Local and "Personalised" Modeling and Knowledge Discovery in Bioinformatics: The Evolving Neuro-Fuzzy Approach

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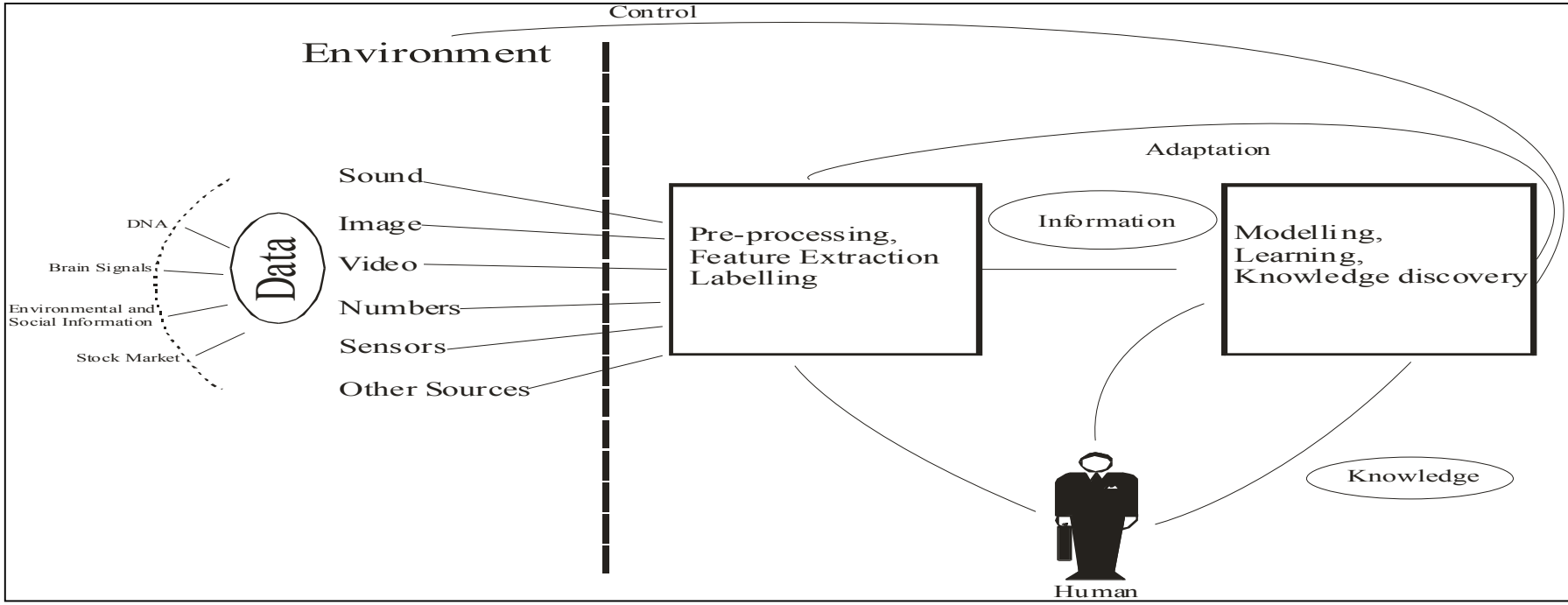
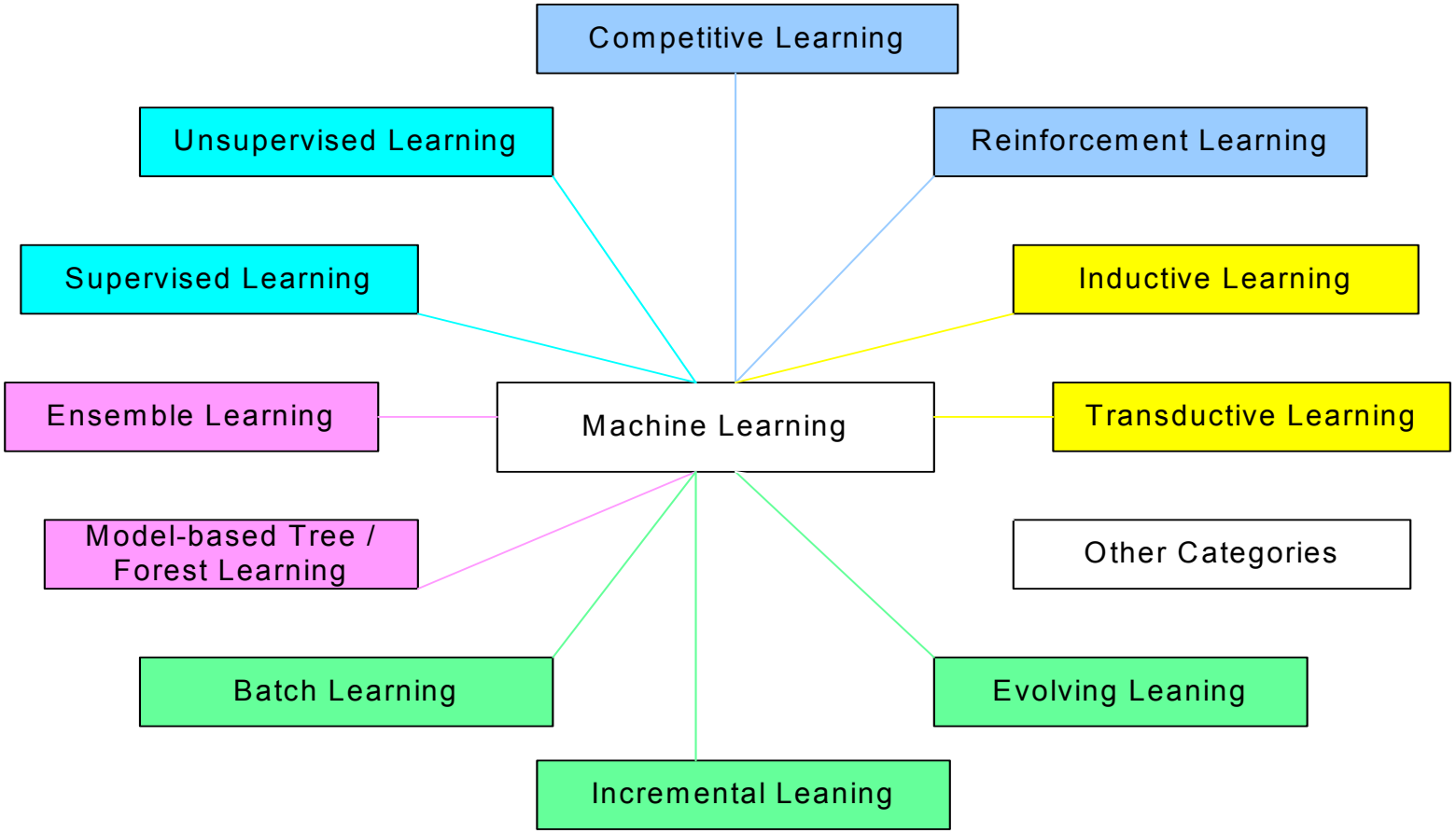
1. Global, local and personalised modelling: Problem definition



