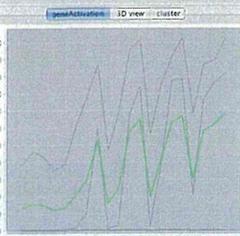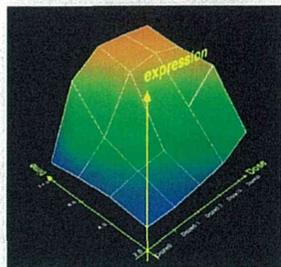# TCDF Cyp1a1 cytochrome P450
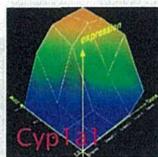
Cyp1a1 Cyp1a2 Aspm

Xenobiotic metabolism
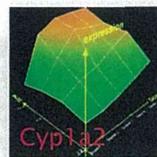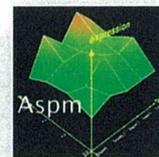
Abnormal Spindle-like, Microcephaly-associated cerebral cortical neurogenesis
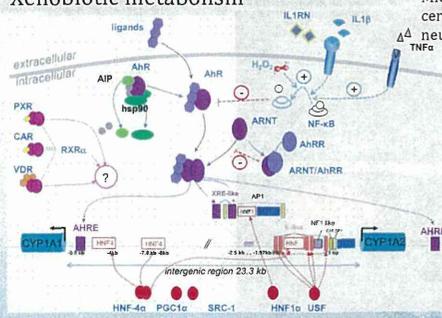
A xenobiotic is a chemical which is found in an organism but which is not normally produced or expected to be present in it. It can also cover substances which are present in much higher concentrations than are usual.

TCDF Abhd6 cluster
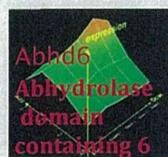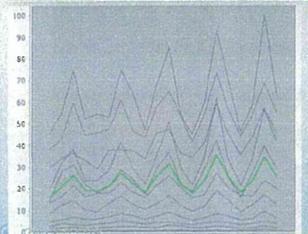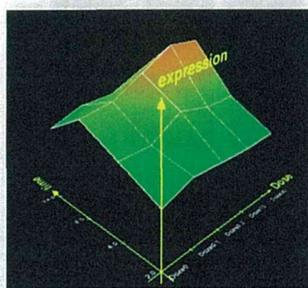
Abhd6 Abhydrolase domain containing 6
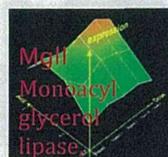
Mgll Monoacyl glycerol lipase
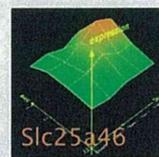
Slc25a46
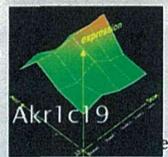
Akr1c19
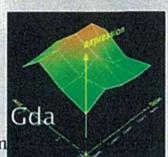
Gda
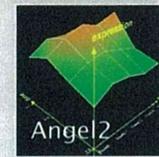
Angel2

Safb2
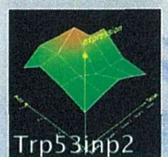
Trp53inp2
transformation related protein 53
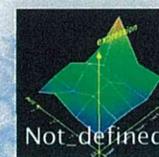
Not_defined

