

## BIOGRAPHICAL SKETCH - N.I.H. FORMAT / APRIL 2014

NAME Petr Kuzmič	TITLE President, BioKin Ltd.
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### EDUCATION

INSTITUTION AND LOCATION	DEGREE	YEAR(S)	FIELD OF STUDY
Institute of Chemical Technology <i>Prague, Czech Republic</i>	M.S.	1979	Medicinal Chemistry
Institute of Organic Chemistry & Biochemistry, Czech Academy of Sciences <i>Prague, Czech Republic</i>	Ph.D.	1984	Physical-Organic Chemistry Bioorganic Chemistry
School of Pharmacy, University of Wisconsin <i>Madison, Wisconsin</i>	Postdoc	1988-9	Bioorganic Chemistry Enzymology

### RESEARCH AND PROFESSIONAL EXPERIENCE

<b>1991-present</b>	<i>President &amp; Owner</i> BioKin, Ltd. – Consulting and Software Development
2014-present	<i>Visiting Scientist</i> Brandeis University – Department of Biology (L. Hedstrom group)
2011-present	<i>Visiting Academic</i> University of Warwick, UK – Molecular Organisation and Assembly in Cells Centre
2001-2002	<i>Lecturer</i> Washington State University, Department of Chemistry
1996-1999	<i>Lecturer</i> University of Wisconsin – Madison, Department of Chemistry
1990-1995	<i>Assistant Scientist</i> University of Wisconsin – Madison, School of Pharmacy
1988-1989	<i>Post-Doctoral Research Associate</i> University of Wisconsin – Madison, School of Pharmacy
1987	<i>Visiting Scholar - National Academy of Sciences U.S.A.</i> University of Wisconsin – Madison, School of Pharmacy
1985-1987	<i>Staff Scientist</i> Institute of Organic Chemistry and Biochemistry – Prague, Czech Republic
1980-1985	<i>Graduate Research Assistant</i> Institute of Organic Chemistry and Biochemistry – Prague, Czech Republic
1977-1979	<i>Research Assistant</i> Institute of Chemical Technology – Prague, Czech Republic

## Consultant

BioKin Ltd. (owned and operated by Dr. Kuzmic as the consultant) has been providing contractual consulting services to US pharmaceutical and biotechnology corporations, usually small-to-medium size. The topics are covered by non-disclosure agreement.

*For example:*

- ArQule, Inc. (Woburn, MA)
- Arris Pharmaceuticals, Inc. (South San Francisco, CA)
- Axys Pharmaceuticals, Inc. (South San Francisco, CA)
- Celera Genomics, Inc. (South San Francisco, CA)
- Chiron Corp. [Novartis] (Emeryville, CA)
- DNAX Research Inst. (Palo Alto, CA)
- Dyax Corp. (Cambridge, MA)
- Hawaii Biotech / Panthera BioPharma (Aiea, HI)
- Phenomix Corp. (San Diego, MA)
- Proteon Therapeutics, Inc. (Waltham, MA)
- Sequoia Pharmaceuticals, Inc. (Gaithersburg, MD)

## Software Developer

Dr. Kuzmic's expertise in enzyme kinetics, assay development, assay optimization, experiment design, and statistical data analysis for drug discovery is embodied in software packages DYNAFIT and BATCHKI. These software packages have been used in hundreds of academic laboratories and numerous corporations.

*For example:*

Amgen	Dyax	Novartis
Anadys	GlaxoSmithKline	Orion
BiogenIDEC	Guilford	Pfizer
BristolMyersSquibb	Hawaii Biotech	Phenomix
Celera Genomics	Millenium	Portola
Chiron	Monsanto	Sequoia
DNAX	Nerviano MedSci	Theravance

## Seminar Speaker

Oral conference presentations and invited lectures or seminars:

Mar 2014 Brandeis University, Waltham, MA  
Jun 2013 Celgene Avilomics Research, Bedford, MA  
Jun 2013 Brandeis University, Waltham, MA  
May 2013 ArQule, Inc., Woburn, MA  
Apr 2013 Novartis Pharmaceuticals, Horsham, U.K.  
Dec 2012 Novartis Pharmaceuticals, Cambridge, MA  
Jul 2012 Novartis Pharmaceuticals, Horsham, U.K.  
Nov 2011 Masaryk University, Brno, Czech Republic  
Apr 2010 Masaryk University, Brno, Czech Republic  
Jul 2009 Max-Planck-Institute for Biomedical Research, Heidelberg  
Jun 2009 *Inhibitors of Protein Kinases* (IPK2009, Warsaw, Poland)  
Sep 2008 University of Dundee, Scotland  
Sep 2008 Czech Academy of Sciences, Prague, Czech Republic  
Jun 2008 Dyax Corp., Cambridge, MA  
Mar 2008 Novartis Pharma, Cambridge, MA  
Jul 2007 Max-Planck-Institute for Biomedical Research, Heidelberg  
Jun 2007 University of Limerick, Ireland  
Mar 2007 Washington State University, Pullman, WA  
Nov 2006 Oregon Health and Science University, Portland, OR  
Dec 2005 University of Montana, Missoula, MT  
Nov 2005 Wayne State University, Detroit, MI  
May 2005 *Steroid Dehydrogenases Workshop* (Schloss Elmau, Germany)  
Dec 2004 Pfizer Inc. (Agouron; La Jolla, CA)  
Sep 2004 *Society for Biomolecular Screening* (SBS10, Orlando, FL)

### Journal Reviewer

- Biochemistry (USA)
- Analytical Biochemistry
- Journal of Theoretical Biology
- Journal of Agricultural and Food Chemistry
- Biochimie
- Enzyme and Microbial Technology

### HONORS

1979 Summa Cum Laude - Institute of Chemical Technology - Prague  
1985 Young Investigator Travel Award - Czech Literary Foundation  
1987 Visiting Scholar - National Academy of Sciences, U.S.A.

## GRANTS

- 2010-14 Masaryk University Lecture Course (“Binding & Kinetics for Experimental Biologists”) - Czech Ministry of Education & The European Union
- 1992 Supercomputer User Access Grant (“Kinetic Mechanism of HIV Proteinase Inhibition”) - U.W. Graduate School and San Diego Supercomputer Center
- 1990 Institutional Research Grant (“Artificial Intelligence System for the Evaluation of Antifolate Activity”) - American Cancer Society

## PROFESSIONAL SOCIETIES

- 2013-present Biochemical Society (London)
- 1990-present American Chemical Society
- 1990-present American Association for the Advancement of Science

## PUBLICATIONS

- [1] Schwartz, P. A., Kuzmič, P., Solowiej, J., Bergqvist, S., Bolanos, B., Almaden, C., Nagata, A., Ryan, K., Feng, J., Dalvie, D., Kath, J., Xu, M., Wani, R., and Murray, B. W. (2014) Covalent EGFR inhibitor analysis reveals importance of reversible interactions to potency and mechanisms of drug resistance. *Proc. Nat. Acad. Sci. U.S.A.* **111**, 173178.
- [2] Kleckner, I. R., McElroy, C. A., Kuzmič, P., Gollnick, P., , and Foster, M. P. (2013) Homotropic cooperativity from the activation pathway of the allosteric ligand-responsive regulatory trp RNA-binding attenuation protein. *Biochemistry* **52**, 8855–8865.
- [3] Salykin, A., Kuzmič, P., Kyrlylenko, O., Musilová, J., Glatz, Z., Dvořák, P., and Kyrlylenko, S. (2013) Nonlinear regression models for determination of nucleotide content in human embryonic stem cell lysates. *Stem Cell Rev. Rep.* **9**, 786793.
- [4] Kuzmič, P. (2011) Optimal design for the dose-response screening of tight-binding enzyme inhibitors. *Anal. Biochem.* **419**, 117–122.
- [5] Rothnie, A., Clarke, A. R., Kuzmič, P., Cameron, A., and Smith, C. J. (2011) A sequential mechanism for clathrin cage disassembly by 70-kDa heat-shock cognate protein (Hsc70) and auxilin. *Proc. Nat. Acad. Sci. U.S.A.* **108**, 6927–6932.
- [6] Kuzmič, P. (2010) A generalized numerical approach to steady-state enzyme kinetics: Applications to protein kinase inhibition. *Biochim. Biophys. Acta* **1804**, 635–641.
- [7] Clé, C., Martin, C., Field, R. A., Kuzmič, P., and Bornemann, S. (2010) Detection of enzyme-catalyzed polysaccharide synthesis on surfaces. *Biocatal. Biotrans.* **28**, 64–71.
- [8] Kuzmič, P. (2009) DYNAPFIT – A software package for enzymology. *Meth. Enzymol.* **467**, 247–280.