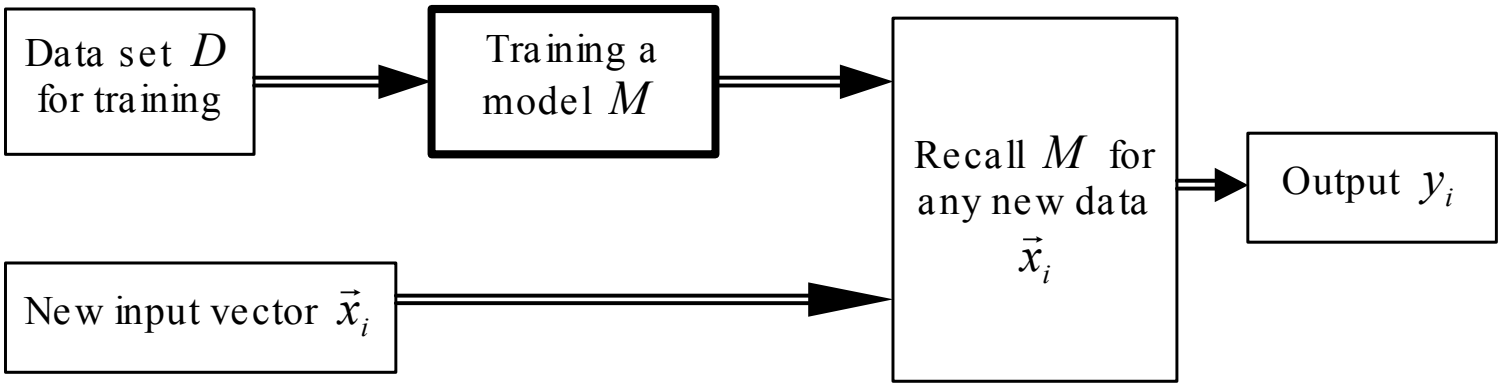
- Adaptive modelling of complex dynamic processes
- Incremental learning and improvement
- Extracting relationship rules, knowledge
- Facilitating discoveries across disciplines – Bioinformatics, Neuroinformatics, Health informatics, Industrial Informatics, Business, Environment

Machine learning algorithms



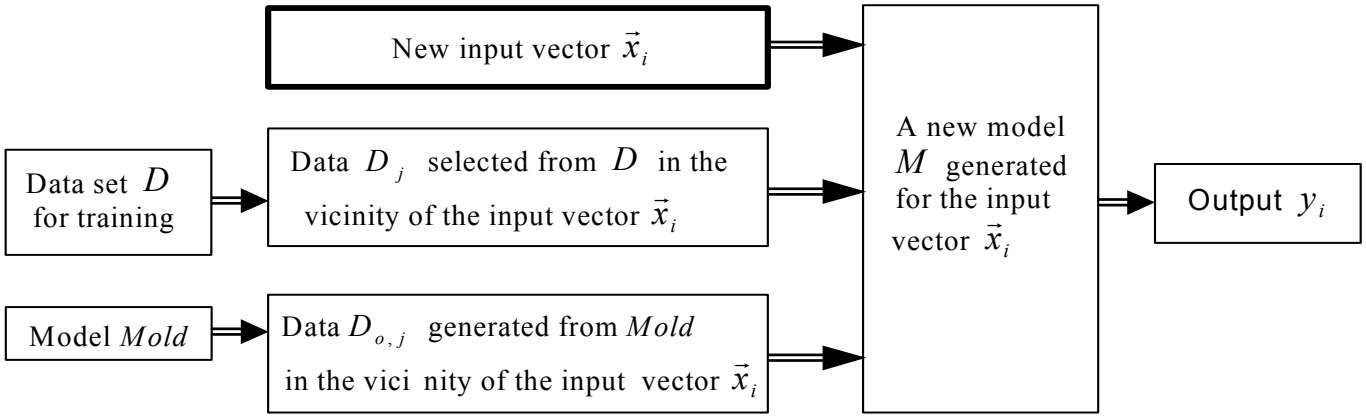
Inductive learning framework

- Inductive Learning extrapolates from a given set of examples so that we can make accurate predictions about future examples.
- Given a **training set** of positive and negative examples of a concept, construct a description that will accurately classify whether future examples are positive or negative. That is, learn some good estimate of function f given a training set {**(x1, y1), (x2, y2), ..., (xn, yn)**} where each **y*i*** is either + (positive) or - (negative).



Transductive learning framework

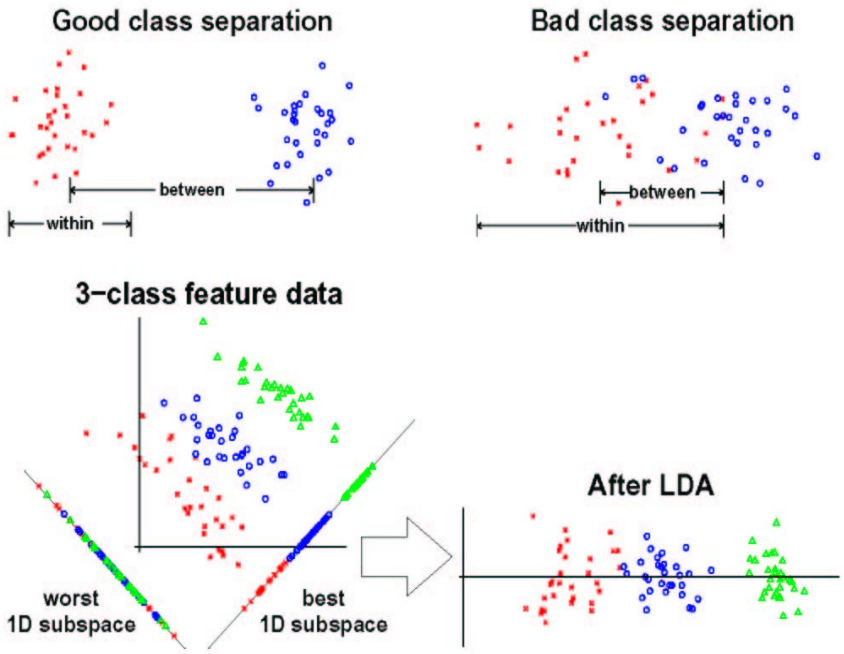
- Transductive learning is concerned with the estimation of a function in a single point of the space only. For every new input vector *xi,* a new model *Mi* is dynamically created from these samples to approximate the function in the locality of point *xi*
- Compared with inductive learning, transductive learning specially takes both labeled data and unlabeled data into account.
- Neuro-fuzzy method for transdictive learning (TWNFI, IEEE TrFS,2004)



Global Models - Statistical Methods

- Linear Discriminant Analysis (LDA)

- Find a linear subspace that maximises class separability among the feature vector projections in the data space.
- Popular separability criterion is ratio of between-class scatter and within-class scatter
- LDA seeks directions efficient for discrimination
- Regression analysis



Support Vector Machines

- The idea of support vector machine is to map the training data into higher dimensional feature space via kernel computation, and constructing a separating hyperplane with maximum margin there.
- The type of the kernel function defines the type of the model: global, or local.
- These kernel functions could be:
  - Polynomial functions

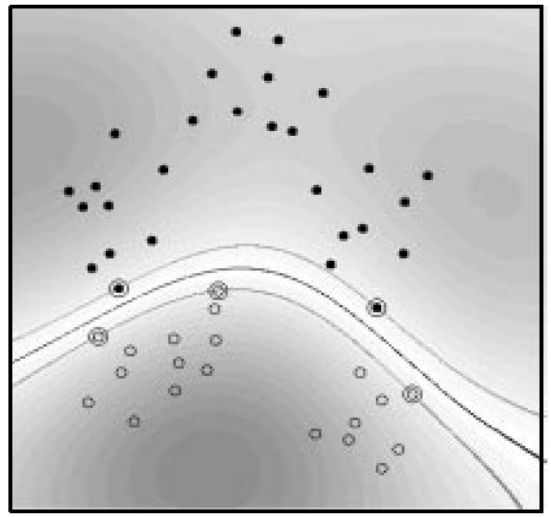
$$K(x_i, x_j) = (x_i \cdot x_j + 1)^d$$

  - Radial bas

$$K(x_i, x_j) = \exp\left(\frac{\|x_i - x_j\|^2}{2\sigma^2}\right)$$

  - Linea

$$K(x_i, x_j) = x_i \cdot x_j$$



Example of a SVM hyperplane

NeuCom: A software environment for data analysis, modeling and knowledge discovery

