Frederick Melvin Parham

Education

Ph.D. Applied and Computational Mathematics, 1989
Princeton University, Princeton, NJ
Research Advisor: Dr. Raymond Pierrehumbert
Thesis Title: Tilted Rossby-wave critical layers in stratified atmospheres

M.A. Applied and Computational Mathematics, 1989
Princeton University, Princeton, NJ
Research Advisor: Dr. Raymond Pierrehumbert

B.S. Mathematics and Computer Science, 1984
Duke University, Durham, NC

Positions

Mathematical Statistician
Biomolecular Screening Branch, Division of the National Toxicology Program, NIEHS, Research Triangle Park, NC
August 2010-present

Performs mathematical analysis involving use of statistical techniques for collecting and analyzing laboratory data from biomedical research.

Areas of research included:
Dose-response analysis of high throughput screening (HTS) assays and genomic assays, including: assays of neurotoxicity and developmental neurotoxicity; mixture models; statistical methods for genomic dose-response analysis
Correlation analysis of high throughput screening (HTS) assays
Effects of PCB exposure on thyroid hormones and neurodevelopmental outcomes

Mathematical Statistician
Environmental Systems Biology Group, NIEHS, Research Triangle Park, NC
Jan. 22, 2006-July 2010

Performed mathematical analysis involving use of statistical techniques for collecting and analyzing laboratory data from biomedical research.

Areas of research included:
Network modeling of microarray data
Performing dose-response and statistical analysis of data from high throughput screening (HTS) assays.

Research Fellow
Laboratory of Computational Biology and Risk Analysis, NIEHS, Research Triangle Park, NC
Feb. 4, 1999 – Jan. 22, 2006

Performed mathematical analysis involving use of statistical techniques for collecting and analyzing laboratory data from biomedical research.

Areas of research included:
Network models of microarray data and pharmacokinetic models.

Information Technology Technical Specialist
OAO Corporation, Research Triangle Park, NC
Jan. 1997- Feb. 4, 1999

Performed mathematical analysis involving use of statistical techniques for collecting and analyzing laboratory data from biomedical research for NIEHS under Central Computing and Scientific Contract.

Areas of research included:
Physiologically based pharmacokinetic (PBPK) models
Performing dose-response modeling of epidemiological data on dioxin
Analyzing epidemiological data on EMF (electromagnetic field) exposure

Technical expert
ISN, Research Triangle Park, NC
Jan. 1994-Jan. 1997

Performed mathematical analysis involving use of statistical techniques for collecting and analyzing laboratory data from biomedical research for NIEHS under Central Computing and Scientific Contract.

Areas of research included:
Physiologically based pharmacokinetic (PBPK) models

Postdoctoral research fellow
Mesoscale Air-Sea Interaction Group, Florida State University, Tallahassee, FL
Supervisor: James J. O'Brien
Jan.1990- Jan. 1992

Performed mathematical modeling of ocean dynamics. Advised others in research group on application of various mathematical and computational techniques.

Honors and Awards

Society of Toxicology Best Paper for 2004, for

Toyoshiba H, Yamanaka T, Sone H, **Parham FM**, Walker NJ, Martinez J, Portier CJ. Gene interaction network suggests dioxin induces a significant linkage between Ah-receptor and retinoic acid receptor beta. Environ Health Perspect 2004; 112: 1217-1224.

Professional Outreach and Professional Society Service

NIEHS representative for a roundtable on 'Establishing 2011-2012 Interagency Comptox Collaborations', 5th Inter-agency Computational Toxicology Colloquium 2010
Centers for Disease Control, Atlanta, GA

Chair of two discussion sessions, 1st Inter-agency Computational Toxicology Colloquium 2008
Centers for Disease Control, Atlanta, GA

Problem presenter, NCSU Industrial Mathematics Modeling Workshop 2002
North Carolina State University, Raleigh, NC

Chair of scientific session ('Power-line frequency field interactions'), World Congress 2000 on Medical Physics and Biomedical Engineering 2000
International Union for Physical and Engineering Sciences in Medicine, Chicago IL