- [9] Sexton, D. J., Chen, T., Martik, D., Kuzmič, P., Kuang, G., Chen, J., Nixon, A. E., Zuraw, B. L., Forteza, R. M., Abraham, W. M., and Wood, C. R. (2009) Specific inhibition of tissue kallikrein 1 with a human monoclonal antibody reveals a potential role in airway diseases. *Biochem. J.* **422**, 383–392.
- [10] Kuzmič, P. (2009) Application of the Van Slyke–Cullen irreversible mechanism in the analysis of enzymatic progress curves. *Anal. Biochem.* **394**, 287–289.
- [11] Kuzmič, P., Lorenz, T., and Reinstein, J. (2009) Analysis of residuals from enzyme kinetic and protein folding experiments in the presence of correlated experimental noise. *Anal. Biochem.* **395**, 1–7.
- [12] Gasa, T. B., Spruell, J. M., Dichtel, W. R., Sorensen, T. J., Philp, D., Stoddart, J. F., and Kuzmič, P. (2009) Complexation between methyl viologen (Paraquat) bis(hexafluorophosphate) and dibenzo[24]crown-8 revisited. *Chem. Eur. J.* **15**, 106–116.
- [13] Kuzmič, P. (2008) A steady state mathematical model for stepwise “slow-binding” reversible enzyme inhibition. *Anal. Biochem.* **380**, 5–12.
- [14] Collom, S. L., Laddusaw, R. M., Burch, A. M., Kuzmič, P., Perry, M. D., and Miller, G. P. (2008) CYP2E1 substrate inhibition: Mechanistic interpretation through an effector site for monocyclic compounds. *J. Biol. Chem.* **283**, 3487–3496.
- [15] Kona, F., Xu, X., Martin, P., Kuzmic, P., and Gatti, D. L. (2007) Structural and mechanistic changes along an engineered path from metallo to nonmetallo 3-deoxy-D-manno-octulosonate 8-phosphate synthases. *Biochemistry* **46**, 4532–4544.
- [16] Jamakhandi, A. P., Kuzmič, P., Sanders, D. E., and Miller, G. P. (2007) Global analysis of protein-protein interactions reveals multiple CYP2E1–reductase complexes. *Biochemistry* **46**, 10192–10201.
- [17] Urbina, H. D., Debaene, F., Jost, B., Bole-Feysot, C., Mason, D. E., Kuzmič, P., Harris, J. L., and Winssinger, N. (2006) Self-assembled small-molecule microarrays for protease screening and profiling. *ChemBioChem* **7**, 1790–1797.
- [18] Kuzmič, P., Millis, S., Cregar, L., and Goldman, M. (2006) Mixed-type noncompetitive inhibition of anthrax Lethal Factor protease by aminoglycosides. *FEBS J.* **273**, 3054 – 3062.
- [19] Kuzmič, P. (2006) A generalized numerical approach to rapid-equilibrium enzyme kinetics: Application to 17 $\beta$ -HSD. *Mol. Cell. Endocrinol.* **248**, 172–181.
- [20] Tang, C., Simo, O., O’Malley, S., Nagata, M., Goldman, M., Cregar, L., Nguyen, D., Kuzmič, P., Moayeri, M., Leppla, S., Liddington, R., Hemscheidt, T., and Jiao, G. S. (2004) Discovery of cationic inhibitors of anthrax Lethal Factor protease. *Abstr. Pap. Am. Chem. Soc.* **228**, U967 – U968.
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- [22] Chu, D., Bungiro, R. D., Ibanez, M., Harrison, L. M., Campodonico, E., Jones, B. F., Mieszczynek, J., Kuzmič, P., and Cappello, M. (2004) Molecular characterization of *Ancylostoma ceylanicum* Kunitz-type serine protease inhibitor: Evidence for a role in hookworm-associated growth delay. *Infect. Immun.* **72**, 2214 – 2221.