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Rule extraction

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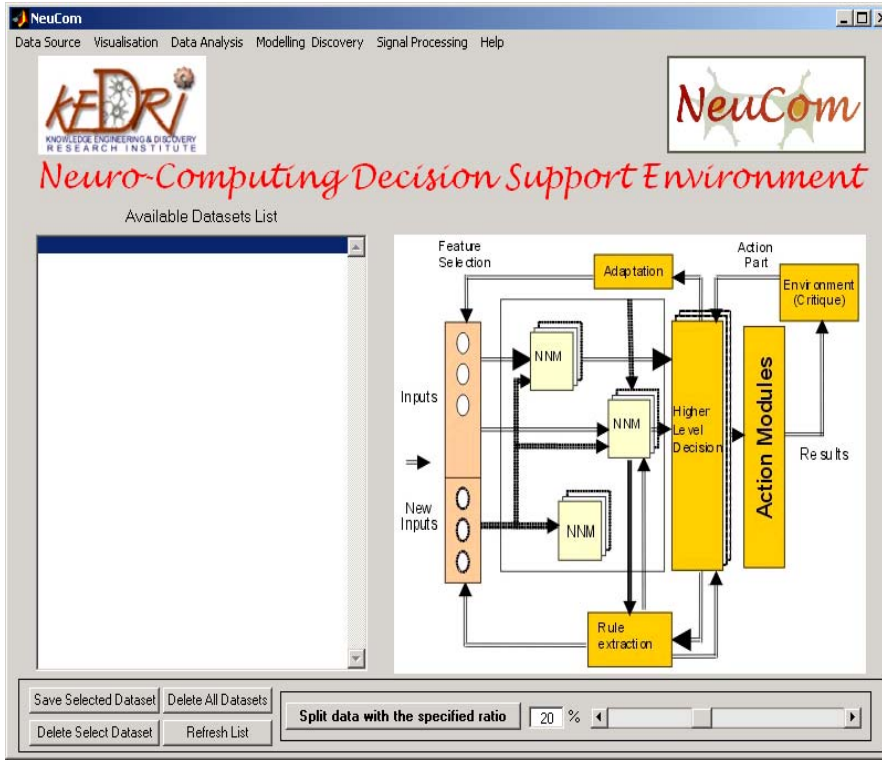
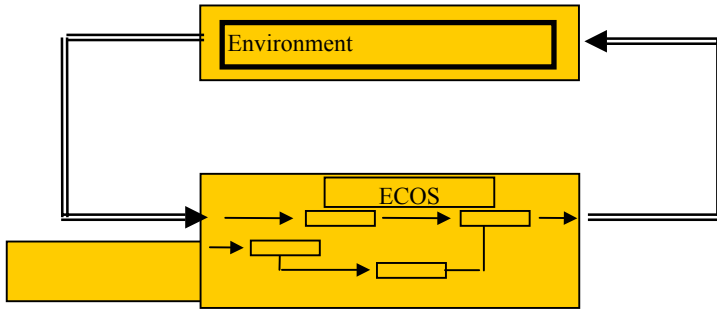


2. Local Learning in ECOS

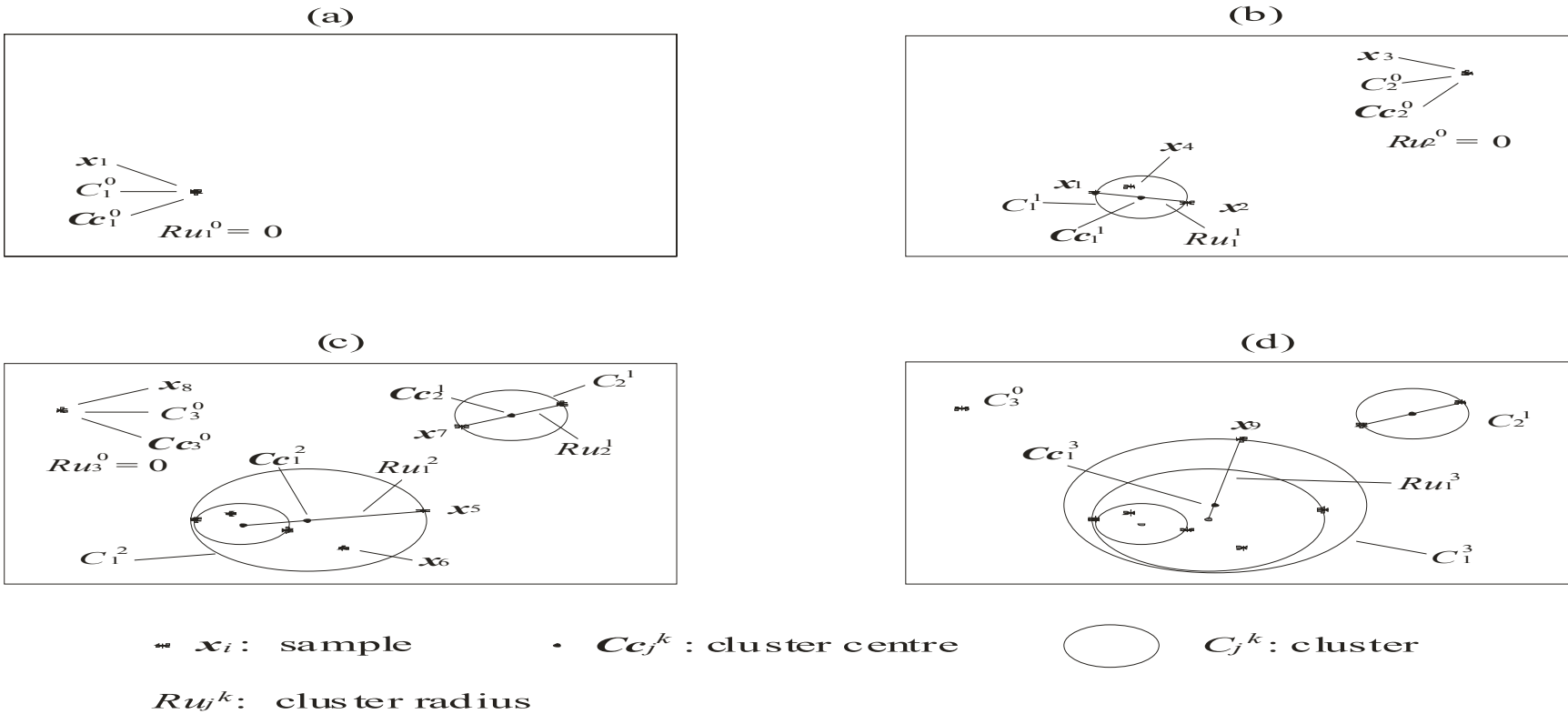
- Creating multiple local models in the problem space, all of them covering the whole space through inductive learning.

