Why you should care about statistics

Jeff Leek

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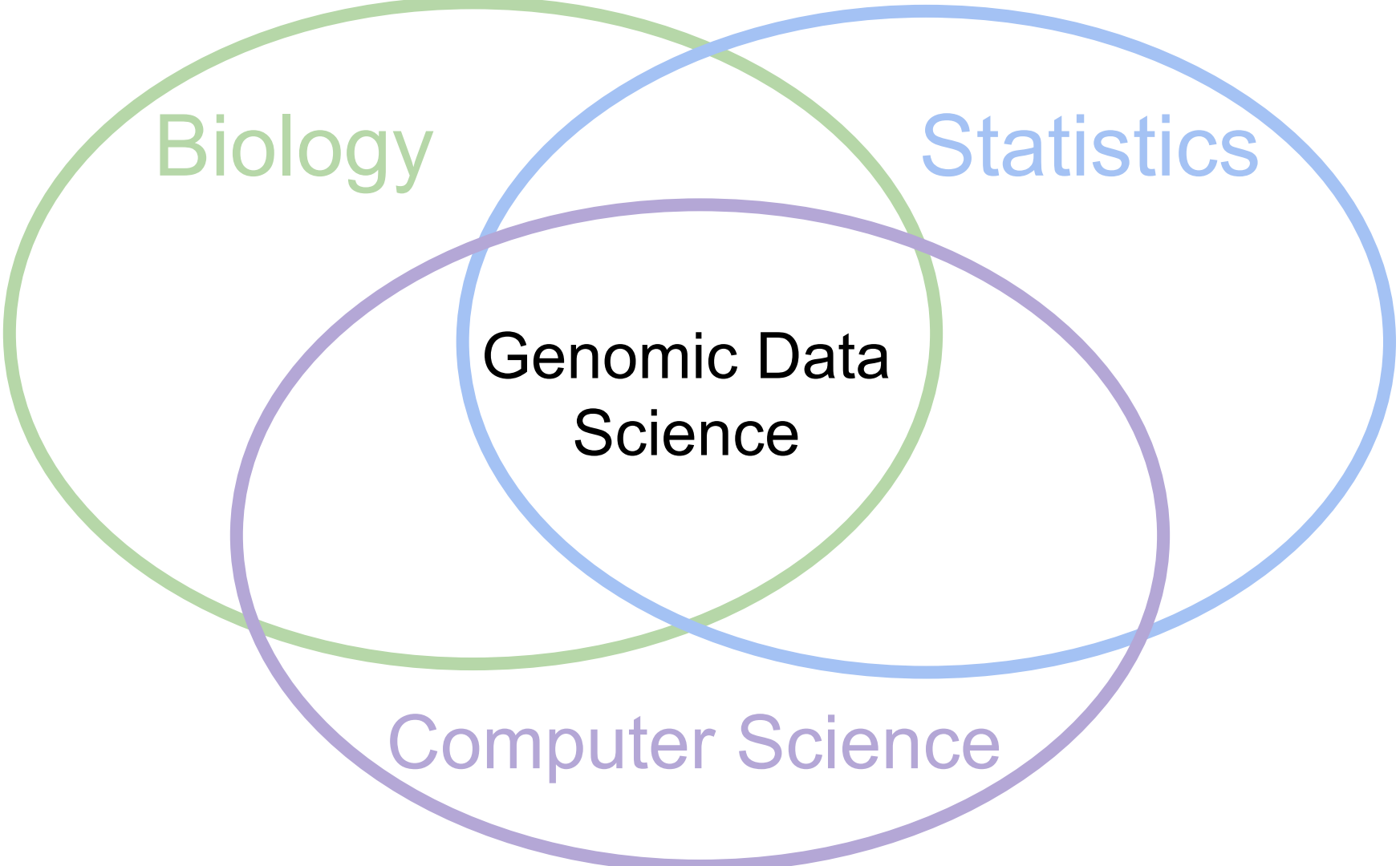
Intersection of three disciplines

- biology
- statistics
- computer science


Biology
Statistics
Genomic Data Science
Computer Science

Seems like an exciting result!

Genomic signatures to guide the use of chemotherapeutics

Anil Potti[1,2], Holly K Dressman[1,3], Andrea Bild[1,3], Richard F Riedel[1,2], Gina Chan[4], Robyn Sayer[4], Janiel Cragun[4], Hope Cottrill[4], Michael J Kelley[2], Rebecca Petersen[5], David Harpole[5], Jeffrey Marks[5], Andrew Berchuck[1,6], Geoffrey S Ginsburg[1,2], Phillip Febbo[1,2,3], Johnathan Lancaster[4] & Joseph R Nevins[1,2,3]

Using *in vitro* drug sensitivity data coupled with Affymetrix microarray data, we developed gene expression signatures that predict sensitivity to individual chemotherapeutic drugs. Each signature was validated with response data from an independent set of cell line studies. We further show that many of these signatures can accurately predict clinical response in individuals treated with these drugs. Notably, signatures developed to predict response to individual agents, when combined, could also predict response to multidrug regimens. Finally, we integrated the chemotherapy response signatures with signatures of oncogenic pathway deregulation to identify new therapeutic strategies that make use of all available drugs. The development of gene expression profiles that can predict response to

image credits:
http://en.wikipedia.org/wiki/Protein
http://en.wikipedia.org/wiki/Genetic_code

