Genomics @ BSPH
Applications

• Gene expression
• Genome-wide Association Studies (GWAS)
• Gene Regulation
• Epigenetics
• Comparative Genomics
Example of Papers


More than 40 collaborative papers in 2007 and 2008
Grants

• Novel Statistical Methods for Gene-Environment Interactions in Complex Diseases PI: Kung-Yee and Ingo (with Ciprian and Tom)
• Hierarchical Models in Health Services Research PI: Tom (with Ingo)
• Software for the Statistical Analysis of Microarray. PI: Rafa
• Preprocessing and Analysis Tools for Contemporary Microarray Applications PI: Rafa (with Ingo, Ciprian, and Hongkai)

Collaborative
• Bioconductor: An Open Computing Resource for Genomics PI: Robert Gentleman
• Center for the Epigenetics of Common Human Diseases PI: Andrew Feinberg
• Genetic study of schizophrenia and bipolar PI: Ann Pulver
• Genetic study of obsessive and compulsive disorder (OCD) PI: Gerry Nestadt
• International genetic study of oral cleft PI: Terri Beaty
• Institute for Clinical and Translational Research. PI: Daniel Ford
• Genome-Wide Association Studies of Asthma In Populations Of African Descent PI: Kathleen Barnes
• DNA Repair, Skin Cancer and Overall Cancer Risk PI: Anthony Alberg
• Genotypic Determinants of Aspirin Response in High Risk Families PI: Lewis Becker

Provost Initiatives
• Nucleating a discipline: Creating leadership in bioinformatics and computational biology PI: Sarah Wheelan
• The Johns Hopkins Individualized Medicine Program. PI: David Valle
Three examples

- Genome-wide Association Studies
- Epigenetics
- Gene Regulation
Genotyping and Association Measures
Affymetrix SNP chip terminology

Genomic DNA:
TACATAGCCATCGGTANGTACTCAATGATGATA

PM probe for Allele A:
ATCGGTAGCCATT\text{CATGAGTTACTA}

PM probe for Allele B:
ATCGGTAGCCATC\text{CATGAGTTACTA}

Genotyping: answering the question about the two copies of the chromosome on which the SNP is located:

Is a person \text{AA, AG or GG} at this Single Nucleotide Polymorphism?
Varying confidence
Methylation
Differential Methylation

Genes

Location

chr10

brain: normal
liver: normal
spleen: normal

M

2.5

1.5

0.5

0.5

-1

25280400
25280800
25281200
25281600

PRTFDC1
Statistics & Gene Regulation
From science to statistics
An example: gene regulation

Transcription factors
Other genes
Activation
Repression
Other Interactions
Biologists: we have a powerful technology, but ...
Statisticians: let us try

Statisticians: we can go further

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GTATGTACTTACCTATGGGTGGTCTACAATCTATGTATGA
TAACATGTGACTCTATAACCTCTTGGGTGGTACATGAA
CTGGGAGGTCTCGGTTCAGAGTCACAGTAGCAGATAATCA
TTAGAGGCAACAATTGCTTTGGTGGTGCAACAAAAAACAG
AACAGCCTTTGGATATTAGCTGCTGGGGGGTGAAGTGTCAC
ATCAGAATTGGGTGGTCTCATACTCCCCAAGAGAGGATAG
```

Joint posterior probability of unknown parameters is:

\[
f(W, \Theta, A, B, R, t, D, N_0 | S, \theta_0) \propto \pi(\theta, t, D, N_0) \pi(q) \pi(W) \pi(\Theta | W)
\]

\[
f(B, R | q) f(A | B, R, \lambda) f(S | W, \Theta, \theta_0, A, B, R)
\]

\[
\propto \exp\left(-\frac{1}{\tau_0}\right) \int_{\mu_0}^1 \int_{\mu_0}^1 \prod_{k=1}^{\lambda} q_0^{(B|R)} r_0^{(\lambda)} \prod_{n=0}^{P(A)} \int_{d_1(B, R, \lambda)}^{d_2(B, R, \lambda)} \theta_0^{(A|\lambda)} \prod_{k=1}^{\lambda} \frac{\Gamma(\theta_k)}{\Gamma(\theta_0)}
\]

Integrate out \( \Theta \) and \( q \):

\[
f(W, A, B, R, \delta, t, D, N_0 | S, \theta_0) \propto \exp\left(-\frac{1}{\tau_1}\right) \prod_{n=0}^{P(A)} \int_{d_1(B, R, \lambda)}^{d_2(B, R, \lambda)} \Gamma(\theta_k) + \alpha_0 \prod_{k=1}^{\lambda} \Gamma(\theta_k + \alpha_0) \prod_{n=0}^{P(A)} \Gamma(\theta_n + \alpha_n)
\]

\[
\frac{\theta_0^{(A|\lambda)}}{\prod_{k=1}^{\lambda} \frac{\Gamma(\theta_k)}{\Gamma(\theta_0)}} \prod_{n=0}^{P(A)} \frac{\Gamma(\theta_n)}{\Gamma(\theta_0)} \Gamma(\Gamma(\theta_k) + \alpha_0) \prod_{k=1}^{\lambda} \Gamma(\theta_k + \alpha_0) \prod_{n=0}^{P(A)} \Gamma(\theta_n + \alpha_n)
\]
Folks: let us take advantage of our local expertise
How to define ourselves?

In the field of functional genomics,

• Perhaps it is not enough to define ourselves only as statisticians.

• We are an integral part of scientific community and we should also see our role in driving the development of science.