BIOGRAPHICAL SKETCH

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NAME: Jeffries, Clark Debs EMAIL: clark_jeffries@med.unc.edu

eRA COMMONS USER NAME (credential, e.g., agency login): JEFFRIES

POSITION TITLE: Research Scientist, Renaissance Computing Institute, Adjunct Professor, Eshelman School of Pharmacy

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Washington, Seattle	BS	08/67	Mathematics
University of Washington, Seattle	MS	06/68	Applied Mathematics
University of Toronto, Toronto	PhD	06/71	Mathematics

A. Personal Statement

I am a mathematician with expertise in predictive machine learning. Methods I invented have been recently applied to clinical high risk datasets, yielding novel approaches to address reproducible classification and to avoid overfitting. I am acquainted with both the promise and pitfalls of machine learning. I am also an expert in various mathematical modeling techniques, especially related to stability theory and graph theory. I am currently a bioinformatics scientist with Renaissance Computing Organization of the University of North Carolina at Chapel Hill. Formerly I was a professor with Mathematical Sciences of Clemson University, then a designer with Microelectronics Division of IBM Corporation. In the first I wrote more than 50 scientific papers and in the second I became among inventors on 117 issued US patents. My current issued patent total is 121, and one more (with D. Perkins pertaining to prodrugs of monomethyl fumarate) being processed, to be assigned to UNC.

The ProDACC facet of the present project will include seeking patterns in data of diverse types. Methods I developed can extract information in robust solutions that differ little or not at all by small uncertainties such as deletion of or noise in measurements for a few subjects. Furthermore, the methods automatically and rationally select parsimonious subsets of biomarkers from sets of tens, hundreds, or thousands. The optimal number of markers can be determined by permutation test results over a range of limits. Importantly, the analyses have survived tests using real data for overfitting and can accommodate mixes of data types (e.g. numerical scores of clinical signs plus blood protein levels). In fact, the algorithm developed does not care about the types of sources, only that the values are z-scores. Findings to date include superior figures of merit (AUC, p-val, mse) vs popular and powerful methods including LASSO. Even better, the methods exhibit superior permutation and cross validation testing performance when applied to examples from real psychiatric data, sometimes making the difference between experimental interpretations that do or do not have a customarily acceptable estimate of false discovery.

The goal of the present application is expansion of the novel method into additional data including time-dependent data (as opposed to baseline).

B. Positions and Honors

Positions and Employment

1987-1992 Lecturer, Assistant Professor, Associate Professor, Clemson University, Clemson, SC
1992-1998 Professor, Mathematical Sciences, Clemson University, Clemson, SC

1998-2004 Algorithm Designer, IBM Microelectronics Division, Research Triangle Park, NC
2005-present Research Scientist, Renaissance Computing Institute, UNC Chapel Hill, NC.
2006-present Adjunct Professor, University of North Carolina Eshelman School of Pharmacy

Other Experience and Professional Memberships

2008-present Society for Neurosciences, member
2016-present American Association for Advancement of Science, member
2017-present, Royal Society of Medicine, overseas fellow

Honors

2003-2004 IBM "Master Inventor" (presently listed as inventor on ~121 issued US patents, 117 with IBM)

C. Contributions to Science

A career in applied mathematics requires curiosity, and my scientific curiosity has led to development of numerous algorithms for—in the broadest sense—detection of patterns in data. Correct detection leads to optimal response, another field of endeavor. Inventions in computer networks have ranged from devising a nickname system ("hash function") for Internet addresses on packets to securing communications with a protocol that cannot be decoded from interceptions (now licensed by IBM, Patent US20080077979, see *Computer Communications* 2006). Successful work at IBM implies the ability to work with hardware and software engineers of very different and complementary types of expertise.

Prior to my IBM days I published papers on ecological networks, galactic rotation, classical electromagnetics, fluid dynamics, and other sciences. However, the goal of my career since 2005 is to collaborate with others to understand and treat schizophrenia. Achieving that would, of course, would require general understanding of a variety of concepts in neuroscience and effective networking with experts.

My interests are to apply machine learning and related methods to high dimensional data to better understand heterogeneity in the psychosis high-risk syndrome. I have developed a novel machine learning approach, called CALF, and applied this approach to data from the NAPLS project. My work has contributed to our understanding of **distinguished networks** of markers (not sets of individually distinguished markers) including: (1) key symptoms driving the emergence of psychosis (disturbances in thought content); (2) blood markers used collectively in risk prediction (especially biomarkers of oxidative stress); and (3) inflammation and hormone markers in blood-brain barrier regulation that may signal the earliest stages of psychotic disorders.

Again, the role involves collaboration with psychiatrists and psychologists with very different and complementary types of expertise.

My contributions in the present application will intersect all three of the above arenas but focus mainly on the third problem, finding network patterns in seemingly unrelated data types. The goal is to describe networks and their changes that foretell by months or years a high risk of transition to schizophrenia.