Publications

Refereed Journals

Pelch K, Wignall JA, Goldstone AE, Ross PK, Blain RB, Shapiro AJ, Holmgren SD, Hsieh JH, Svoboda D, Auerbach SS, **Parham FM**, Masten SA, Walker V, Rooney A, Thayer KA. A scoping review of the health and toxicological activity of bisphenol A (BPA) structural analogues and functional alternatives. Toxicology 424, DOI: 10.1016/j.tox.2019.06.006. Aug 2019

Phillips JR, Svoboda DL, Tandon A, Patel S, Sedykh A, Mav D, Byron K, Yauk C, Yang L, Thomas RS, Gift JS, Davis JA, Olysyzk L, Merrick BA, Paules RS, **Parham F**, Saddler T, Shah RR, Auerbach SS. BMDExpress 2: Enhanced transcriptomic dose-response analysis workflow.Bioinformatics. DOI: 10.1093/bioinformatics/bty878. May 2019

Behl M, Ryan K, Hsieh JH, **Parham F**, et al. Screening for developmental neurotoxicity at the National Toxicology Program: The future is here. Toxicological Sciences 167 (1), pp 6:14, DOI: 10.1093/toxsci/kfy278. Jan. 2019.

Sirenko O, **Parham F**, et al. Functional and mechanistic neurotoxicity profiling using human iPSC-derived neural 3D cultures. Toxicological Sciences 167 (10), pp 58-76, DOI: 10.1093/toxsci/kfy218. Jan. 2019.

Hsieh JH, Ryan K, Sedykh A, Lin JA, Shapiro AJ, **Parham F**, Behl M. Application of benchmark concentration (BMC) analysis on zebrafish data - a new perspective for quantifying toxicity in alternative animal models.Toxicological Sciences 167(1) pp. 92-104. DOE: 10.1093/toxsci/kfy258. Jan. 2019.

Sirenko O, Grimm FA, Ryan KR, Iwata Y, Chiu WA, **Parham F**, Wignall JA, Anson B, Cromwell EF, Behl M, Rusyn I, Tice RR. In vitro cardiotoxicity assessment of environmental chemicals using an organotypic human induced pluripotent stem cell-derived model. TAP 2017.

Parham F, Portier CJ, Chang Z, Mevissen M. The use of signal-transduction and metabolic pathways to predict human disease targets from electric and magnetic fields using in vitro data in human cell lines. Front. Public Health 2016.

Sand S, **Parham F**, Portier CJ, Tice RR, Krewski D. Comparison of points of departure for health risk assessment based on high-throughput screening data. Environmental Health Perspectives 2016.

Ryan KR, Sirenko O, **Parham F**, Hsieh JH, Cromwell EF, Tice RR, Behl M. Neurite outgrowth in human induced pluripotent stem cell-derived neurons as a high-throughput screen for developmental neurotoxicity or neurotoxicity. Neurotoxicology 2016.

Wise A, **Parham F**, Axelrad DA, Guyton KZ, Portier C, Zeise L, Zoeller RT, Woodruff TJ. Upstream adverse effects in risk assessment: A model of polychlorinated biphenyls, thyroid hormone disruption and neurological outcomes in humans. Environmental Research 2012; 117:90-99.

Parham F, Wise A, Axelrad DA, Guyton KZ, Portier C, Zeise L, Zoeller RT, Woodruff TJ. Adverse effects in risk assessment: Modeling polychlorinated biphenyls and thyroid hormone disruption outcomes in animals and humans. Environmental Research 2012; 116:74-84.

Parham F, Austin C, Southall N, Huang R, Tice R, Portier C. Dose-response modeling of high-throughput screening data. Journal of Biomolecular Screening 2010; 14:1216-1227.

Thomas R, Gohlke JM, Stopper GF, **Parham FM**, Portier CJ. Choosing the right path: enhancement of biologically relevant sets of genes or proteins using pathway structure. Genome Biology 2009; 10: R44.

Gohlke JM, Armant O, **Parham FM**, Smith MV, Zimmer C, Castro DS, Nguyen L, Parker JS, Gradwohl G, Portier CJ, Guillemot F. Characterization of the proneural gene regulatory network during mouse telencephalon development. BMC Biology 2008; 6:#15.