TCDF Slc46a3 cluster
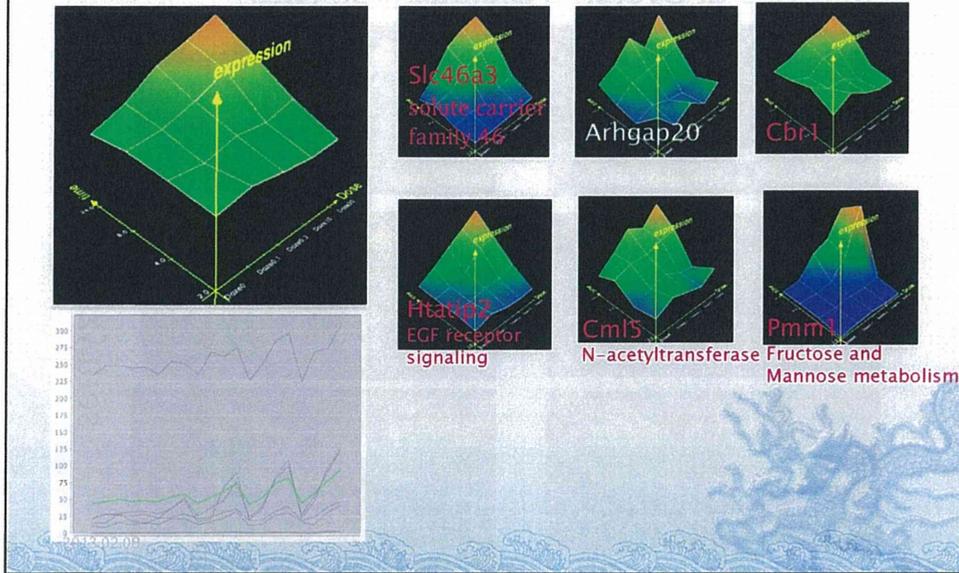
TCDF Ptplad1 cluster
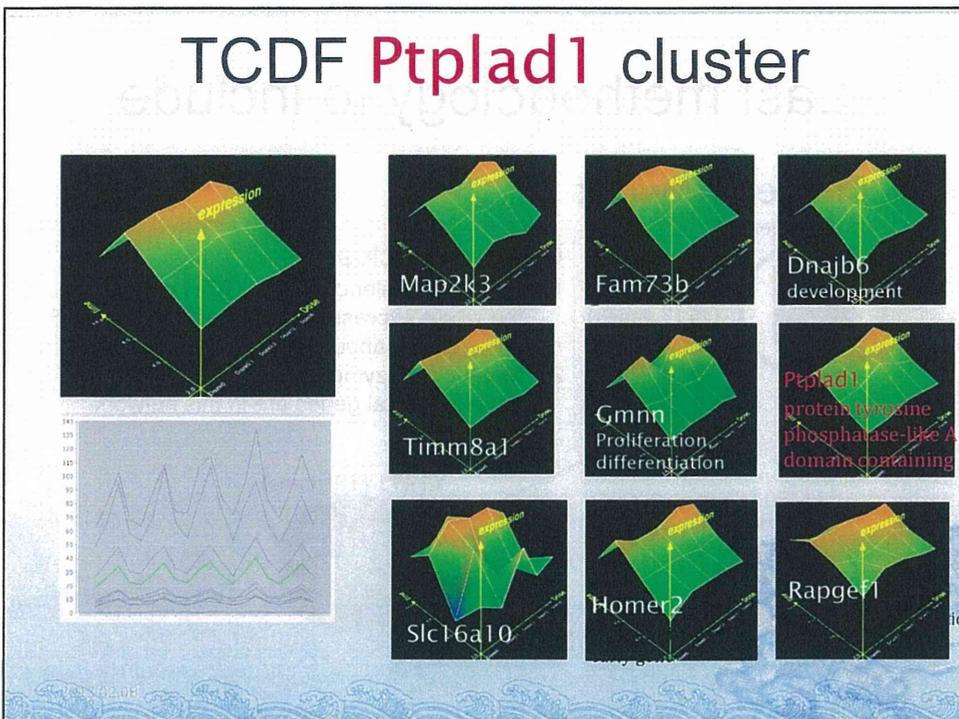
New genes shared regulated by TCDD
and TCDF chemicals (600) -> gene network
analysis at Systems Biology Inst. (SBI)

