BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Russ B. Altman

eRA COMMONS USER NAME: ALTMAN.RUSS

POSITION TITLE: Professor of Bioengineering, Genetics, Medicine, Biomedical Data Science, and (by courtesy) of Computer Science

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Harvard College	A.B.	06/1983	Biochemistry & Molecular Biology
Stanford University Medical School	Ph.D.	06/1989	Medical Information Sciences
Stanford University Medical School	M.D.	06/1990	Medicine

A. Personal Statement

My area of professional expertise is biomedical informatics and data science, the creation of methods to analyze molecular, cellular and organismal data of importance to problems in medicine and health. My specific application area of interest is drug action, including molecular analysis of protein structure and dynamics, datamining (including natural language processing) for discovery of unexpected drug actions, functional genomics (particularly pharmacogenomics) to understand drug action, and the impact of human variation on drug response. We build the PharmGKB resource (http://www.pharmgkb.org/) of curated information about how human genetic variation impacts drug-response phenotypes. We develop and use a broad array of machine learning algorithms for natural language processing, clustering, classification and deep learning. I am also Co-PI of an FDA Center of Excellence in Regulatory Science & Innovation. This proposal focuses on development of methods for extracting knowledge from literature and its use in systems modeling.

B. Positions and Honors

RESEARCH AND/OR PROFESSIONAL EXPERIENCE

1982	Undergraduate Research Assistant. Supervisor: Prof. William N. Lipscomb, Nobel Laureate, Harvard Department of Chemistry
1982-1983	Undergraduate Research Assistant. Supervisor: Prof. Stephen C. Harrison, Harvard Department of Biochemistry and Molecular Biology
1984-1988	Graduate Research Assistant to Bruce G. Buchanan, Stanford Dept. of Computer Science
1989-1992	Post-Doctoral fellow (part time). Prof. Oleg Jardetzky, Stanford Magnetic Resonance Laboratory
1990-1992	Intern and Resident, Stanford University Medical Center
1992-1999	Assistant Professor of Medicine (& Computer Science, by courtesy), Stanford University
1993-1997	Member, Executive Steering Committee, San Diego Supercomputer Center
1994-1995	Organizing Committee, 2nd & 3rd Intl. Conf. on Intelligent Systems for Molecular Biology
1996-	Organizing Committee, Pacific Symposium on Biocomputing
1996	Founding Board of Directors, International Society for Computational Biology (ISCB)
1997	Molecular Science Thrust Leader, National Partnership for Advanced Computer Infrastructure
1999-2004	Associate Professor of Medicine (& Computer Science, by courtesy) tenure, Stanford University
2000-2018	Director, Biomedical Informatics Program, Stanford University
2000-2002	President, International Society for Computational Biology
2004-	Professor of Genetics, Bioengineering, & Medicine (& Comp. Sci., by courtesy)
2007-2012	Chair, Department of Bioengineering, Stanford University
2013-2014	President, American Society for Clinical Pharmacology and Therapeutics
2013-2014	Chair, Science Board to the Food and Drug Administration

2015- Co-Chair, Drug Forum of Institute of Medicine
2016- Founding Co-Editor-in-Chief (with M. Levitt) Annual Review of Biomedical Data Science

HONORS AND AWARDS

1983 Phi Beta Kappa, Harvard College Chapter
1983 Summa Cum Laude, Harvard College
1983 NIH Medical Scientist Training Program pre-doctoral fellowship at Stanford
1987 Departmental Ph.D. oral exams passed "with high distinction"
1991 Howard Hughes Fellowship for Physicians
1993 Charles E. Culpeper Scholarship in Medical Science
1996 National Science Foundation CAREER Award
1997 U.S. Presidential Early Career Award for Scientists and Engineers (NIH)
1998 Western Society for Clinical Investigation, Annual Young Investigator Award
1998 Fellow, American College of Medical Informatics
1999 Fellow, American College of Physicians
2000 Stanford Graduate Teaching Award
2005 General Internal Medicine, Honorable Mention for Clinical Teaching
2009 Fellow, American Institute of Medical and Biological Engineering
2009 Member, Institute of Medicine of the National Academies
2010 Fellow, International Society for Computational Biology
2014 Stanford Medical School Mentorship Award
2014 Fellow, American Association for the Advancement of Science

C. Contribution to Science

I have ~374 papers on PubMED (as of 6/1/2019) at NCBI (https://tinyurl.com/y4v72t8o). Five key areas of contribution over the last decade include:

