Genomics of Cultured Species: From Discovery to Mechanism

Plant and Animal Genome

January 13 2012
Contributors

• Molecular Biology
  – AnnaLaura Mancia
  – Marion Beal
  – Megan Peck
  – Sonomi Hikima
  – Greg Warr
  – Paul Gross
  – Artur Veloso
  – Chris Johns
  – Greg Warr

• Physiology
  – Brett Macey
  – Karen Burnett
  – Lou Burnett
  – Charles K. Rathburn

• Computers
  – Hal Trent
  – David McKillen
  – Stephen Ficklin
  – Meg Stanton
  – Eddie Duffy

• Mathematicians
  – Jonas Almeida
  – Eberhart Voit
  – Matt Cook

• Ecology
  – Fred Holland
  – Denise Sanger
  – Ann Blair
  – Guy DiDonato
Where We Are Going Today

- Impacts of Development on Oysters in Tidal Creeks
- Impacts of Environmental Conditions (physical and chemical) on Oysters
- Impacts of Environmental Conditions and Disease on Oysters
The Problem

- Given 15,000 genes on a microarray, find a set (size unknown) that is an optimal solution (maps to) for an output state.
- Verifying that a given set “fits” the output is easy
- Finding the optimal set(s) is impractical-
My Bias

- The transcriptome is a dynamically interacting network and nothing is ‘independent’
- Hence linear analysis tools such as ANOVA’s are not appropriate
HIDDEN NODES
Run 10 ANN models using all genes.

Compute Sensitivities

Select top 250 genes,

Randomly remove 10% of the individuals

Run 20 ANN models on 90% of the individuals 250 genes

Compute model $R^2$

Model Cross Validation

ROC Curves
Let’s map Gene Expression to Individual Environmental Conditions (physical and chemical)

Then Reverse the Logic and Map Environmental Conditions to Individual Genes
Genes

Environmental parameters
R-squares

Gill

Hepatopancreas
Genes

Environmental parameters
Collective behavior of genes can predict water quality in both gill and hepatopancreas with some precision. Collective behavior of water quality parameters are much less successful in predicting expression levels of individual genes. This implies that the value of transcriptomic data is not in expression of individual genes, but rather their collective behavior—this behavior cannot be extracted from ANOVA.
Focal Adhesion Complex

Akrit Sodhi, Silvia Montaner and J. Silvio Gutkind
Nature Reviews Molecular Cell Biology 5, 998-1012 (December 2004)
ER stress proteins → eIF2α kinase → P-eIF2α → Translation arrest
DNA damage  Hypoxia  rNTP depletion  Spindle damage

ATM  CHK1  CHK2  p19ARF

p53  mdm2

Active p53

Angiogenesis  Growth Arrest  DNA Repair  Apoptosis

Thierry Soussi p53.free.fr/p53_info/ p53_Pathways.html
Differentiated tissues

+O₂ (Glucose) → Pyruvate → CO₂
-0₂ (Glucose) → Pyruvate → Alanine, Succinate Octopine

Anaerobic Glycolysis
2 moles ATP

Oxidative Phosphorylation
36 moles ATP

Proliferative tissues

+-0₂ (Glucose) → Pyruvate → CO₂

85%

Alanine, Succinate Octopine

Aerobic Glycolysis
4 moles ATP
The transcriptome is saying that development and climate change should impact

Metabolic processes
The generation of lipids, amino acids etc needed for growth
Growth rates
Reproduction
Biomineralization

Does it???
The Impact of *Perkinsus* and Environmental Conditions in the Gulf of Mexico
An attempt to find more in the data using PCA. Are the two groups in all locales surveyed. Boys and girls? - OOPS
Average R-squares and sensitivity of individual genes, N=558

Mapping Environmental variables, Perkinsus Gene Expression and Oyster Genotypes to Individual Oyster Gene Expression
How do you know Perkinsus gene expression is related to infection?

I got data from Shaolin Wang which has 23 Perkinsus genes and RFTM scores from Ximing Guo. Mapping Perkinsus gene expression to RFTM data generates an Model $R^2 = 1.0$, $Cv R^2=1.0$. 
Shaolin’s data: Mapping Perkinsus gene expression to 1462 Oyster genes

Senescence Protein is a deacetylase for p53 promoting its up regulation
We cannot ignore the disease status when working with oysters

I wonder how much misleading or incomplete information is out there with the title

‘Response of Oysters to Environmental ............’

‘Temperature and Salinity Effects on Oyster ..........’
Modified Modularity Clustering
Finding Genes that Co-Vary in GOM study

http://mmc.gnets.ncsu.edu/

Cytoscape connections of the modules
Cytoscape connection of individual genes within all modules, \( r^2 \geq 0.5 \)

Module 3
Module 3
Mainly microtubule associated and cellular trafficking
Predictive behavior from Ann models-All models are wrong, some models are useful
How do you know the transition to an alternative Transcriptomic state is due to Oyster genes and not Perkinsus genes?
No obvious separation within populations and certainly nothing that correlates with the oyster PCA—hence the transition is not due to levels of Perkinsus gene expression.
Why I made a point of the rapid transition. If the transcriptomic transitions were not steep and concerted, then we would not see clusters in PCA.
Southern oyster populations do not suffer declines as a result of Perkinsus infection even though 100% are infected. These oysters are intertidal and routinely experience temperatures above 40°C during low tides in the summer. If the GOM data can be taken at face value, it implies that somewhere around 32°C Perkinsus becomes inactive. It isn’t that southern oysters are immune to Perkinsus, but rather the environment provides a high temperature thermal refuge.