Rheb
Ras homolog enriched in brain

Coq10b
coenzyme Q10 homolog B

N4bp2
NEDD4 binding protein 2

Marveld1

Dnajb6
DnaJ homolog subfamily B member 6

Clpx caseinolytic peptidase X
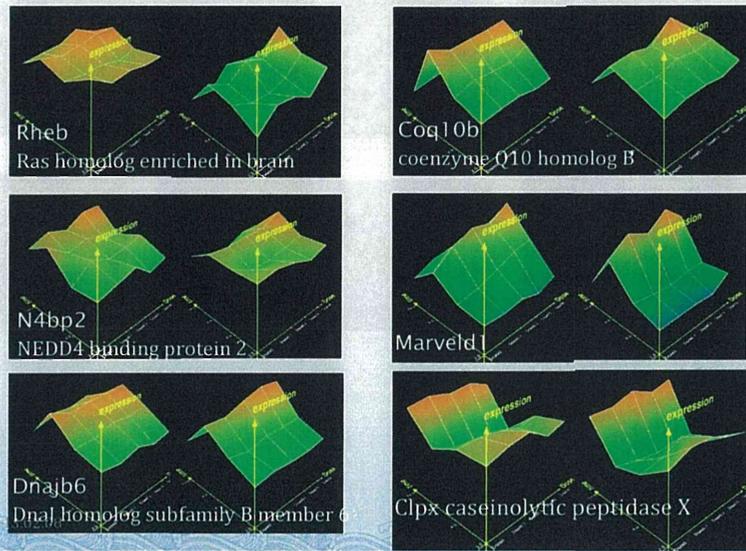
Metabolic enzymes

Last methodology to include

◈ Cluster network

Cl 3(5 genes)

Ahr

Cl5 (3 genes)

Cyp1a1

Cl250 (15 genes)

Dbp

Cl 471 (13 genes)

Current conclusions:
1. Toxicity Equivalency Factor (TEF) on
the whole expression profile of TCDD, TCDF
chemicals is about 3.
2. Metabolic enzymes, transcription factors,
developmental genes are in this network.

http://localhost:8080/AGCT_HP2/index.html

NEW!

AGCT A Geometric Clustering Tool

Spectral clustering Delaunay triangulation Principal component analysis Cluster expression profile

| Result and Demo | Downloads | FAQ |

Rise in quality and quantity of data being produced elevated demands towards the intelligence of the algorithms and their computational power. Tangibility and 3D visualization of data has become an indispensable feature of biological software, recently acquiring techniques from computer graphics/vision fields.

Systematic analysis of gene expression data demanding sophisticated tools based on solid mathematics and flexible control that can handle stochasticity, plasticity and modularity of genetic machine. Several gene clustering methods, such as, **Hierarchical** clustering (Eisen et al 1998), **K-means** clustering (Tavazoie et al 1999), **Self-Organizing Map (SOM)** (Tamayo et al 1999), **Affinity propagation**(Frey et al 2007) implemented in software tools such as GeneCluster, GenePattern, Arena3D, Mev4TM, Bioconductor, etc. are well known.

Ab initio discovery of causalities in high dimensional data without *a priori* knowledge of these causalities and powerful visualization of the results in an intuitive and interactive manner has become important at the current stage of progress in Biological Science.