1. I have served as the original PI, now Co-PI, of the **Pharmacogenomics Knowledgebase** (PharmGKB, http://www.pharmgkb.org/) Resource. This is a premier human-curated knowledge base of how human genetic variation impacts drug response phenotypes. It gets ~30K unique IP hits each month, publishes review articles on drug pathways and genes of significance to pharmacogenomics (and thus precision medicine), and is the basis for several clinical implementation research efforts, including the Clinical Pharmacogenetic Implementation Consortium guidelines (CPIC). We also have made primary contributions to PGx discovery. We have written more than 150 papers as part of the PharmGKB project, available at https://tinyurl.com/yyupc9yr

a. Johnson JA, …, Altman RB; Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing. Clin Pharmacol Ther. 2011 Oct;90(4):625-9. Epub 2011 Sep 7. Review. PMID: 21900891; PMCID: PMC3187550.
b. Daneshjou R, …, Altman RB. Pathway analysis of genome-wide data improves warfarin dose prediction. BMC Genomics. 2013;14 Suppl 3:S11. doi: 10.1186/1471-2164-14-S3-S11. Epub 2013 May 28. PMID: 23819817; PMCID: PMC3829086.
c. Bergmeijer TO, …, Altman RB, …, Klein TE, Shuldiner AR; ICPC Investigators. Genome-wide and candidate gene approaches of clopidogrel efficacy using pharmacodynamic and clinical end points-Rationale and design of the International Clopidogrel Pharmacogenomics Consortium (ICPC). Am Heart J. 2018 Apr;198:152-159. doi: 10.1016/j.ahj.2017.12.010. Epub 2017 Dec 17. PubMed PMID: 29653637; PubMed Central PMCID: PMC5903579.
d. Amare AT, …, Altman RB, …, Klein TE, Weinshilboum RM, Biernacka JM, Baune BT. Association of the Polygenic Scores for Personality Traits and Response to Selective Serotonin Reuptake Inhibitors in Patients with Major Depressive Disorder. Front Psychiatry. 2018 Mar 6;9:65. doi: 10.3389/fpsyt.2018.00065. eCollection 2018. PubMed PMID: 29559929; PubMed Central PMCID: PMC5845551.

2. My group has lead in the creation of methods to analyze the scientific literature, in support of extracting information about the relationship between genes, drugs and phenotypes (in particular, diseases). These are

the critical entities for our work in pharmacogenomics and translational medicine. There is a large volume of unstructured knowledge in the published literature, and too often it is not captured and integrated optimally in the creation and testing of hypotheses. Our work has focused on extracting high quality, semantically clear relationships between key entities. We have focused on both abstracts in PubMED as well as full text, as available. We have released recently a compendium of more than 2 million high quality and typed relationships between genes, drugs and diseases. We have also shown the ability of novel text mining algorithms to search full text to find relationships between entities. We have then used these extracted relationships to support curation of PharmGKB and the generation of networks that can be used to understand the systematic response to drugs. We have written ~38 papers available at https://tinyurl.com/yxauw6wr.

a. Percha B, Altman RB. A global network of biomedical relationships derived from text. Bioinformatics. 2018 Aug 1;34(15):2614-2624. doi: 10.1093/bioinformatics/bty114. PubMed PMID: 29490008; PubMed Central PMCID: PMC6061699.
b. Mallory EK, Zhang C, Ré C, Altman RB. Large-scale extraction of gene interactions from full-text literature using DeepDive. Bioinformatics. 2016 Jan 1;32(1):106-13. doi: 10.1093/bioinformatics/btv476. Epub 2015 Sep 3. PubMed PMID: 26338771; PubMed Central PMCID: PMC4681986.
c. Lyalina S, Percha B, LePendu P, Iyer SV, Altman RB, Shah NH. Identifying phenotypic signatures of neuropsychiatric disorders from electronic medical records. J Am Med Inform Assoc. 2013 Dec;20(e2):e297-305. doi: 10.1136/amiajnl-2013-001933. Epub 2013 Aug 16. PubMed PMID: 23956017; PubMed Central PMCID: PMC3861917.
d. Percha B, Garten Y, Altman RB. Discovery and explanation of drug-drug interactions via text mining. Pac Symp Biocomput. 2012:410-21. PubMed PMID: 22174296; PubMed Central PMCID: PMC3345566.