Gohlke JM, **Parham FM**, Portier CJ. A direct comparison of algorithm-based and literature-based systems biology approaches: Applications in neurodevelopment. Neurotoxicology 2006; 27: SI 908-908.

Portier CJ, Toyoshiba H, Sone H, **Parham F**, Irwin RD, Boorman GA. Comparative analysis of gene networks at multiple doses and time points in livers of rats exposed to acetaminophen. ALTEX 2006; 23: Suppl. 380-384.

Toyoshiba H, Sone H, Yamanaka T, **Parham FM**, Irwin RD, Boorman GA, Portier CJ. Gene interaction network analysis suggests differences between high and low doses of acetaminophen. TAP 2006; 215: 306-316.

Gohlke JM, **Parham FM**, Portier CJ. Combining microarrays with comparative genomics to elucidate gene regulatory networks for normal and perturbed forebrain development. Birth Defects Research A 2006; 76: 316-316

Yamanaka T, Toyoshiba H, Sone H, **Parham FM**, Portier CJ. The TAO-Gen algorithm for identifying gene interaction networks with application to SOS repair in *E. coli*. Environ Health Perspect 2004; 112: 1614-1621.

Toyoshiba H, Yamanaka T, Sone H, **Parham FM**, Walker NJ, Martinez J, Portier CJ. Gene interaction network suggests dioxin induces a significant linkage between Ah-receptor and retinoic acid receptor beta. Environ Health Perspect 2004; 112: 1217-1224.

Brunssen SH, Morgan DL, **Parham FM**, Harry GJ. Carbon Monoxide Neurotoxicity: Transient Inhibition of Avoidance Response and Delayed Microglia Reaction in the Absence of Neuronal Death. Toxicology 2003; 194: 51-63**.**

Koo JW, **Parham F**, Kohn MC, Masten SA, Brock JW, Needham LL, Portier CJ. The association between biomarker-based exposure estimates for phthalates and demographic factors in a human reference population. Environ Health Perspect 2002; 110: 405-410.

Parham FM, Matthews HB, Portier CJ. A physiologically based pharmacokinetic model of p,p '-dichlorodiphenylsulfone. TAP 2002; 181:153-163.

Kohn MC, **Parham F**, Masten SA, Portier CJ, Shelby MD, Brock JW, Needham LL. Human exposure estimates for phthalates. Environ Health Perspect 2000; 108: A440-A442.

Portier CJ, **Parham FM**. Comments on a biochemical model of cyclophosphamide hematotoxicity. J Toxicol Environ Health A 2000; 61:525-528.

Walker N, Portier CJ, Edler L, Jung D, Needham L, Masten S, **Parham F**, Lucier G. Half-lives and body burdens for dioxin and dioxin-like compounds in humans estimated from an occupational cohort in Germany. Organohalogen Compounds 1999; 42:129-138.

Parham, FM, Portier CJ. A dioxin dose-response calculation from published epidemiological data. Organohalogen Compounds 1999; 44:405-406.

Parham FM, Portier CJ. Using structural information to create physiologically based pharmacokinetic models for all polychlorinated biphenyls : II: Rates of Metabolism. TAP 1998; 151:110-116.

Parham FM, Kohn MC, Matthews HB, DeRosa C, Portier CJ. Using structural information to create physiologically based pharmacokinetic models for all polychlorinated biphenyls : I: Tissue:blood partition coefficients. TAP 1997; 144:340-347.

Freeman GB, Dill JA, Johnson, JD, Kurtz PJ, **Parham FM,** Mathews HB. Comparative

Contributed to NTP Technical Report on the Toxicology and Carcinogenesis Studies of Bromodichloromethane (CAS No. 75-27-4) in Male F344/N Rats and Female B6C3F$_1$ Mice, NTP TR 532, NIH Publication No. 06-4468, 2006.