(AGCT) A Gene *geometric* Clustering Tool is a benchmark for *ab initio* discovery of gene clusters where the problem of 'guess' is substituted with multiple optimization routines and the results of several algorithms can be seen at a glance. It works as a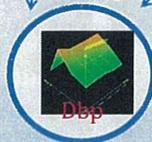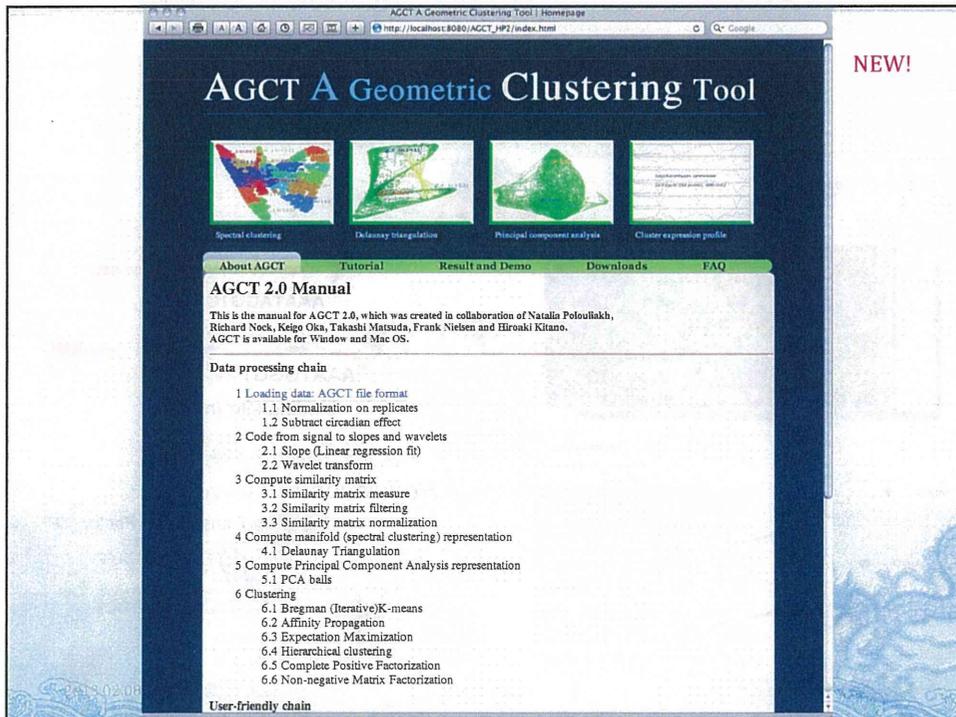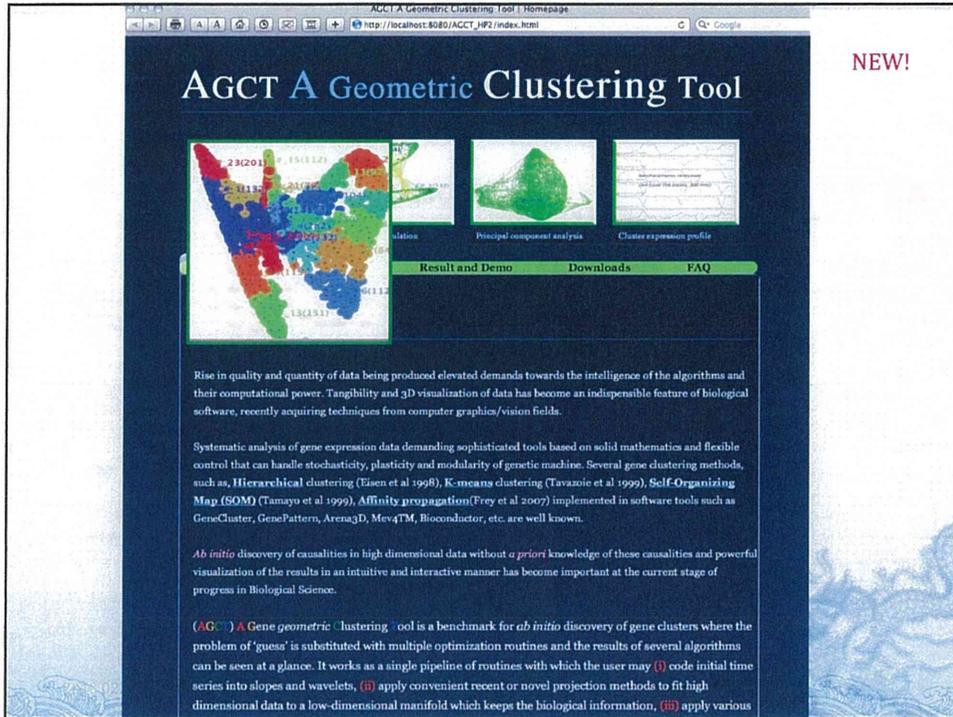 single pipeline of routines with which the user may (i) code initial time series into slopes and wavelets, (ii) apply convenient recent or novel projection methods to fit high dimensional data to a low-dimensional manifold which keeps the biological information, (iii) apply various

