

Simon David William Frost

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- EDUCATION
- ◇ **Trinity College, University of Cambridge, UK.**
B.A. (Hons), 1st class in Natural Sciences (Zoology), awarded June 1992.
 - ◇ **Merton College, University of Oxford, UK.**
D.Phil. in Mathematical Biology, awarded January 1996.
Thesis title: *The Within Host Dynamics of HIV Infection.*
Thesis supervisor: Dr. Angela McLean.
- TRAINING
- ◇ October - December 1995: Visiting Scholar,
Department of Epidemiology and Biostatistics, University of California, San Francisco, USA.
Mentor: Dr. Sally Blower.
 - ◇ 1996: NATO Postdoctoral Fellowship,
Department of Ecology and Evolutionary Biology, Princeton University, NJ, USA.
Mentor: Professor Andrew Dobson.
 - ◇ January - September 1997: Postdoctoral Research Associate,
Department of Zoology, University of Oxford, UK.
Mentor: Professor John Krebs.
 - ◇ October 1997 - September 2000: MRC Training Fellowship,
Institute of Cell, Animal, and Population Biology, University of Edinburgh, UK.
Mentor: Professor Andrew Leigh Brown.
 - ◇ October 2000 - September 2001: Postdoctoral Researcher,
Department of Pathology, University of California, San Diego, USA.
Mentor: Dr. Douglas Richman.
- APPOINTMENTS
- ◇ October 2001 - June 2004: Assistant Project Scientist (Research Faculty),
Department of Pathology, University of California, San Diego, USA.
 - ◇ July 2004 - present: Adjunct Assistant Professor,
Department of Pathology, University of California, San Diego, USA.
- RESEARCH INTERESTS
- ◇ Population genetics and phylogenetics.
 - ◇ Semiparametric Bayesian models.
 - ◇ Machine learning.
 - ◇ Agent based modelling.
 - ◇ Viral evolution and dynamics.
 - ◇ Epidemiology of infectious diseases.

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- RESEARCH PROJECTS
- ◇ Modelling of neutralizing antibody responses to human immunodeficiency virus.
Collaborators: Dr. Douglas D. Richman (UCSD), Dr. Christos Petropoulos (ViroLogic, Inc.).
 - ◇ Dynamics and evolution of hepatitis C virus during interferon therapy.
Collaborators: Dr. Gerond Lake-Bakaar (Cornell) and Dr. Dan Weinrich (Harvard).
 - ◇ Stoichiometry of antibody-mediated neutralization of HIV-1 in vitro.
Collaborator: Dr. Pascal Poignard (Scripps Research Institute, La Jolla, CA).
 - ◇ Modelling of disease transmission within sexual networks. Part of a NIDA funded program, Sexual Acquisition and Transmission of HIV Cooperative Agreement (SATH-CAP).
Collaborators: Drs. Steve Shoptaw and Pamina Gorbach (University of California, Los Angeles).
 - ◇ Correlating viral genotype with viral phenotype using machine learning techniques.
Collaborator: Professor Andrew Leigh Brown (University of Edinburgh, UK).
 - ◇ Developing methodology for detecting positive selection on sequence data.
Post-doctoral Researcher: Dr. Sergei Kosakovsky Pond (UCSD).
 - ◇ Evolution of interferon-related genes and their promoter regions.
Collaborator: Dr. Christopher Woelk (UCSD).
 - ◇ Genomic complexity of coastal marine ecosystems.
Collaborators: Drs. Robert Naviaux and Jacques Corbeil (UCSD).
- SOFTWARE PROJECTS
- ◇ Development of phylogenetic models of sequence evolution within the HyPhy software package.
URL: <http://www.hyphy.org>
Role in project: Model design and applications.
Collaborators: Dr. Sergei Kosakovsky Pond (UCSD) and Dr. Spencer Muse (North Carolina State University).
 - ◇ Web-based tools for the analysis of selection pressure on sequence data.
URL: <http://www.datamonkey.org>
Role in project: Model design and applications.