3. My group has created the **FEATURE suite of programs** for understanding the molecular mechanism of proteins, particularly with respect to drug binding, druggability and drug design. WebFEATURE is a publicly available interface for analyzing protein structures for functional sites (http://feature.stanford.edu/webfeature/). The PocketFEATURE program uses pocket similarity between proteins to predict whether ligands for one pocket will bind a similar pocket (https://simtk.org/home/pocketfeature). The DrugFEATURE program analyzes a protein pocket and determines the likelihood that it will specifically bind a small molecule drug (https://simtk.org/home/drugfeature). The FragFEATURE program analyzes a protein pocket and determines small molecule fragments that are likely to bind in different sections within the pocket (https://simtk.org/home/frag-feature). We have ~30 papers as part of this effort available at: https://tinyurl.com/y595xynu

a. Liu T, Altman RB. Using multiple microenvironments to find similar ligand-binding sites: application to kinase inhibitor binding. PLoS Comput Biol. 2011 Dec;7(12):e1002326. PMID: 22219723; PMCID: PMC3248393.
b. Liu T, Altman RB. Relating Essential Proteins to Drug Side-Effects Using Canonical Component Analysis: A Structure-Based Approach. J Chem Inf Model. 2015 Jul 27;55(7):1483-94. doi: 10.1021/acs.jcim.5b00030. PMID: 26121262; PMCID: PMC4875781.
c. Liu T, Oprea T, Ursu O, Hasselgren C, Altman RB. Estimation of Maximum Recommended Therapeutic Dose Using Predicted Promiscuity and Potency. Clin Transl Sci. 2016 Dec;9(6):311-320. doi: 10.1111/cts.12422. PMID: 27736015; PMCID: PMC5161261.
d. Lo YC, Liu T, Morrissey KM, Kakiuchi-Kiyota S, Johnson AR, Broccatelli F, Zhong Y, Joshi A, Altman RB. Computational Analysis of Kinase Inhibitor Selectivity using Structural Knowledge. Bioinformatics. 2018 Jul 9. doi: 10.1093/bioinformatics/bty582. PMID: 29985971.

4. Our group has engaged in a program of **translational bioinformatics** to show how systems pharmacology approaches can be used to understand the relationship of molecular mechanism to adverse events. We have shown that we can link data mining of the FDA adverse events database and electronic medical records to extract and validate novel and unexpected drug interactions. We have used crowdsourcing to prioritize adverse events based on their severity. We have created algorithms for linking molecular networks to drugs and diseases in order to generate and understand pathways of drug response, and how drug interactions may result from intersections of underlying molecular mechanisms of individual drug responses. We have more than 40 papers as part of this effort, available at: https://tinyurl.com/ya4okyc4

a. White RW, …, Altman RB, Horvitz E. Web-scale pharmacovigilance: listening to signals from the crowd. J Am Med Inform Assoc. 2013 May 1;20(3):404-8. PMID: 23467469; PMCID: PMC3628066.
b. Tatonetti NP, …, Altman RB. Detecting drug interactions from adverse-event reports: interaction between paroxetine and pravastatin increases blood glucose levels. Clin Pharmacol Ther. 2011 Jul;90(1):133-42. PMID: 21613990; PMCID: PMC3216673.
c. Han L, Maciejewski M, Brockel C, Gordon W, Snapper SB, Korzenik JR, Afzelius L, Altman RB. A probabilistic pathway score (PROPS) for classification with applications to inflammatory bowel disease. Bioinformatics. 2018 Mar 15;34(6):985-993. doi: 10.1093/bioinformatics/btx651. PubMed PMID: 29048458; PubMed Central PMCID: PMC5860179.
d. Bagley SC, Sirota M, Chen R, Butte AJ, Altman RB. Constraints on Biological Mechanism from Disease Comorbidity Using Electronic Medical Records and Database of Genetic Variants. PLoS Comput Biol. 2016 Apr 26;12(4):e1004885. doi: 10.1371/journal.pcbi.1004885. eCollection 2016 Apr. PubMed PMID: 27115429; PubMed Central PMCID: PMC4846031.

5. We have helped demonstrate **how whole human genomes can be annotated**, and the issues of genome annotation in the context of next generation sequencing. This leadership has been through highly collaborative papers showing the first clinical analysis of a whole human genome, the analysis of a family quartet of genomes, an analysis of a series of genomes with an analysis of accuracy, and papers on the appropriate interpretation and triage of variations discovered in genome sequencing applications, both for pharmacogenomics and more broadly. We have 14 papers as part of this effort available at https://tinyurl.com/y77rarch

a. Ashley EA, …, Altman RB. Clinical assessment incorporating a personal genome. Lancet. 2010 May 1;375(9725):1525-35. PMID: 20435227; PMCID: PMC2937184.
b. Dewey FE, …, Altman RB, …, Quertermous T. Clinical interpretation and implications of whole-genome sequencing. JAMA. 2014 Mar 12;311(10):1035-45. PMID: 24618965; PMCID: PMC4119063.
c. MacArthur DG, …, Altman RB, …, Gunter C. Guidelines for investigating causality of sequence variants in human disease. Nature. 2014 Apr 24;508(7497):469-76. PMID: 24759409; PMCID: PMC4180223.
d. McDonagh EM, Whirl-Carrillo M, Altman RB, Klein TE. Enabling the curation of your pharmacogenetic study. Clin Pharmacol Ther. 2015 Feb;97(2):116-9. PMID: 25670512; PMCID: PMC4352230.