Contributed to dose-response section of EPA dioxin risk assessment document -- http://www.epa.gov/ncea/pdfs/dioxin/part2/drich8.pdf
http://cfpub.epa.gov/ncea/iris_drafts/dioxin/nas-review/pdfs/part2/dioxin_pt2_ch08_dec2003.pdf

Contributed to NTP Technical Report on the Toxicology and Carcinogenesis Studies of *p,p'*-Dichlorodiphenyl Sulfone (CAS No. 80-07-9) in F344/N Rats and B6C3F$_1$ Mice (Feed Studies), NTP TR 501, NIH Publication No. 01-4435, 2001.

Portier CJ, Wolfe MS, Boorman GA, Bernheim NJ, Galvin MJ, Newton SA, **Parham FM**, Olden KO, eds. NIEHS report on health effects from exposure to power-line frequency electric and magnetic fields. Research Triangle Park, North Carolina: National Institute of Environmental Health Sciences; NIH publication no. 99-4493. 1999;508

Contributed to Portier CJ, Wolfe MS, eds. Assessment of Health Effects from Exposure to Power-Line Frequency Electric and Magnetic Fields: Working Group Report. Research Triangle Park, North Carolina: National Institute of Environmental Health Sciences; NIH publication no. 98-3981. 1998.

Invited Talks at conferences and professional society meetings

Talk on in vitro data analysis methods at workshop Integrated Testing Strategies for Developmental Neurotoxicity, Research Triangle Park, NC, September 2017.

Parham F, "Analysis of replicate high throughput screening data"; Tox21 quarterly meeting, Research Triangle Park, NC, July 2012.

Parham F, "Thyroid hormone disruption as an upstream indicator of chemical toxicity"; Moving Upstream: Using upstream biological signals to assess chemical toxicity, Oakland, CA, November, 2009.

Parham F, "Overview of NIEHS CompTox Activities"; 1st Inter-agency Computational Toxicology Colloquium, Centers for Disease Control, Atlanta, GA, February 2008.

Parham F, Portier CJ, "A meta-analysis of the epidemiology of childhood leukemia and EMF"; World Congress 2000 on Medical Physics and Biomedical Engineering, Chicago, IL, June 2000.

Contributed presentations at conferences and professional society meetings

Behl M, Ryan K, Hsieh JH, Parham F, Shapiro AJ, Collins BJ, Sipes NS, Birnbaum LS, Bucher JR, Foster PMD, Walker NJ, Paules RS, Tice RR, "A novel approach to evaluate mechanistic data for developmental neurotoxicity", Poster presentation at NASEM workshop Strategies and

Tools for Conducting Systematic Review of Mechanistic Data to Support Chemical Assessments, Washington, DC, December 2018.

Ryan KR, Hsieh JF, Parham F, Shapiro A, Sipes N, Collins B, Maull E, Paules R, Walker N, Behl M, "Strategies and advancements to evaluate developmental neurotoxicity at the National Toxicology Program", Poster presentation at Teratology Society Annual Meeting, Clearwater, FL, June 2018

Hsieh J, Lin J, Sedykh A, Parham F, Shapiro A, Sipes NS, Ryan K, Behl M, Paules RS, Auerbach SS, "A non-parametric approach for selecting benchmark responses for in vitro or alternative animal model data", Poster presentation at Society of Toxicology annual meeting, San Antonio, TX, March 2018.

Saddler T, Parham F, Shapiro A, Devito M, Auerbach S, "PubChem-Heatmap: A chemical data density viewer for surveying literature across classes of chemicals", Poster presentation at Society of Toxicology annual meeting, San Antonio, TX, March 2018.

Shapiro AJ, Hsieh J, Addington J, Ryan K, Behl M, "A transparent and reusable data analysis/data visualization infrastructure for developmental neurotoxicity screening using in vitro and alternative animal model systems", Poster presentation at Society of Toxicology annual meeting, San Antonio, TX, March 2018.

Parham F, Auerbach S, Svoboda D, Hsieh JH, "Comparison of metrics of chemical similarity in high-throughput assays", Poster presentation at Society of Toxicology annual meeting, Baltimore, MD, March 2017.

Ryan K, Sirenko O, Parham F, Cromwell E, Hsieh JH, DeLaura S, Tice R, Behl M, "Prioritizing compounds for targeted developmental neurotoxicity testing through utilization of human induced pluripotent stem cells in a high throughput high content screening assay", Poster presentation at Triangle Society for Neuroscience spring meeting, Research Triangle Park, NC, April 2015.