- Examples:
  - Local regressions
  - ECOS - modular connectionist-based systems that evolve their structure and functionality in a continuous, self-organised, on-line, adaptive, interactive way from incoming information; they can process both data and knowledge in a supervised and/or unsupervised way.
- N. Kasabov, Evolving connectionist systems – methods and applications in bio-informatics, brain study and intelligent machine, Springer Verlag, 2002

'*Throw the "chemicals" and let the system grow'* Prof. *Walter Freeman, UC at Berkeley.*



Local learning based on clustering of input (or input-output) vectors and learning local models

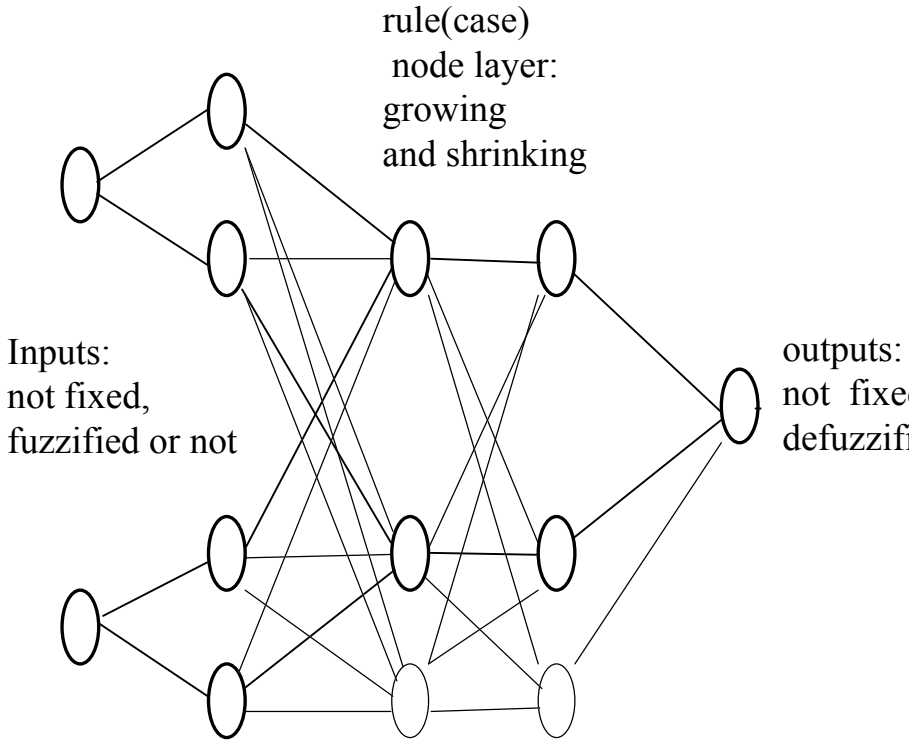


An evolving clustering process using ECM with consecutive examples x1 to x9 in a 2D space (Kasabov and Song, DENFIS, IEEE Tr FS, 2002)

Evolving Fuzzy Neural Network (EFuNN)

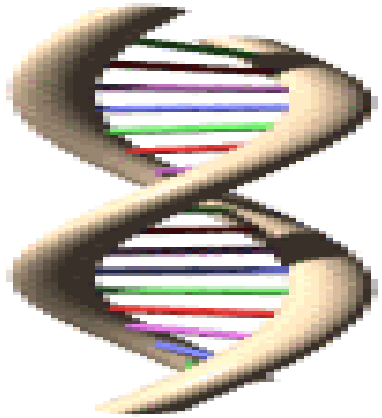
- Learning is based on clustering in the input space and a function estimation for this cluster
- Prototype rules represent the clusters and the functions associated with them
- Different types of rules: e.g. – Zadeh-Mamdani, or Takagi-Sugeno
- The system grows and shrinks in a continuous way
- Feed-forward and feedback connections (not shown)
- Fuzzy concepts may be used
- Not limited in number and types of inputs, outputs, nodes, connections
- On-line/off line training
- *ECF – evolving classifier function – a partial case of EFuNN – no output MF*

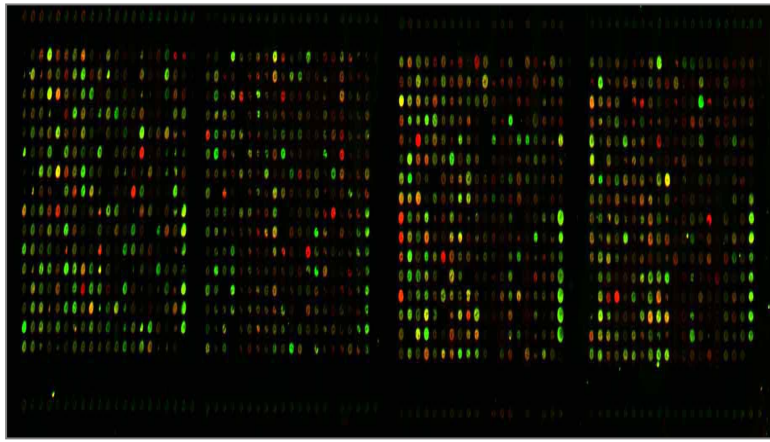
- N. Kasabov, IEEE Tr SMC, 2001,

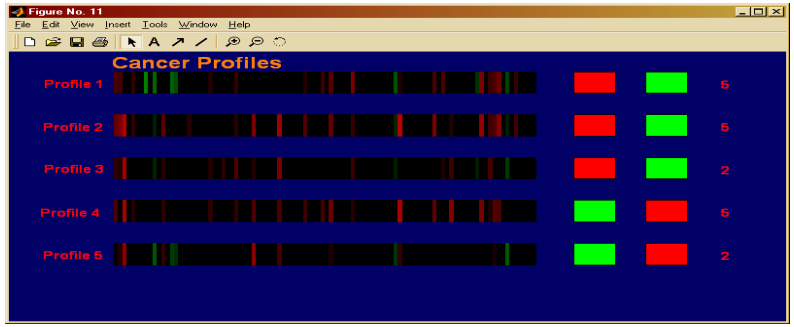


Gene Expression Data Analysis, Modellling and Profiling

- Problems:
  - large data bases;
  - data always being added and modified;
  - different sources of information
- Local models are suitable – each cluster is represented as a [rule = profile]
- Applications for markers and drug discoveries
- PEBL (www.peblnz.com)