- [23] Williams, C. R., Snyder, A. K., Kuzmič, P., O'Donnell, M., and Bloom, L. B. (2004) Mechanism of loading the Escherichia coli DNA polymerase III sliding clamp - I. Two distinct activities for individual ATP sites in the gamma complex. *J. Biol. Chem.* **279**, 4376 – 4385.
- [24] Kuzmič, P., Hill, C., and Janc, J. W. (2004) Practical robust fit of enzyme inhibition data. *Methods Enzymol.* **383**, 366 – 381.
- [25] Kuzmič, P., Hill, C., Kirtley, M. P., and Janc, J. W. (2003) Kinetic determination of tight-binding impurities in enzyme inhibitors. *Anal. Biochem.* **319**, 272 – 279.
- [26] Lake-Bakaar, G., Ruffini, L., and Kuzmič, P. (2003) Effect of Ribavirin and Amantadine on early hepatitis C virus RNA rebound and clearance in serum during daily high-dose interferon. *Dig. Dis. Sci.* **48**, 126 – 139.
- [27] Ahn, J., Won, T. W., Kaplan, D. E., Londin, E. R., Kuzmič, P., Gelernter, J., and Gruen, J. R. (2002) A detailed physical map of the 6p reading disability locus, including new markers and confirmation of recombination suppression. *Hum. Genet.* **111**, 339 – 349.
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- [42] Kuzmič, P. (1993) Kinetic assay for HIV proteinase subunit dissociation. *Biochem. Biophys. Res. Commun.* **191**, 998 – 1003.
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- [46] Moss, M. L., Palmer, R. E., Kuzmič, P., Dunlap, B. E., Henzel, W., Kofron, J. L., Mellon, W. S., Royer, C. A., and Rich, D. H. (1992) Identification of actin and *hsp-70* as Cyclosporine-A binding-proteins by photoaffinity-labeling and fluorescence displacement assays. *J. Biol. Chem.* **267**, 22054 – 22059.
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- [48] Kuzmič, P., Moss, M. L., Kofron, J. L., and Rich, D. H. (1992) Fluorescence displacement method for the determination of receptor ligand-binding constants. *Anal. Biochem.* **205**, 65 – 69.
- [49] Kuzmič, P., Ng, K. Y., and Heath, T. D. (1992) Mixtures of tight-binding enzyme-inhibitors – Kinetic analysis by a recursive rate-equation. *Anal. Biochem.* **200**, 68 – 73.
- [50] Kofron, J. L., Kuzmič, P., Kishore, V., Gemmecker, G., Fesik, S. W., and Rich, D. H. (1992) Lithium-chloride perturbation of *cis-trans* peptide-bond equilibria: Effect on conformational equilibria in Cyclosporine-A and on time-dependent inhibition of cyclophilin. *J. Am. Chem. Soc.* **114**, 2670 – 2675.

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- [55] Kuzmič, P. and Souček, M. (1986) Photo-cyanation of 3,4-di-methoxy-1-nitro-benzene. A quantitative study. *Collect. Czech. Chem. Commun.* **51**, 358 – 367.
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