Collaborators: Dr. Sergei Kosakovsky Pond (UCSD).
 - ◇ Development of SimPy, a discrete event simulation package written in Python.
URL: <http://simpy.sourceforge.net>
Role in project: optimisation and parallelisation of multi-agent simulations.
Collaborators: Dr. Klaus Muller and Professor Tony Vignaux (Victoria University, New Zealand).
 - ◇ Design and implementation of an HIV sequence database for a multi-centre study in North America on primary HIV Infection.
Collaborators: Dr. Susan Little (UCSD), Dr. Victor De Gruttola (Harvard School of Public Health).
 - ◇ Development of Bayesian semiparametric models within the WinBUGS software package.
Extension of WinBUGS to allow parallel processing via the Message Passing interface protocol.
URL: <http://www.simonfrost.com>
- PUBLICATIONS
- Frost, S.D.W. and McLean, A.R. (1994a) Quasispecies dynamics and the emergence of drug resistance during zidovudine therapy of HIV infection. *AIDS* 8, 323-332.
- Frost, S.D.W. and McLean, A.R. (1994b) Germinal centre destruction as a major pathway of HIV pathogenesis. *J. AIDS* 7, 236-244.
- McLean, A.R. and Frost, S.D.W. (1995) Zidovudine and HIV: mathematical models of within-host population dynamics. *Rev. Med. Virol.* 5, 141-148.
- Frost, S.D.W. and Michie, C.A. (1996) Lymphocyte dynamics, apoptosis and HIV infection. *Trends Microbiol.* 4, 77-82.

PUBLICATIONS,
CONTINUED

- Krebs, J.R., Anderson, R.M., Clutton-Brock, T., Morrison, W.I., Young, D., Donnelly, C.A., Frost, S.D.W. and Woodroffe, R. (1997) Bovine tuberculosis in cattle and badgers. Report to the Ministry of Agriculture, Fisheries and Food. MAFF Publications, London, UK.
- Krebs, J.R., Anderson, R.M., Clutton-Brock, T., Donnelly, C.A., Frost, S., Morrison, W.I., Woodroffe, R. and Young, D. (1998) Badgers and bovine TB: conflicts between conservation and health. *Science* 279, 817-818.
- Frost, S.D.W. (1999) The Immune System as an Inducible Defense. Chapter 8 in: Harvell, C.D. and Tollrian, R., eds. *The Ecology and Evolution of Inducible Defenses*. Princeton University Press.
- Woodroffe, R, Frost, S.D.W. and Clifton-Hadley, R.C. (1999) Attempts to control tuberculosis in cattle by removing infected badgers: constraints imposed by live test sensitivity. *J. Appl. Ecol.* 36, 494-501.
- Gunthard, H.F., Frost, S.D.W., Leigh Brown, A.J., Ignacio, C.C., Kee, K., Perelson, A.S., Spina, C.A., Havlir, D.V., Hezareh, M., Looney, D.J., Richman, D.D. and Wong, J.K. (1999) Evolution of envelope sequences of HIV-1 in cellular reservoirs in the setting of potent antiviral therapy. *J. Virol.* 11, 9404-9412.
- Smith, D.B., Basaras, M., Frost, S.D.W., Haydon, D., Cuceanau, N., Prescott, L., Kamenka, C., Millband, D., Sathar, M.A. and Simmonds, P. (2000) Phylogenetic analysis of GBV-C/hepatitis G virus. *J. Gen. Virol.* 81, 769-780.
- Frost, S.D.W., Nijhuis, M., Schuurman, R., Boucher, C.A.B. and Leigh Brown, A.J. (2000) Evolution of lamivudine resistance in human immunodeficiency virus type-1 infected individuals: the relative roles of drift and selection. *J. Virol.* 74, 6262-6268.
- Frost, S.D.W. (2001) Bayesian modeling of HIV evolution and dynamics. *AIDS Cyber J* 4(2).