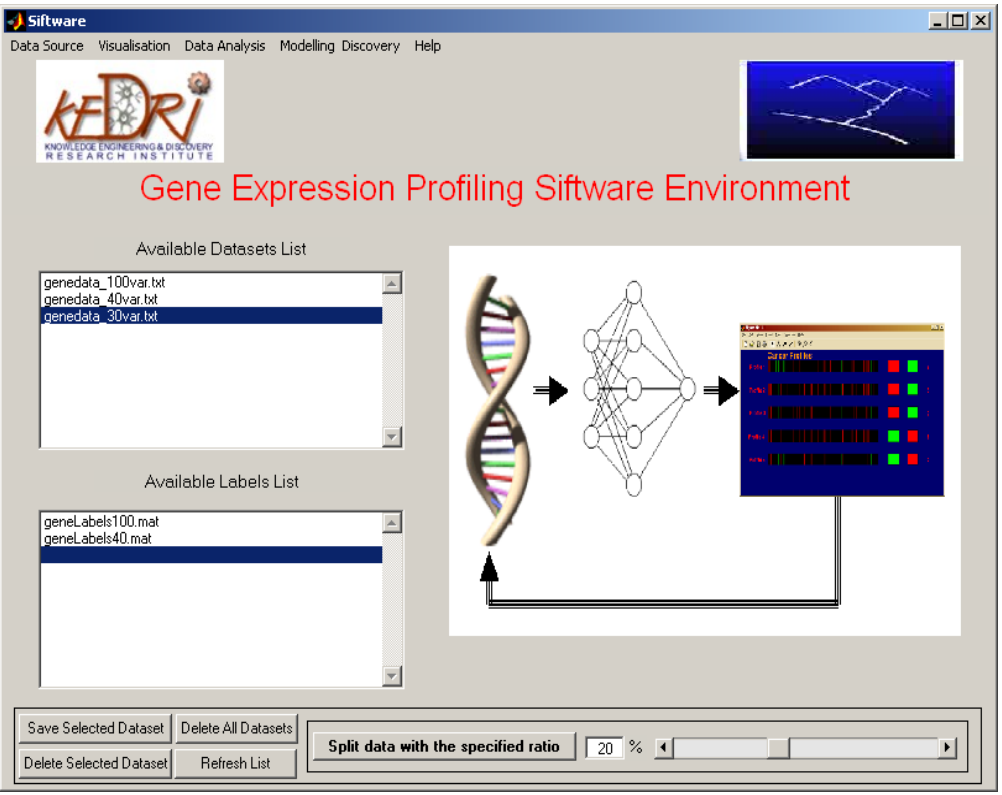


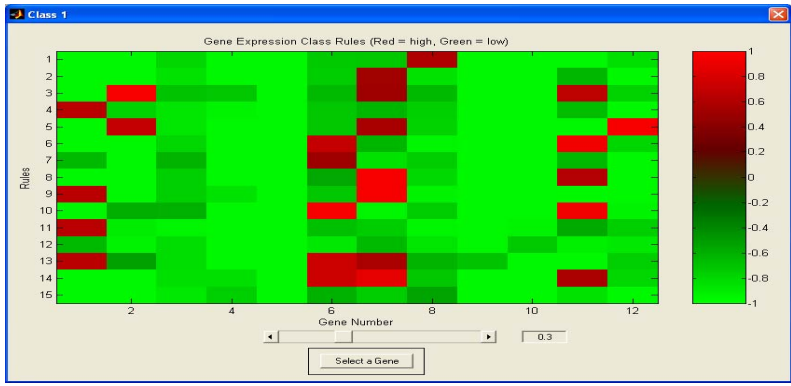


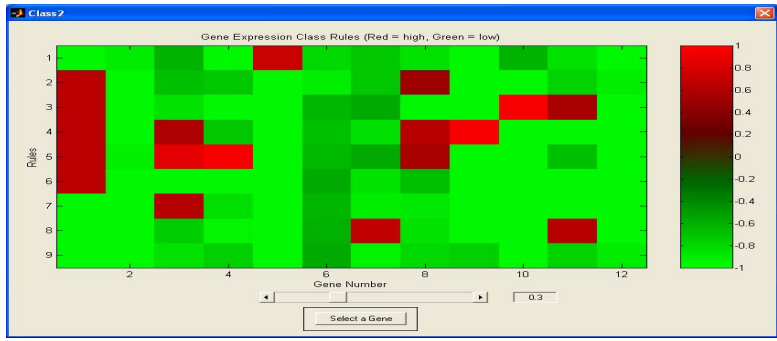
SIFTWARE – A software systems for gene expression data analysis, modelling and profiling

(License available from PEBL, www.peblnz.com)

Case example: DLBCL outcome prediction, data from: M. Ship et al, Nature Medicine, vol.8, n.1, January 2002, 68-74

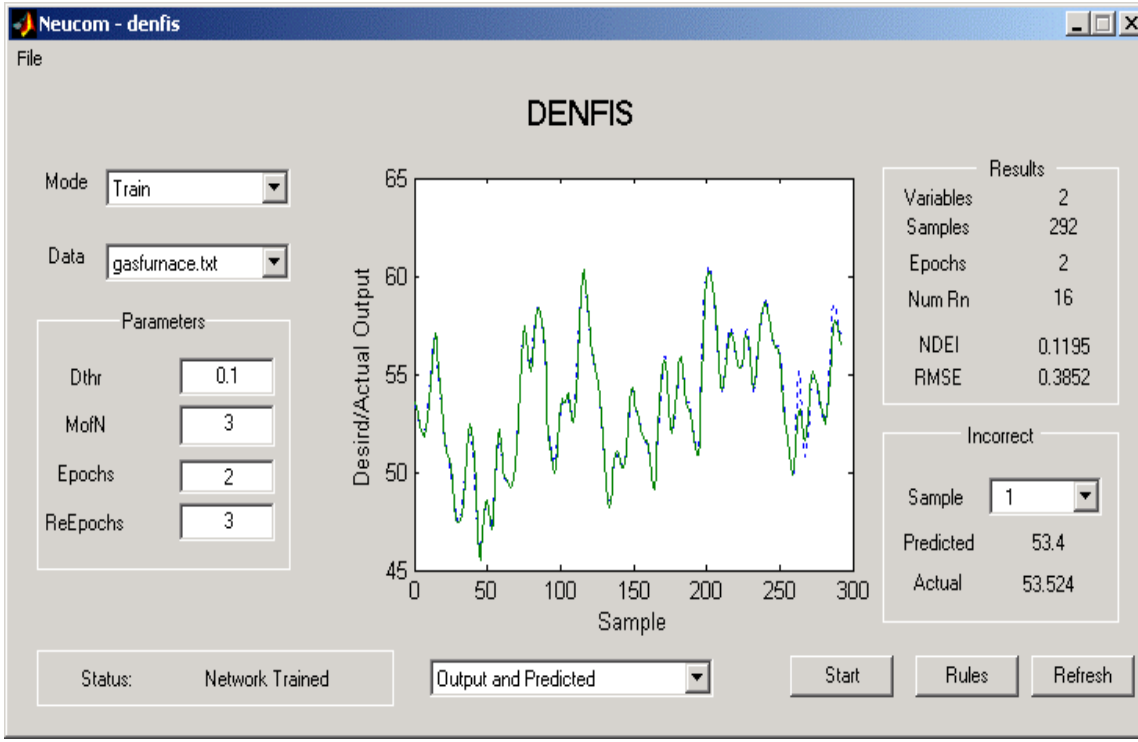






Dynamic Evolving Neuro-Fuzzy Systems (DENFIS)

- Modeling, prediction and knowledge discovery from dynamic time series
- Cluster –based local modelling where each cluster evolves a model (a function) of the same type
- Kasabov, N., and Song, Q., DENFIS: Dynamic Evolving Neural-Fuzzy Inference System and its Application for Time Series Prediction, IEEE Transactions on Fuzzy Systems, 2002, April



Local, incremental learning of cluster-based fuzzy rules in DENFIS

- Input vector: $\mathbf{x} = [x1, x2, \ldots, xq]$
- Result of inference:

$$y = \frac{\sum_{i=1,m} [\omega i \, fi\,(x1, x2, \ldots, xq)]}{\sum_{i=1,m} \omega i}$$