Major problems in the analysis

DERIVING CHEMOSENSITIVITY FROM CELL LINES: FORENSIC BIOINFORMATICS AND REPRODUCIBLE RESEARCH IN HIGH-THROUGHPUT BIOLOGY

By Keith A. Baggerly* and Kevin R. Coombes†

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High-throughput biological assays such as microarrays let us ask very detailed questions about how diseases operate, and promise to let us personalize therapy. Data processing, however, is often not described well enough to allow for exact reproduction of the results, leading to exercises in "forensic bioinformatics" where aspects of raw data and reported results are used to infer what methods must have been employed. Unfortunately, poor documentation can shift from an inconvenience to an active danger when it obscures not just methods but errors. In this report, we examine several related papers purporting to use microarray-based signatures of drug sensitivity derived from cell lines to predict patient response. Patients in clinical trials are currently being allocated to treatment arms on the basis of these results. However, we show in five case studies that the results incorporate several simple errors that may be putting patients at risk. One theme that emerges is that the most common errors are simple (e.g., row or column offsets); conversely, it is our experience that the most simple errors are common. We then discuss steps we are taking to avoid such errors in our own investigations.

Annals of Applied Statistics

An ongoing saga

NORTH CAROLINA DURHAM COUNTY	IN THE GENERAL COURT OF JUSTICE SUPERIOR COURT DIVISION 11 CVS 4727

Richard Aiken, Jean K. Carroll, Executrix of the Estate of Harold G. Carroll, Jean K. Carroll, Individually, Peggy Cox, as Administratrix of the Estate of Paul F. Cox, Peggy Cox, Individually, Helene L. Fligel, Jason Gannon, as Personal Representative of the Estate of Jennifer L. Gannon, John Haddock, as Executor of the Estate of Karen Heath, Walter Jacobs, as Executor of the Estate of Juliet J. Jacobs, Walter Jacobs, Individually, Polly Johnson, as Executor of the Estate of Malcom W. Johnson, and Polly Johnson, Individually,

Plaintiffs

vs.

COMPLAINT
(JURY TRIAL DEMANDED)

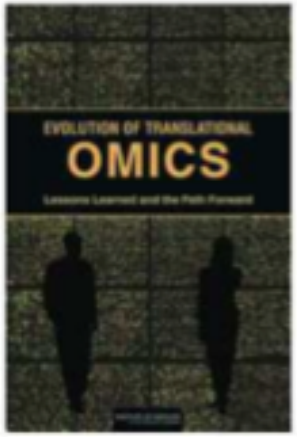
This situation spurred an IOM report

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Advising the nation • Improving health

For more information visit www.iom.edu/translationalomics

Evolution of Translational Omics

Lessons Learned and the Path Forward



Sequencing the human genome opened a new era in biomedical science. Researchers have begun to untangle the complex roles of biology and genetics in specific diseases, and now better understand why particular therapies do or do not work in individual patients. New technologies have made it feasible to measure an enormous number of molecules within a tissue or cell; for example, genomics investigates thousands of DNA sequences, and proteomics examines large numbers of proteins. Collectively, these technologies are referred to as *omics*.

Caring about statistics

Abstract

Background

Many groups, including our own, have proposed the use of DNA methylation profiles as biomarkers for various disease states. While much research has been done identifying DNA methylation signatures in cancer vs. normal etc., we still lack sufficient knowledge of the role that differential methylation plays during normal cellular differentiation and tissue specification. We also need thorough, genome level studies to determine the meaning of methylation of individual CpG dinucleotides in terms of gene expression.

Results

In this study, we have used (insert statistical method here) to compile unique DNA methylation signatures from normal human heart, lung, and kidney using the Illumina Infinium 27 K methylation arraysand compared those to gene expression by RNA sequencing. We have identified unique signatures of global DNA methylation for human heart, kidney and liver, and showed that DNA methylation data can be used to correctly classify various tissues. It indicates that DNA methylation reflects tissue specificity and may play an important role in tissue differentiation. The integrative analysis of methylation and RNA-Seq data showed that gene methylation and its transcriptional levels were comprehensively correlated. The location of methylation markers in terms of distance to transcription start site and CpG island showed no effects on the regulation of gene expression by DNA methylation in normal tissues.

RELEVANT TO RESEARCH IN YEAR

	FIELD	NOTEWORTHY APPLICATIONS
1983	**Artificial Intelligence**	machine learning, natural language processing, vision, mathematical models of cognition and learning
	Chemistry	chemical and biomolecular engineering
	Computational Science	computational fluid mechanics, computational materials sciences
	Earth and Planetary Science	climate modeling, seismology, geographic information systems
	Marketing	online advertising, consumer behavior
	Physical Sciences	astronomy, particle physics, geophysics, space sciences
	Signal Processing	compressed sensing, inverse imagining
	Statistics	
2013	**Biology**	genomics, proteomics, ecoinformatics, computational cell biology
	Economics	macroeconomic policy, taxation, labor economics, microeconomics, finance, real estate
	Engineering	sensor networks (traffic control, energy-efficient buildings, brain-machine interface)
	Environmental Sciences	deforestation, climate change, impacts of pollution
	Humanities	digital humanities, archeology, land use, cultural geography, cultural heritage
	Law	privacy, security, forensics, drug/human/CBRNe trafficking, criminal justice, incarceration, judicial decision making, corporate law
	Linguistics	historical linguistics, corpus linguistics, psycholinguistics,