- Gunthard, H.F., Havlir, D.V. Fiscus, S., Zhang, Z.-Q., Eron, J., Mellors, J., Gulick, R., Frost, S.D.W., Leigh Brown, A.J., Schleif, W., Valentine, F., Jonas, J., Meibohm, A., Ignacio, C.C., Isaacs, R., Gamagami, R., Emini, E., Haase, A., Richman, D.D. and Wong, J.K. (2001) Residual Human Immunodeficiency Virus-1 RNA and DNA in Lymph Node and HIV RNA in Genital Secretions and in Cerebro Spinal Fluid after Two Years of Suppression of Viremia in the Merck 035 cohort. *J. Inf. Dis.* 183, 1318-1327.
- Frost, S.D.W., Gunthard, H.F., Wong, J.K., Havlir, D., Richman, D.D. and Leigh Brown, A.J. (2001) Evidence for positive selection driving the evolution of HIV env under potent antiviral therapy. *Virology* 284:250-258.
- Ruiz, L., Carcelain, G., Martinez-Picado, J., Frost, S., Marfil, S., Paredes, R., Romeu, J., Ferrer, E., Morales-Lopetegui, K., Zayat, M.K., Autran, B. and Clotet, B. (2001) HIV-specific CD8+ T cells and HIV dynamics after three structured treatment interruptions in chronic HIV infection. *AIDS* 15:F19-F27.
- Frost, S.D.W., Dumaurier, M.-J., Wain-Hobson, S. and Leigh Brown, A.J. (2001) Genetic drift and within-host metapopulation dynamics of HIV-1 infection. *Proc. Natl. Acad. Sci. USA* 98:6975-6980.
- Frost, S.D.W., Martinez-Picado, J., Ruiz, L., Clotet, B., and Leigh Brown, A.J. (2002) Viral dynamics during structured therapy interruptions of chronic human immunodeficiency virus type 1 infection. *J. Virol.* 76:968-979.
- Prado, J.G., Wrin, T., Beauchaine, J., Ruiz, L., Petropoulos, C.J., Frost, S.D.W., Clotet, B., D.Aquila, R.T., and Martinez-Picado, J. (2002) Amprenavir resistant HIV-1 exhibits lopinavir cross-resistance and reduced replication capacity. *AIDS* 16:1009-1017.
- Martinez-Picado, J., Morales-Lopetego, K., Wrin, T., Prado, J.G., Frost, S.D.W., Petropoulos, C.J., Clotet, B., and Ruiz, L. (2002) Selection of drug-resistant HIV-1 mutants in response to repeated structured treatment interruptions. *AIDS* 16:895-899.

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- PUBLICATIONS,
CONTINUED
- Quigg, M., Frost, S.D.W., McDonagh, S., Burns, S.M., Clutterbuck, D., McMillan, A., Leen, C.S., and Leigh Brown, A.J. (2002) Association of antiretroviral resistance genotypes with response to therapy comparison of three models. *Antiviral Therapy* 7:151-157.
- Frost, S.D.W. (2002) Dynamics and evolution of HIV-1 during structured therapy interruptions. *AIDS Reviews* 4:119-127.
- Martinez-Picado, J., Frost, S.D.W., Izquierdo, N., Morales-Lopetegui, K., Marfil, S., Puig, T., Cabrera, C., Clotet, B., and Ruiz, L. (2002) Viral evolution during structured treatment interruptions in chronically HIV-infected individuals. *J. Virol.* 76:12344-12348.
- Leigh Brown, A.J., Frost, S.D.W., Mathews, W.C., Dawson, K., Hellman, N.S., Daar, E.S., Richman, D.D., and Little, S.J. (2003) Transmission fitness of drug resistant HIV and the prevalence of resistance in the antiretroviral-treated population. *J. Infect. Dis.* 187:683-686.
- Ellis, R.J., Childers, M.E., Zimmerman, J.D., Frost, S.D.W., Deutsch, R., and McCutchan, J.A. (2003) Human immunodeficiency virus-1 RNA levels in cerebrospinal fluid exhibit a set point in clinically stable patients not receiving antiretroviral therapy. *J. Infect. Dis.* 187:1818-1821.