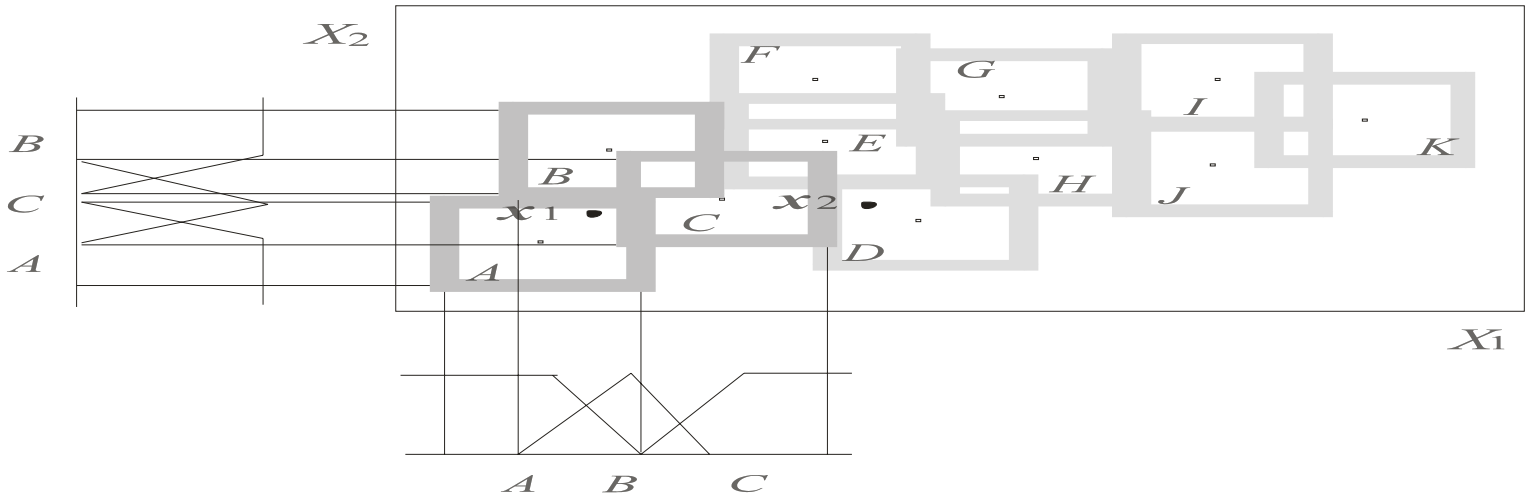
- A partial case is using linear regression functions:

$$y = \beta 0 + \beta 1\, x1 + \beta 2\, x2 + \ldots + \beta q\, xq.$$

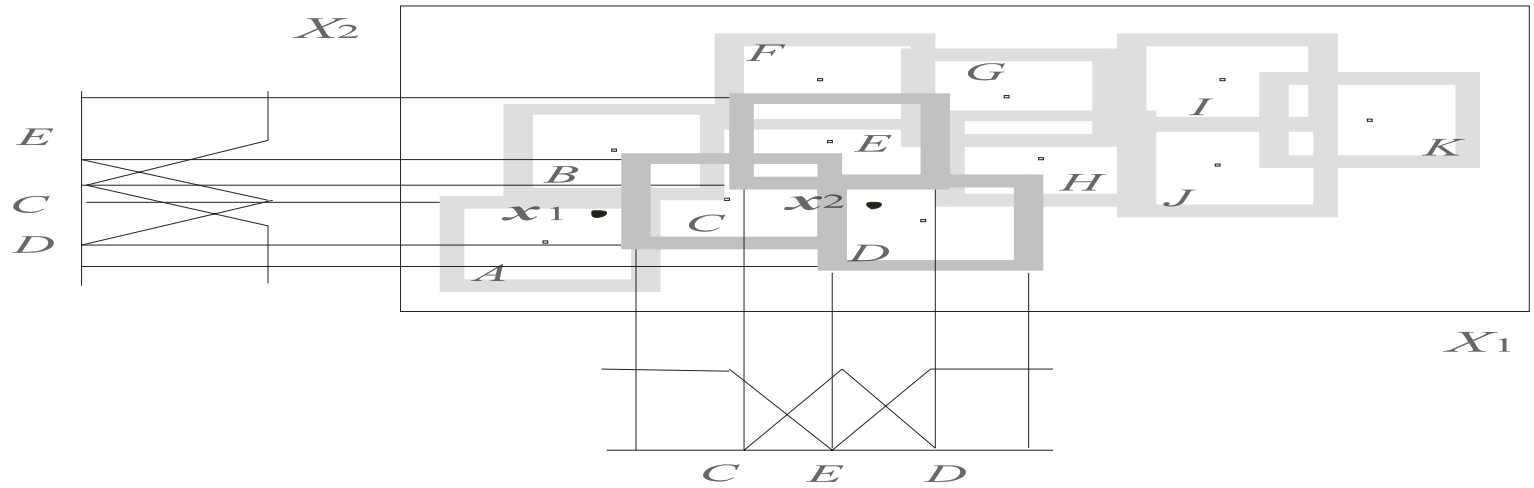
- Fuzzy rules: IF x is in cluster Cj THEN yj = fj (**x**)
- Incremental learning of the function coefficients through least square error

Learning and Inference in DENFIS

(a) Fuzzy rule group 1 for a DENFIS



(b) Fuzzy rule group 2 for a DENFIS

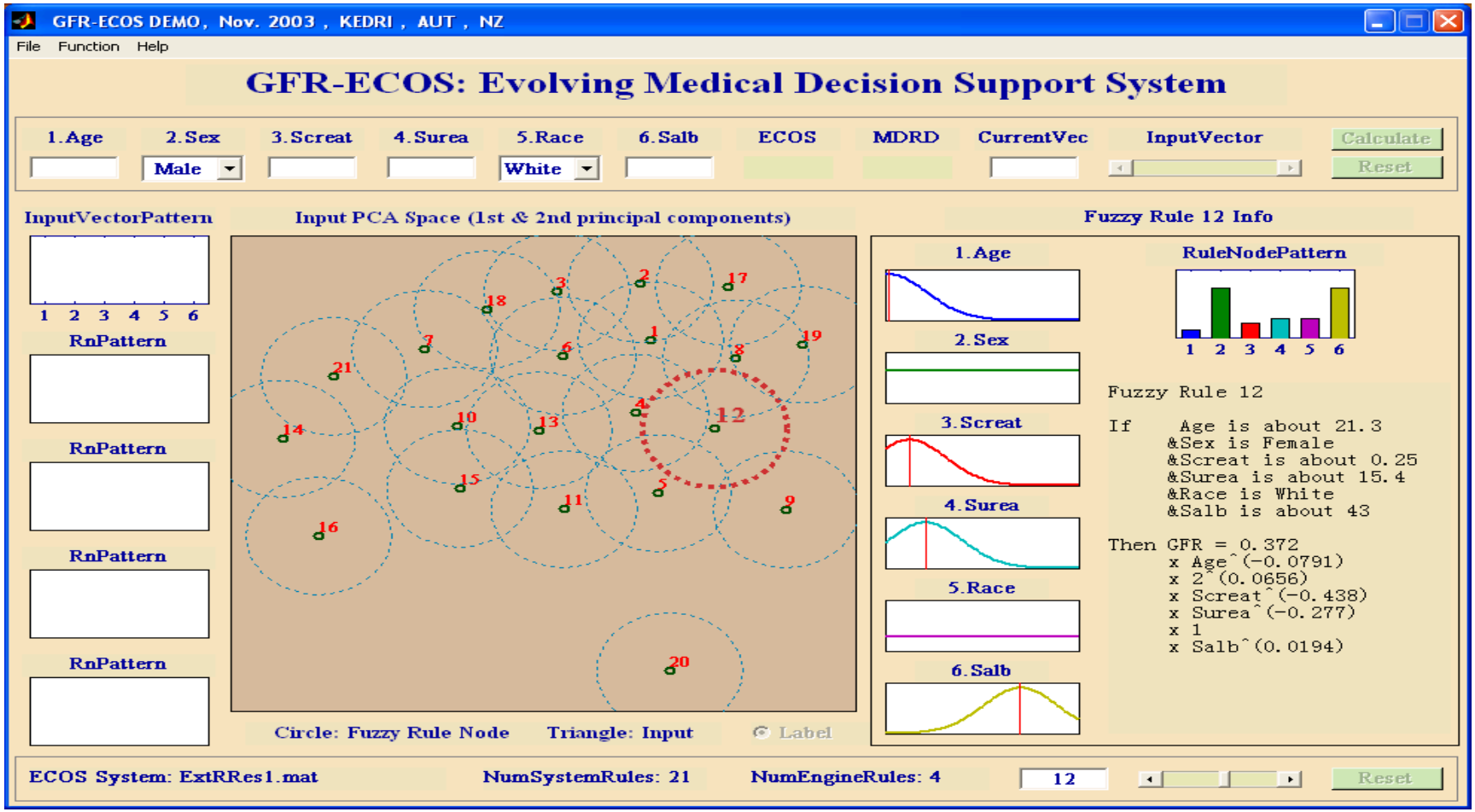


The case study on GFR prediction for renal medical decision support

A real data set from a medical institution is used here for experimental analysis. The data set has 447 samples, collected at hospitals in New Zealand and Australia. Each of the records includes six variables (inputs): age, gender, serum creatinine, serum albumin, race and blood urea nitrogen concentrations, and one output - the glomerular filtration rate value (GFR). All experimental results reported here are based on 10-cross validation experiments with the same model and parameters and the results are averaged. In each experiment 70% of the whole data set is randomly selected as training data and another 30% as testing data.