---

http://localhost:8080/AGCT_HP2/index.html

NEW!

AGCT A Geometric Clustering Tool

Spectral clustering Delaunay triangulation Principal component analysis Cluster expression profile

| About AGCT | Tutorial | Result and Demo | Downloads | FAQ |

AGCT 2.0 Manual

This is the manual for AGCT 2.0, which was created in collaboration of Natalia Polouliakh, Richard Nock, Keigo Oka, Takashi Matsuda, Frank Nielsen and Hiroaki Kitano.
AGCT is available for Window and Mac OS.

Data processing chain

1 Loading data: AGCT file format
    1.1 Normalization on replicates
    1.2 Subtract circadian effect
2 Code from signal to slopes and wavelets
    2.1 Slope (Linear regression fit)
    2.2 Wavelet transform
3 Compute similarity matrix
    3.1 Similarity matrix measure
    3.2 Similarity matrix filtering
    3.3 Similarity matrix normalization
4 Compute manifold (spectral clustering) representation
    4.1 Delaunay Triangulation
5 Compute Principal Component Analysis representation
    5.1 PCA balls
6 Clustering
    6.1 Bregman (Iterative)K-means
    6.2 Affinity Propagation
    6.3 Expectation Maximization
    6.4 Hierarchical clustering
    6.5 Complete Positive Factorization
    6.6 Non-negative Matrix Factorization

User-friendly chain

CellDesigner Plug-in

FROM CLUSTER TO TRANSCRIPTION REGULATION

Transcription regulation of clusters

gene a

AAAT**A**GGT**C**T

gene b

AAAT**G**GG**T**AT

binding site (motif)

Human, Mouse, Rat data

if Regulation conserved !!!

Transcription Factor (TF)

Evolutionary time scale (in millions of years ago, MYA) is approximate

ear

Promoter and Enhancer!

Negative Feedback Regulation Ensures the One Receptor-One Olfactory Neuron Rule in Mouse
Shou Serizawa *et al. Science 302, 2088 (2003);*

The homology (H) region that activates the MOR28 cluster.
(A) Structures of seven transgenic constructs are compared.
(B) MOR28 in each construct is shown as expressed (+) or not (−).
(C) Nucleotide sequences were compared between mouse and human for the upstream regulatory region.
A 2-kb homology (H) was identified (dot matrix) 75 kb upstream of MOR28.

Sequence HOmology in higher Eukaryotes
真核生物比較ゲノム解析ツール

Pic on SHOE by my friend K. Hamachi

スケッチ作家
京都市立芸術大学

Paris

Tsurugaoka Hachiman Jingu

1. AGCT is registered in Garuda.

2. Software A is loading file suitable for AGCT

Why software joins Garuda platform

- To develop an open & common software and data platform for biological and medical research
- Consistent GUI, APIs, and other development framework
- Provide a consistent user experience
- Enables efficient and quality software development
- Effective dissemination of tools and resources

Systems Toxicology
Inferring Gene Regulatory Networks from
Percellome Experimental Data

Takeshi Hase, Samik Ghosh, Hiroaki Kitano

The Systems Biology Institute

Application of Network Reconstruction Technique to Percellome

• Possible areas

- – How the gene interaction network changes over different dosage of the perturbation?
- – Build tissue specific gene networks
- – How network structure changes over time in a tissue for a specific dose of the perturbation