- Leigh Brown, A.J., Frost, S.D.W., Mathews, W.C., Dawson, K., Hellmann, N.S., Daar, E.S., Richman, D.D., and Little, S.J. (2003) Changing transmission fitness of drug-resistant human immunodeficiency virus against a background of evolving antiretroviral therapy - Reply. *J. Infect. Dis.* 188:1258-1259.
- Lake-Bakaar, G., and Frost, S.D.W. (2003) Viral kinetics and hepatitis C. *Hepatology* 38:1589-1590.
- Leigh Brown, A.J., Frost, S.D.W., Good, B., Daar, E.S., Simon, V., Markowitz, M., Collier, A.C., Connick, E., Conway, B., Margolick, J.B., Routy, J.-P., Corbeil, J., Hellmann, N.S., Richman, D.D., and Little, S. J. (2004) Genetic basis of hypersusceptibility to protease inhibitors and low replicative capacity of human immunodeficiency virus type 1 strains in primary infection. *J. Virol.* 78:2242-2246.
- IN PRESS
- Kosakovsky Pond, S.L., and Frost, S.D.W. (2005) A simple hierarchical approach to modeling distributions of substitution rates. *Mol. Biol. Evol.*
- Kosakovsky Pond, S.L., and Frost, S.D.W. (2005) A genetic algorithm approach to detecting lineage-specific variation in selection pressure. *Mol. Biol. Evol.*
- Kosakovsky Pond, S.L., Frost, S.D.W., and Muse, S.V. (2005) HyPhy: hypothesis testing using phylogenies. *Bioinformatics.*
- SUBMITTED
MANUSCRIPTS
- Kosakovsky Pond, S.L., and Frost, S.D.W. Not so different after all: a comparison of methods for detecting amino-acid sites under selection.
- Frost, S.D.W., Little, S.J., Kosakovsky Pond, S.L., Chappey, C., Liu, Y., Wrin, T., Petropoulos, C.J., and Richman, D.D. Characterization of HIV-1 envelope variation and neutralizing antibody responses during transmission of HIV-1 subtype B.
- Frost, S.D.W., Ruffini, L., Richman, D.D., and Lake-Bakaar, G. Dynamics of hepatitis C virus, serum alanine aminotransferase and interferon during high dose interferon-alpha therapy.
- Martinez-Picado, J., Wrin, T., Frost, S.D.W., Clotet, B., Ruiz, L., Leigh Brown, A.J., Petropoulos, C.J., and Parkin, N.T. Phenotypic hypersusceptibility to multiple protease inhibitors and low replicative capacity in chronically HIV-1 infected patients.
- COMPUTER
SKILLS
- ◇ Computer languages: Eiffel, Python, Lua, C, Component Pascal, Ox.
 - ◇ Statistical packages: R/S-Plus, WinBUGS.
 - ◇ Computer systems: MS-Windows, Linux.
 - ◇ Databases: MySQL, SQLite.
 - ◇ Bioinformatics: Alignment (e.g. BLAST, Clustal), phylogenetics (e.g. PHYLIP, PAUP*, PAML, HyPhy, MrBayes), motif search (e.g. MEME, AlignACE).

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- PRESENT TEACHING I provide mentorship for Dr. Sergei Kosakovsky Pond, a postdoctoral fellow who joined UCSD in July 2003 as part of the Bioinformatics initiative at the UCSD Antiviral Research Center. In addition, I supervise a number of graduate students and postdoctoral researchers within the Department of Pathology and School of Medicine.
- PAST TEACHING Oxford: I gave weekly one-on-one tutorials in 'Evolution and Taxonomy' and 'Parasites and Pathogens' and group (c. 20 students) demonstrations in computer classes of statistics (using Minitab) and computer modelling (which included phylogenetics, bioinformatics, dynamical systems and image analysis) to Zoology undergraduates.