Local, adaptive GFR Renal Function Evaluation System based on DENFIS: GFR-DENFIS

(Marshal, Song, Ma, McDonell and Kasabov, Kidney International, May 2005)

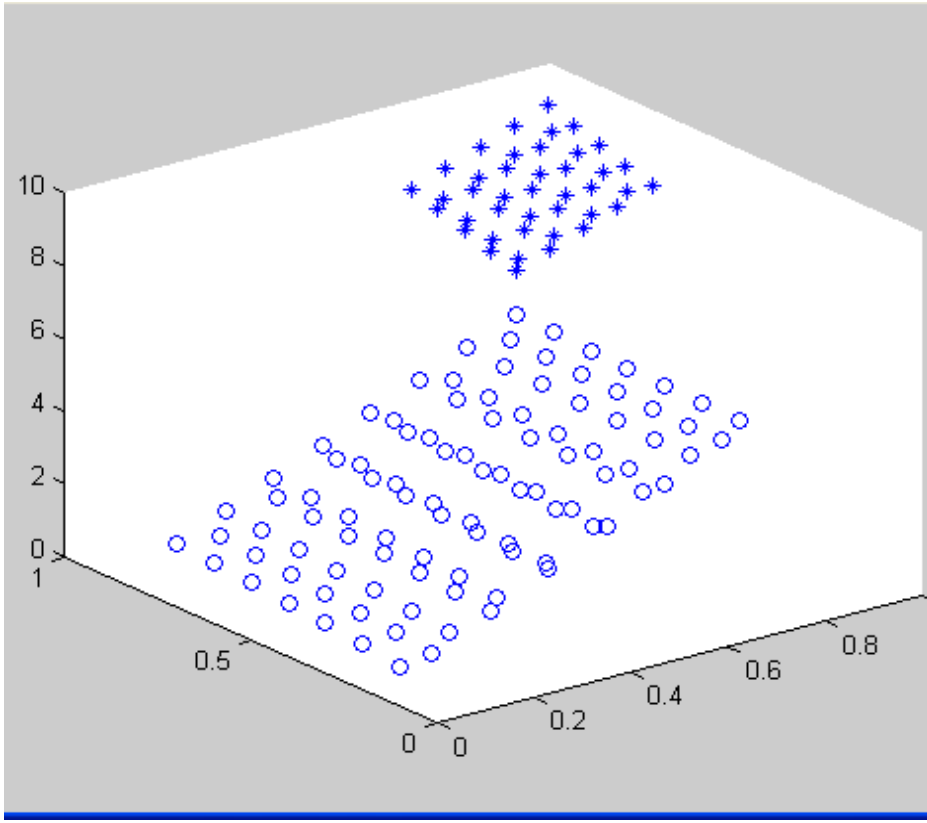


3. Data and model integration through local learning and modelling

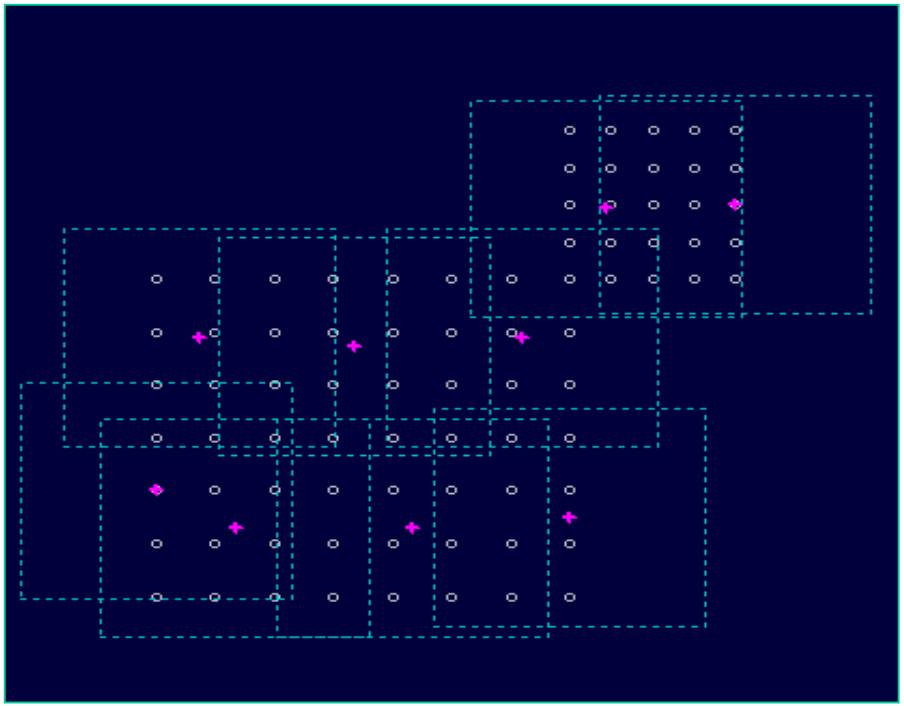
A case study of a model M (formula) and a data set D of new data integration through an ECOS.

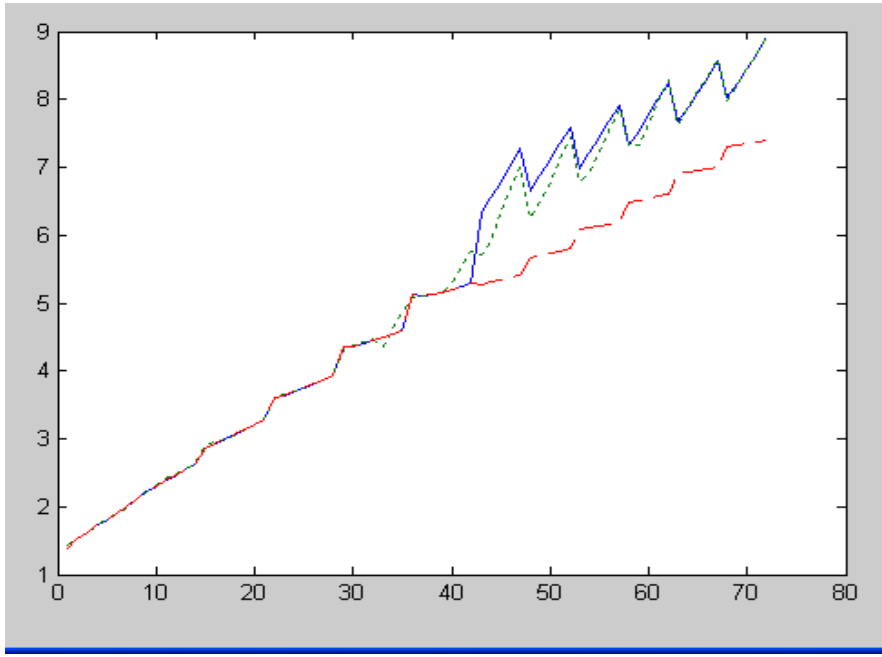
- **Model M:** A 3D plot of data D_0 (data samples denoted as "o") generated from a model M (formula) $y = 5.1x_1 + 0.345x_1^2 - 0.83x_1 \log_{10} x_2 + 0.45x_2 + 0.57 \exp(x_2^{0.2})$ in the sub-space of the problem space defined by x_1 and x_2 both having values between 0 and 0.7, and

