Donald E. Knuth has called (in the title of his best-known work) *The Art of Computer Programming* (D.E. Knuth, vols 1–4, Addison-Wesley, Reading, Massachusetts, USA, 1968–2005). Essentially, it does not matter what programming language one is using—elegant programs can be written in any language. And yes, Warren's code is truly elegant.

For Warren, programming was not just a job or a means to another goal—it was like playing a musical instrument. The programs he designed were symphonies in computational space: integrated, complex

and elegant at the same time. What's more, these masterpieces can be played by everyone.

Before Warren moved on to graduate school at the University of California at San Francisco (UCSF), he had already started to work on what would eventually become PyMOL. Based on a rough idea of "defining objects and displaying them on a graphics terminal" and a rather clumsy and simple implementation that I had written in the mid-1980s to feed molecular information to a noisy refrigerator-sized Evans & Sutherland vector graphics computer, he took the concept and made it truly useful and accessible to everybody. PyMOL was the first intuitive molecular graphics program for the laptop era with the kind of click-and-drag functionality that we are now all accustomed to. And of course the rest is history: PyMOL has developed into one of the most widely used molecular visualization systems around.

The first time I (J.A.W.) met Warren was when he showed up at my office at Genentech. His hands were sweating and he was shaking as he announced that he had to work in my lab as a rotation student in the Biophysics Program at UCSF, where I had an adjunct appointment. Frankly, I was a little reluctant, as I knew he had virtually no wet-lab experience. But I couldn't resist his intense passion, incredible smarts and no-fear attitude.

One of the most amazing things about protein-protein interfaces is their promiscuity—that is, the fact that the same interface can bind multiple partners whose folds can be completely different. Warren's project was to use peptide-phage display to see whether naive peptides would seek out a well-known promiscuous epitope at the Fc region of antibodies. He selected for peptide binders, optimized them and rigorously characterized them using multiple biophysical methods, including solving the X-ray structure of the peptide bound to the Fc. Remarkably, his peptide, shown by the X-ray structure to be a simple  $\beta$ -hairpin, bound exactly over the promiscuous epitope! By comparing the contact properties of four natural Fc-binding ligands to that of his naive peptide, he began to define the minimal binding properties. Importantly, he revealed the highly adaptive nature of these interfaces. To visualize this adaptive property, he began to further develop the software for PyMol in his spare time. In particular he developed a special application he called RigiMol—one of the first molecular movie programs that allows one to morph between static structures. For Warren's superb thesis, published as a first-author paper in *Science* entitled "Convergent solutions to binding at a protein-protein interface" (W.L. DeLano, M.H. Ultsch, A.M. de Vos and J.A. Wells, *Science* **287**, 1279–1283, 2000), he was awarded the annual Julius Krevans Award for the best PhD thesis at UCSF. Not bad for a computational geek.

Warren was a driven adventurer. About the time he graduated in 1998, I decided to leave Genentech for a start-up company, Sunesis Pharmaceuticals. Warren said he *had* to join as one of the first founding scientists, and he flew into the opportunity. He was seemingly doing everything, from working at the bench to evaluating novel fragment-based discovery technologies to setting up our computational group. He even insisted on physically setting up our first IT system, pulling wires to work stations, connecting routers and our company e-mail

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Warren DeLano speaking at the Open Source Bioinformatics conference 2005 part of the Annual Meeting of the International Society for Computational Biology (<http://open-bio.org/bosc2005/finalProgram/images/WarrenDeLano.JPG>).

service and developing our website, all just so he could learn it. As the company grew from 10 to 20 to 50 to 70 employees, Warren was intimately involved in recruiting people, including his sister Jennifer (who has comparable DeLano traits) and others to take over parts of his job. This way he could focus on his true love, molecular graphics and visualization tools. It was a sad but not unexpected day for all of us at Sunesis, and a great day for the computational bioscience community, when in 2002 he decided to leave. This way he could devote his full time to the development and dissemination of PyMOL and embellishments through his own company DeLano Scientific, his ultimate adventure.

Warren's impact on crystallographic software spreads beyond PyMOL and CNS, spanning almost two decades. Paul Adams retained him as a consultant in the very early days of the Phenix project. There ensued many lively and passionate discussions about how to develop a new crystallographic software system with the current computational tools. Warren's insight and experience developing PyMOL were major contributors to the decision to use Python as the scripting language in Phenix. This choice also made it easy for the Phenix developers to integrate PyMOL with Phenix.

PyMOL is Open Source ([http://en.wikipedia.org/wiki/Open\\_source](http://en.wikipedia.org/wiki/Open_source)), part of a movement that produced the popular Netscape and

Mozilla browser systems and, of course, the GNU/Linux operating system. Early on, Warren made the decision to make his programs accessible to all, in full, including source code. He felt that for pursuit of academic freedom it is essential to have all information about a scientific program fully accessible, promoting innovation. This is an ideal that we can all aspire to.

One must also recognize Warren as a humanist and thinker, perhaps best summarized in a recent posting by UCSF structural biologist Linda Brinen on the CCP4 bulletin board (<https://www.jiscmail.ac.uk/cgi-bin/webadmin?A2=ind0911&L=CCP4BB&T=0&F=&S=&P=36748>):

*I—like so many others—[am] shocked, saddened and shaken by this news. Warren's passing is a great loss to his friends, family and to our scientific community.*

*Nearly exactly one year ago, when an MRI found that I had a brain tumor, Warren wrote me an e-mail, part of which I will share here, because it sums up part of him and his approach to life:*

*"...I am so sorry to read your startling news.*

*Not a one of us is excused from life-altering biology and random accidents, any of which can strike suddenly without warning. For that reason, we must never take anything for granted. Not a single day. Not a single friend.*

*But as you well know, there are only two things we can do in defiance of chance, whether in sickness or in health:*

*1. Do everything you feel is important in life, today, or as soon as possible.*

*2. Never give up. Ignore the odds. Always believe you will survive and thrive.*

*...I am personally counting on you to get through this just fine and be back in action..."*

*Warren will be remembered well... and I wish for him to be at peace.*

*—Linda*

Warren is survived by his wife Beth Pehrson, mother Margaret DeLano, father James DeLano, Jr., stepmother Cathy Groves DeLano, stepfather Tom Snouse, sister Jennifer DeLano and brother Brendan DeLano, as well as five aunts and eight cousins. He left this world with much undone that he wanted to do. He also left us some magnificent science and the huge challenge of living up to his ideals of Open Scientific Software. Warren was a truly visionary thinker, and to be deprived of his future work is a huge blow to the scientific community.

#### ACKNOWLEDGMENT

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