Understanding Human Development through Gene Expression

DGEMap
Developmental Gene Expression Map

www.dgemap.org

The Story

The goal is to understand human development. The story starts with wet-lab experiments. To reach the goal many other research components are required. Some of these are illustrated here. Developing a deep understanding will require many cycles of hypothesis, analyse and test to reach the goal of a predictive theory of development. This will demand development and integration of biological, physical, chemical, computational, and mathematical science; biomedical research must embrace all these scientific diciplines. The key is integration at all levels: data, computational, and people. This is the challenge for e-Science.

The project

DGEMap is a FP6/EU-funded design study that aims to deliver a design for a pan-European infrastructure to support gene expression studies in early human development. This design requires detailed analysis and of the biological experiments, the data mapping and curation, the interoperability environment and data integration with in this case an analysis of the ethical basis for the research.
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Team

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Publications

J.I. van Hemert and R.A. Baldock. Mining spatial gene expression data for association rules. 1st International Conference on Bioinformatics Research and Development (2007) in press.

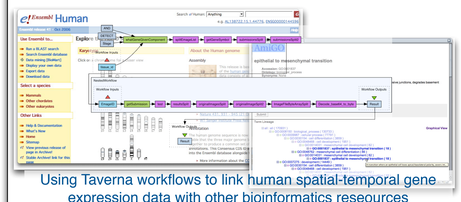
J.H. Christiansen, Y. Yang, S. Venkataraman, L. Richardson, P. Stevenson, N. Burton, R.A. Baldock and D.R. Davidson. EMAGE: a spatial database of gene expression patterns during mouse embryo development. Nucl. Acids Res. 34 (2006): D637.

S. Lindsay, S. Sarma, M. Martínez-de-la-Torre, J. Kerwin, M. Scott, J. Luis Ferran, R.A. Baldock and L. Puelles. Anatomical and gene expression mapping of the ventral pallium in a 3-dimensional model of developing human brain. Neuroscience (2005), 136, p625-632.

J. Kerwin, M. Scott, J. Sharpe, L. Puelles, S. C Robson, M. Martinez-de-la-Torre, J. Luis Ferran, G. Feng, R.A. Baldock, T. Strachan, D.R. Davidson, S. Lindsay, 3 dimensional modelling of early human brain development using optical projection tomography, BMC Neuroscience 5 (2004) p27.

Biological Understanding

Bioinformatics & Ontologies



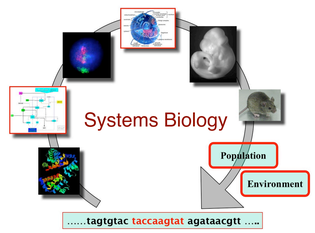
Using Taverna workflows to link human spatial-temporal gene expression data with other bioinformatics reseources

Integrative Biology

?

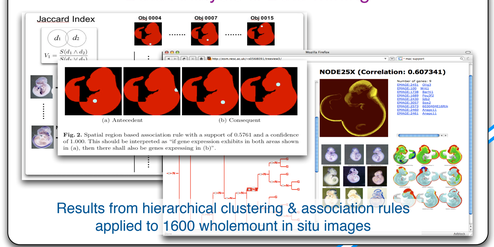
Identify and model the outcomes of gene expression networks, eg on growth or differentiation in specific developing tissues

Full Biological Understanding



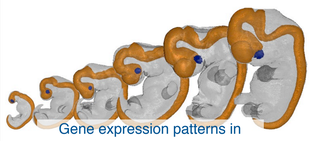
From DNA to cells, to the whole organism, to population and environments, back to DNA

Data Analysis & Data Mining



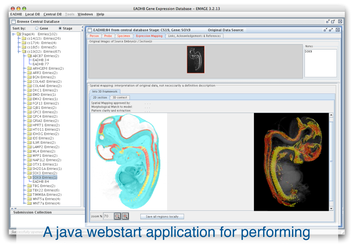
Results from hierarchical clustering & association rules applied to 1600 wholemount in situ images

Computational Modelling



Gene expression patterns in successive developmental stages

Gene Expression Database



A java webstart application for performing spatial queries on gene expression patterns

Data Integration

- Delivery models
- Security models
- Distributed query processing
- Data descriptions
- Schema integration
- Meta-data handling

OGSA-DAI

Brain Atlas

FieldName01	*Description01*
FieldName02	*Description02*
FieldName03	*Description03*
FieldName04	*Description04*
FieldName05	*Description05*

Ensembl

FieldName01	*Description01*
FieldName02	*Description02*
FieldName03	*Description03*
FieldName04	*Description04*
FieldName05	*Description05*

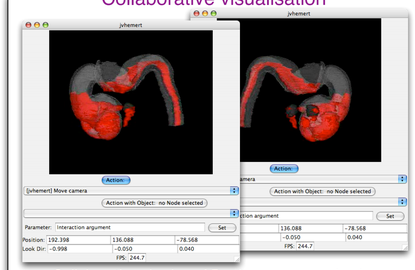
Genes

HHIP	*Description01*
SHH	*Description02*
BMP2	*Description03*
BMP4	*Description04*
BMP7	*Description05*
WNT3	
WNT5A	
WNT8A	
WNT8B	
WNT2B	

Anatomy

Heart	*Description01*
Trunk	*Description02*
Brain	*Description03*
Eye	*Description04*
Limb	*Description05*

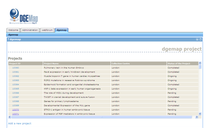
Collaborative visualisation



Collaborative viewing of Pax6 gene expression in a human embryo using the RAVE system from WeSC

To understand how genes affect human development, in situ hybridisation is performed to locate the spatial regions genes are expressed in.

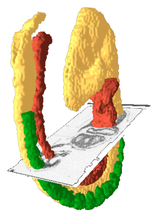
A unique resource of human embryos



An on-line repository for collaborative in-situ experiments on human tissue

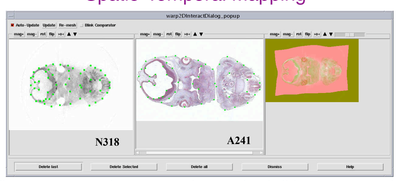
High throughput in situ hybridisation experiments

3D Reconstructions



Embryo reconstructed from individually stained sections

Spatio-Temporal Mapping



The gene expression patterns from stained slides are mapped on to 3D spatial-temporal models of human embryos

Research Components

Here we illustrate the research components that will be required to contribute to the ultimate goal of understanding the process of human development. Many contributions are unknown - how do we model the complex system of a developing embryo? What mathematical techniques can be applied? - ideas exist, but clear answers do not exist. Here we have organised components roughly according to biological and computation complexity. DGEMap aims to contribute to the design, development and integration of these components.

Information Technology Complexity

Newcastle University
The University of Edinburgh
National e-Science Centre
MRC Medical Research Council
Policy Ethics And Life Sciences