Perkins DO, Jeffries CD, Do KQ. Potential roles of redox dysregulation in the development of schizophrenia. Mol Psychiatry. 2020. To appear in Molecular Psychiatry.

Jeffries CD, Perkins DO, Fournier M, Do KQ, Cuenod M, Khadimallah I, Domenici E, Addington J, Bearden CE, Cadenhead KS, Cannon TD, Cornblatt BA, Mathalon DH, McGlashan TH, Seidman LJ, Tsuang M, Walker EF, Woods SW. Networks of blood proteins in the neuroimmunology of schizophrenia. Transl Psychiatry. 2018 Jun 6;8(1):112. doi: 10.1038/s41398-018-0158-y.

Zheutlin AB, Jeffries CD, Perkins DO, Chung Y, Chekroud AM, Addington J, Bearden CE, Cadenhead KS, Cornblatt BA, Mathalon DH, McGlashan TH, Seidman LJ, Walker EF, Woods SW, Tsuang M, Cannon TD. The Role of microRNA Expression in Cortical Development During Conversion to Psychosis. Neuropsychopharmacology. 2017 Oct;42(11):2188-2195. doi: 10.1038/npp.2017.34.

Perkins DO, Jeffries CD, Addington J, Bearden CE, Cadenhead KS, Cannon TD, Cornblatt BA, Mathalon DH, McGlashan TH, Seidman LJ, Tsuang MT, Walker EF, Woods SW, Heinssen R. Towards a psychosis risk blood diagnostic for persons experiencing high-risk symptoms: preliminary results from the NAPLS project. Schizophr Bull. 2015 Mar;41(2):419-28. doi: 10.1093/schbul/sbu099. PMID: 25103207

Cannon TD, Chung Y, He G, Sun D, Jacobson A, van Erp TG, McEwen S, Addington J, Bearden CE, Cadenhead K, Cornblatt B, Mathalon DH, McGlashan T, Perkins D, Jeffries C, Seidman LJ, Tsuang M, Walker E, Woods SW, Heinssen R; North American Prodrome Longitudinal Study Consortium. Progressive reduction in cortical thickness as psychosis develops: a multisite longitudinal neuroimaging study of youth at elevated clinical risk. Biol Psychiatry. 2015 Jan 15;77(2):147-57.

Jeffries CD, Perkins DO, Chandler SD, Stark T, Yeo E, Addington J, Bearden CE, Cadenhead KS, Cannon TD, Cornblatt BA, Mathalon DH, McGlashan TH, Seidman LJ, Walker EF, Woods SW, Glatt SJ, Tsuang M. Insights into psychosis risk from leukocyte microRNA expression. Transl Psychiatry. 2016 Dec 13;6(12):e981. doi: 10.1038/tp.2016.148. PMID: 27959328

Cannon TD, Yu C, Addington J, Bearden CE, Cadenhead KS, Cornblatt BA, Heinssen R, Jeffries CD, Mathalon DH, McGlashan TH, Perkins DO, Seidman LJ, Tsuang M, Walker EF, Woods SW1, Kattan MW1. An Individualized Risk Calculator for Research in Prodromal Psychosis. Am J Psychiatry. 2016 Oct 1;173(10):980-988. Epub 2016 Jul 1.

Perkins DO, Jeffries CD, Cornblatt BA, Woods SW, Addington J, Bearden CE, Cadenhead KS, Cannon TD, Heinssen R, Mathalon DH, Seidman LJ, Tsuang MT, Walker EF, McGlashan TH. Severity of thought disorder predicts psychosis in persons at clinical high-risk. Schizophr Res. 2015 Dec;169(1-3):169-77. doi: 10.1016/j.schres.2015.09.008. PMID: 26441004

Jeffries CD, Fried HM, Perkins DO. Nuclear and cytoplasmic localization of neural stem cell microRNAs. RNA. 2011 Apr;17(4):675-86.

Complete List of Published Work in MyBibliography
https://www.ncbi.nlm.nih.gov/sites/myncbi/clark.jeffries.1/bibliography/40151870/public/?sort=date&direction=ascending.

Complete List of Issued US Patents
http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=%2Fnetahtml%2FPTO%2Fsearch-bool.html&r=0&f=S&l=50&TERM1=jeffries%2C+clark&FIELD1=INNM&co1=AND&TERM2=&FIELD2=&d=PTXT

D. Research Support

Research Support

U01 MH082004-10, National Institute of Mental Health (NIMH)
12/01/07-06/30/20
5/9 Predictors and Mechanisms of Conversion to Psychosis
Role: Co-Investigator, data analysis and data integration

3-U01-MH082004-05S1, National Institute of Mental Health
5/9 Predictors and Mechanisms of Conversion to Psychosis
Role: Co-Investigator, modeling rs-fMRI data to distinguish psychosis converters from nonconverters

6/01/2009-
San Francisco Foundation
Role: PI, develop approaches to better understand the causes of schizophrenia