D. Research Support

Active

R01 LM05652 (PI: Altman) Role: PI 07/01/94-06/30/19 NIH/NLM
Text mining for high-fidelity curation and discovery of gene-drug-phenotype relationships The main goal is to apply methods and develop methods for annotating biological structures so that active sites, binding sites and interaction sites in biological structures can be automatically identified and annotated.

R24 GM061374 (Co-PI: Altman) 04/01/00 – 07/31/19 NIH/NIGMS
PharmGKB: pharmacogenomic knowledge for precision medicine
The Stanford Pharmacogenomics Knowledge Base (PharmGKB, http://www.pharmgkb.org/), an integrated data resource to support the NIGMS Pharmacogenetic Research Network and Database Initiative focuses on how genetic variation contributes to variation in the response to drugs, and will produce data from a wide range of sources, therefore interlinking genomic, molecular, cellular and clinical information about gene systems important for modulating.

UCSF / FDA (PI: Giacomini, Kathleen) Role: Co-PI 04/15/2014 – 08/31/2019 Subcontract.
UCSF-Stanford Center of Excellence in Regulatory Science and Innovation.
Goal: Stanford will engage in research collaborations with UCSF and FDA scientists to pursue projects in the area of regulatory science, with a focus on informatics.

NIH / NCATS (PI: Altman) 01/01/18 – 12/28/19
Stanford Effort for Biomedical Data Translator
The Biomedical Data Translator (BDT) will deliver capabilities for hypothesis generation by combining rich data with powerful inferential reasoning.

R01 GM102365 NIH/NIGMS (PI: Altman) 09/01/2012 – 03/31/2022

Combining systems biology and structural biology to find new therapeutics
Goal: To combine systems biology approaches with structure-based approaches to find new purposes for existing drugs, and to better predict off-target effects of drugs.

COMPLETED

HHSF223201510108C (PI: Altman) FDA 10/01/15- 9/30/18
Improving the Efficiency and Rigor of Pharmacovigilance at FDA
The overall goal of this project is to use natural language processing (NLP) and machine learning to triage reports to FAERS in order to identify high-value reports.

U54 (Co-PI: Altman) NIH/Northwestern University (Subcontract) 07/01/2016 – 06/30/2021
African American Cardiovascular Pharmacogenetics CONsorTium (ACCOuNT): Discovery and Translation
The PharmGKB team will manage the data for this project by providing data coordination, curation, harmonization, standardization and dissemination support for each consortium.

U54-HL117798 (PI: Altman) NIH/University of Pennsylvania / Subcontract 08/01/2012-05/31/2017
Personalization of Therapeutic Efficacy and Risk.
The goal is to build an integrated network of genes, drugs and phenotypes that will be an important asset in integrating information from multiple integrated efforts to understand the individual response to NSAIDs.

IC2014-1387 (PI: Altman) Pfizer 12/17/2015-12/16/2017
Strategic Effort in Precision Immunology –I-GPS
The vision for this collaboration is to create analytic methods for understanding drug response at the molecular level and quantitatively based on retrospective and prospective data analysis.

Genentech, Inc. (PI: Altman) 02/01/2016-03/01/2017
Identifying new drug targets and assessing drug efficacy and safety with systems pharmacology
This project will have three parts: (1) side effect prediction of Genentech small molecules administered as a single agent; (2) side effect prediction and data-driven dose selection of Genentech small molecules administered in combination; (3) identification of genetic signatures of drug response and new indications for Genentech drugs.
Role: PI

P50 MH094267 (PI: Altman) NIH/University of Chicago / Subcontract 09/22/11 – 10/31/16
Conte Center for Computational Systems Genomics of Neuropsychiatric Phenotypes
The goal is to consolidate in a single modeling framework a number of disparate approaches for analysis of complex neuropsychiatric disorders.

U10 HL105198 (Co-PI: Altman) NIH/University of Maryland, Baltimore / Subcontract 8/30/2011 – 8/31/2016
Pharmacogenomics of Anti-platelet Intervention-2 (PAPI-2) Study
The overall goal of the TPP is to operationalize the work of the PGRN Clinical Pharmacogenomics Implementation Committee (CPIC) by translating widely accepted actionable pharmacogenetic discoveries into real-world clinical practice.