Tice RR, Sirenko O, Parham F, Cromwell EF, Hsieh J, DeLaura S, Behl M, Ryan K, "Using human-induced pluripotent stem cells (iPSC) in high-content screening (HCS) to prioritize chemicals for developmental neurotoxicity testing", Poster presentation at Society of Toxicology annual meeting, San Diego, CA, March 2015.

Sirenko O, Ryan KR, Parham F, DeLaura S, Behl M, Cromwell EF, and Tice RR, "In vitro assessment of neurotoxicity hazards of environmental compounds using human iPSC-derived neurons", Poster presentation at International Society for Stem Cell Research meeting, Vancouver, Canada, June 2014.

Ryan KR, Parham F, Hsieh J-H, Sirenko O, DeLaura S, Cromwell EF, Tice RR, Behl M, "Chemical effects on neurite outgrowth using human iPSC-derived neurons - A screening approach to identify potential developmental neurotoxicants", Poster presentation at DNT4 conference on developmental neurotoxicity, Philadelphia, PA, May 2014.

Sirenko 0, Ryan KR, Parham F, Behl M, Anson B, Cromwell EF, Tice RR, "In vitro assessment of cardiotoxicity hazards of environmental compounds using fast fluorescence imaging of beating iPSC-derived cardiomyocytes", Poster presentation at Society of Toxicology Annual meeting, Phoenix, AZ, March 2014.

Ryan KR, Parham F, Sirenko O, Behl M, Anson B, Cromwell EF, Tice RR, "In vitro cardiotoxicity assessment of environmental chemicals using human induced pluripotent stem cell (iPSC)-derived cardiomyocytes", Poster presentation at FutureTox II, Chapel Hill, NC, January 2014.

Ryan KR, Parham F, Sirenko O, Behl M, Anson B, Cromwell EF, Tice RR, "In vitro Assessment of Environmental Compound-Induced Cardiotoxicity Potential Using Human Induced Pluripotent Stem Cell (iPSC)-Derived Cardiomyocytes", Poster presentation at American Society for Cell Biology annual meeting, New Orleans, LA, December 2013.

Parham F, DeVito M, Huang R, Xia M, Collins B, Rider C, Tice R, "Generalized concentration addition models some but not all interactions of mixtures of androgen- and estrogen-receptor active compounds in high throughput screening assays", Poster presentation at Society of Toxicology annual meeting, San Antonio, TX, March 2013.

Mevissen M, Parham F, Chang X, "Signaling pathways linked to EMF exposure overlap with pathways linked to heat", Poster presentation at NIEHS Genomics Day, Research Triangle Park, NC, September 2012.

Mevissen M, Möller AM, Parham F, Chang X, Thomas R, Murbach M, Kuster, Portier CJ, "The Use of Signal-Transduction and Metabolic Pathways to Predict Human Disease Targets from Electric and Magnetic Fields", Poster presentation at EMF Health Risk Research: Lessons Learned and Recommendations for the Future, Swiss Federal Institute of Technology Zurich, Zurich, Switzerland, November 2011.

Mevissen M, Parham F, Chang X, Portier CJ, "EMF and Health: Predicting Human Disease Using Microarrays and Pathway Analysis", Poster presentation at Bioelectromagnetics Society annual meeting, Halifax, Canada, June 2011.

Parham F, Wise A, Axelrad DA, Guyton KZ, Portier C, Zeise L, Zoeller RT, Woodruff TJ, "Integrating human and toxicological evidence on PCBs, thyroid hormone disruption and developmental neurological effects", Poster presentation at Society of Toxicology annual meeting, Washington, DC, March 2011.

Chang X, Thomas R, Foley J, Parham FM, Portier CJ, "AHr-mediated gene expression in the developing mouse heart", Poster presentation at Society of Toxicology Annual meeting, Salt Lake City, UT, March 2010.

Thomas R, Gohlke J, Parham F, Portier C, "Incorporation of biochemical interaction network information helps in identification of biologically-relevant pathways and improves the toxicity

classification of chemicals", Poster presentation at Society of Toxicology annual meeting, Baltimore, MD, March 2009.