- Princeton: I gave undergraduate level teaching in epidemiological (spatial models of disease spread) and immunological models (the dynamics of immunological memory).
- Edinburgh: I gave undergraduate demonstrations in host-parasite evolution and basic population genetics, as well as a lecture course option in HIV genetics and evolution for 4th year honours students.
- Other teaching experience: I have also worked on 'Modern Approaches to the Epidemiology of Infectious Disease' in May 1994 and September 1995, a three week course run by the University of Oxford to teach mathematical epidemiology to a broad audience of physicians, veterinarians, non-clinical scientists and public health workers. I worked as a demonstrator (1994, 1995) and as a course assistant (1995).
- ACTIVE SUPPORT
- ◇ "Modeling HIV Escape from Neutralizing Antibodies."
Funding source: NIH R01 AI57164
Annual direct costs: USD 200,000
Time period: 07/01/2004-06/30/2009
Role: PI
 - ◇ "Biomathematical Analysis of Viral Dynamics and Evolution."
Funding source: NIH R01 AI47745
Annual direct costs: USD 225,000
Time period: 08/20/2001-31/5/2005
Role: Co-Investigator (PI: Dr. Douglas Richman)
 - ◇ "Southern California Primary Infection Program - Statistical Leadership and Support."
Funding source: NIH U01 AI43638
Annual direct costs: USD 1,100,853
Time period: 08/01/2002-06/30/2007
Role: Co-Investigator (PI: Dr. Douglas Richman)
 - ◇ "UCSD HIV Clinical Research Facility"
Funding source: UC AIDS Research Program
Annual direct costs: USD 433,815
Time period: 01/01/2003-12/31/2005
Role: Co-Investigator, Bioinformatics section (PI: Dr. J. Allen McCutchan)
 - ◇ "HIV/STD Risk Behaviors in Methamphetamine User Networks."
Funding source: NIH/UCLA
Annual direct costs: USD 14,928
Time period: 10/01/2003-09/30/2008
Role: PI (Subcontract to UCLA, PI: Drs. Steven Shoptaw and Pamina Gorbach)

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- PAST SUPPORT
- ◇ "Computational Analysis of Selection Pressure on Viral Sequence Data."
Funding source: NIAID/CFAR
Amount of total award: USD 25,000
Time period: 01/01/2002-31/12/2002
Role: PI
 - ◇ Junior Fellowship.
Funding source: Medical Research Council, UK.
Amount of total award: GBP 92,000
Time period: 10/01/1997-09/30/2000
Role: Postdoctoral fellowship
 - ◇ Postdoctoral Fellowship to Princeton University.
Funding source: NATO
Amount of total award: GBP 16,000
Time period: 01/01/1996-12/31/1996
Role: Postdoctoral fellowship
- PENDING SUPPORT
- ◇ "Identifying selection pressures on viral genomes."
Funding source: NSF/NIGMS.
Amount requested: USD 850,000
Time period: 01/01/2005-12/31/2009
Role: PI
- PROFESSIONAL ACTIVITIES
- With Dr. Doug Richman (UCSD), I was the Co-Chair of the 10th International Discussion Meeting on HIV Dynamics and Evolution held at Lake Arrowhead, CA, April 13th-16th 2003. This involved raising funding for the conference, and developing the programme, which can be seen at <http://ari.ucsd.edu/cfar/hivdynamics>. I am on the Organizing Committee for the 2004 meeting, held in Stockholm, Sweden from April 29th - May 2nd, 2004.
- I am also a reviewer for Nature, Science, Proceedings of the National Academy of Sciences, Journal of Theoretical Biology, Molecular Biology and Evolution, Journal of Molecular Evolution, Proceedings of the Royal Society Series B (Biological Sciences), and Journal of Virology.
- PROFESSIONAL MEMBERSHIPS
- ◇ 1997-present: Junior Member of the Isaac Newton Institute for Mathematical Sciences, Cambridge, UK.
- REFERENCES
- Available on request.