Easterling M, Walker NJ, Parham FM, Portier CJ, "PBPK models for mixtures of dioxin-like chemicals", Society of Toxicology annual meeting, Seattle, WA, March 2008.

Parham F, Portier CJ, "Dose-response modeling of high-throughput screening data", Poster presentation at EPA Computational Toxicology Forum (2007), Research Triangle Park, NC, May 2007.

Gohlke JM, Parham FM, Parker JS, Smith MV, Portier CJ, "Elucidation of a gene regulatory network for forebrain development using bioinformatics approaches for the analysis of compiled microarray datasets", Poster presentation at Society of Toxicology annual meeting, San Diego, CA, March 2006.

Easterling M, Walker NJ, Parham FM, Portier CJ, "A PBPK model for a mixture of dioxin-like chemicals", Poster presentation at Society of Toxicology annual meeting, New Orleans, LA, March 2005.

Sone H, Toyoshiba H, Yamanaka T, Parham F, Irwin R, Boorman G, Portier CJ, "Comparative analysis of gene networks at multiple doses and time points in livers of rats exposed to acetaminophen", Poster presentation at Society of Toxicology annual meeting, New Orleans, LA, March 2005.

Parham F, Miller MC, Bell D, Paules R, Portier C, "Using network-based algorithms to compare oxidative stress gene interactions using data from two microarray platforms", Oral presentation at Total Microarray Data Analysis conference, Washington DC August 2004.

Toyoshiba H, Yamanaka T, Parham FM, Martinez JM, Sone H, Walker NJ, Portier CJ, "Quantifying gene expression networks using Bayesian methods: Known network structure", Poster presentation at Society of Toxicology annual meeting, Baltimore, MD, March 2004.

Yamanaka T, Toyoshiba H, Parham F, Martinez JM, Sone H, Portier C, "Quantifying gene expression: Identifying network structure", Poster presentation at Society of Toxicology annual meeting, Baltimore, MD, March 2004.

Parham F, Toyoshiba H, Yamanaka T, Portier C, "A GUI-based program for analysis of DNA microarray data using Bayesian networks", Oral presentation at Atlantic Symposium on Computational Biology and Genome Informatics (Joint Conference on Information Sciences), Cary, NC, August 2003.

Portier CJ, Ye F, Parham F, Kupper L, "The equal slopes test: a unified statistical method for evaluating extrapolation below a point of departure in dose-response analysis", Poster presentation at Society for Risk Analysis annual meeting, Seattle, WA, December 2001.

Parham FM, "Effects of different models of the gut on the accuracy of PBPK models of PCBs", Poster presentation at Society of Toxicology Annual Meeting, Seattle, WA, March 1998.

Parham FM, Matthews HB, Portier CJ, "Using structure activity data to create PBPK models for all polychlorinated biphenyls", Poster presentation at International Congress of Toxicology, Seattle, WA, July 1995.

Software products created

Generated data on correlation coefficients and related measures (confidence intervals, etc.) of various measures of activity in Tox21 assays for use in data browser web site.
Created PathFind and PathScope, GUI-based programs for analyzing microarray data using Bayesian networks, and made them available for public distribution.

Publications Submitted or In Preparation

Submitted to Toxicology and Applied Pharmacology: Parham FM, Portier CJ. A physiologically based pharmacokinetic model of anthraquinone in rats used to derive dose metrics for a two-stage cancer model.

Peer reviews
Served as peer reviewer for articles for the following journals
Environmental Health Perspectives
Environmental Research
Environmental Science and Technology
Environmental Toxicology and Pharmacology
QSAR & Combinatorial Science
Regulatory Toxicology and Pharmacology
Risk Analysis
Toxicological Sciences
Toxicology Letters

Other professional activities

Trans-NIEHS Combined Exposures Working Group

Exposure Science in the 21st Century (ES21) interagency workgroup (modeling subgroup)

NIEHS Predictive Toxicology and Disease Faculty

Predictive Toxicology and Disease group (part of NIEHS Cross-Divisional Implementation Planning program, 2012-2013)