- New data D (samples denoted as "*") defined by x_1 and x_2 having values between 0.7 and 1;



After integration through incremental learning in ECOS, the system performs better on the new data





Prototype rules extracted from DENFIS and EFuNN after model and data integration

Takagi-Sugeno fuzzy rules (DENFIS):

- Rule 1: IF x_1 is (-0.05, 0.05, 0.14) and x_2 is (0.15,0.25,0.35) THEN $y = 0.01 + 0.7x_1 + 0.12x_2$
- Rule 2: IF x_1 is (0.02, 0.11, 0.21) and x_2 is (0.45,0.55, 0.65) THEN $y = 0.03 + 0.67x_1 + 0.09_{x2}$
- Rule 3: IF x_1 is (0.07, 0.17, 0.27) and x_2 is (0.08,0.18,0.28) THEN $y = 0.01 + 0.71x_1 + 0.11x_2$
- Rule 4: IF $x_1$is (0.26, 0.36, 0.46) and x_2 is (0.44,0.53,0.63) THEN $y = 0.03 + 0.68x_1 + 0.07x_2$
- Rule 5: IF $x_1$is (0.35, 0.45, 0.55) and x_2 is (0.08,0.18,0.28) THEN $y = 0.02 + 0.73x_1 + 0.06x_2$
- Rule 6: IF $x_1$is (0.52, 0.62, 0.72) and x_2 is (0.45,0.55,0.65) THEN $y = -0.21 + 0.95x_1 + 0.28x_2$
- Rule 7: IF $x_1$is (0.60, 0.69,0.79) and x_2 is (0.10,0.20,0.30) THEN $y = 0.01 + 0.75x_1 + 0.03x_2$

- **New rules:**
- **Rule 8: IF $x_1$is (0.65,0.75,0.85) and x_2 is (0.70,0.80,0.90) THEN $y = -0.22 + 0.75x_1 + 0.51x_2$**
- **Rule 9: IF $x_1$is (0.86,0.95,1.05) and x_2 is (0.71,0.81,0.91) THEN $y = 0.03 + 0.59x_1 + 0.37x_2$**

Zhade-Mamdani fuzzy rules (ECF, EFuNN):

Rule 1: IF x_1 is (Low 0.8) and x_2 is (Low 0.8) THEN y is (Low 0.8), radius R_1=0.24; N_{1ex}= 6

Rule 2: IF x_1 is (Low 0.8) and x_2 is (Medium 0.7) THEN y is (Small 0.7), R_2=0.26, N_{2ex}= 9

Rule 3: IF x_1 is (Medium 0.7) and x_2 is (Medium 0.6) THEN y is (Medium 0.6), R_3 = 0.17,N_{3ex}=17

Rule 4: IF x_1 is (Medium 0.9) and x_2 is (Medium 0.7) THEN y is (Medium 0.9), R_4 = 0.08, N_{4ex}=10

Rule 5: IF x_1 is (Medium 0.8) and x_2 is (Low 0.6) THEN y is (Medium 0.9), R_5= 0.1, N_{5ex} = 11

Rule 6: IF x_1 is (Medium 0.5) and x_2 is (Medium 0.7) THEN y is (Medium 0.7), R_6= 0.07,N_{6ex}= 5

New rules:

Rule 7: IF x1 is (High 0.6) and x2 is (High 0.7) THEN y is (High 0.6), R_7 = 0.2, N_{7ex} = 12

Rule 8: IF x1 is (High 0.8) and x2 is (Medium 0.6) THEN y is (High 0.6), R_8=0.1,N_{8ex}= 5

Rule 9: IF x1 is (High 0.8) and x2 is (High 0.8) THEN y is (High3 0.8), R_9= 0.1, N_{9ex} = 6

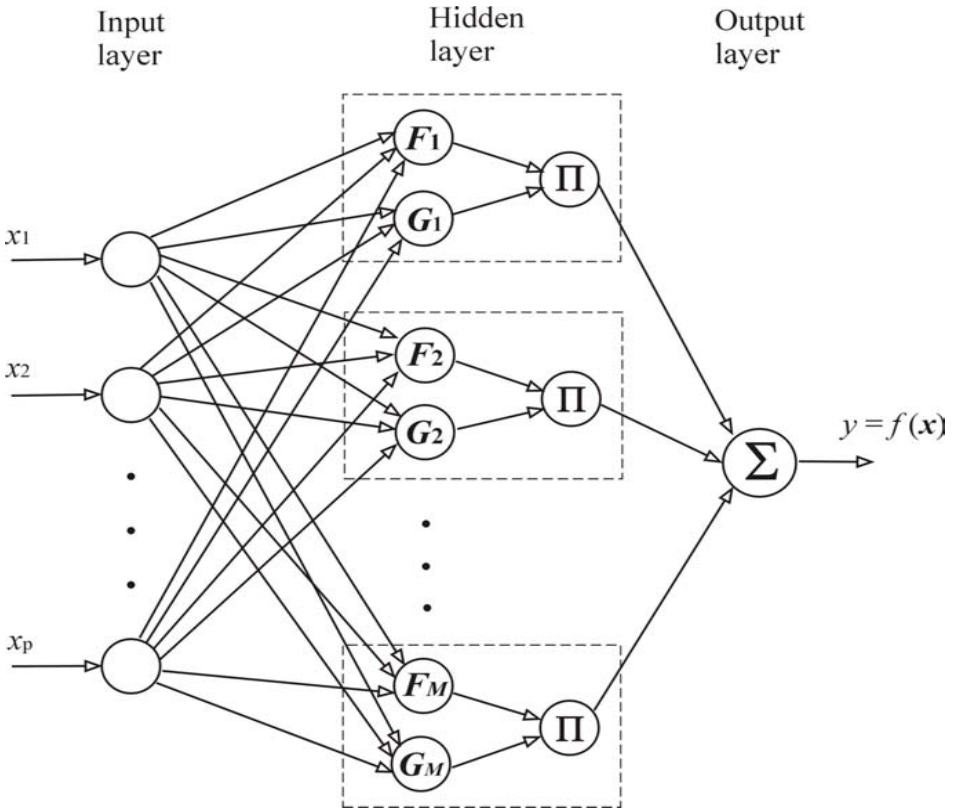
4. Integration of regression formulas and kernel methods in a local learning RK-KBNN

(Song, Kasabov, Ma, Marshall, AI in Medicine, December, 2005)

- *Cluster-based local learning, where each cluster has a different shape and a different type of model (function) evolved*
- *A local function F is selected to approximate data in a local Gaussian kernel*
- $Y(xi) = G1(xi)\ F1(xi) + G2(xi)F2(xi) + \ldots + GM(xi)\ FM(xi)$

where:

$$G_l(\mathbf{x}_i) = \alpha_l \prod_{j=1}^{P} \exp[-\frac{(x_{ij} - m_{lj})^2}{2\sigma_{lj}^2}]$$

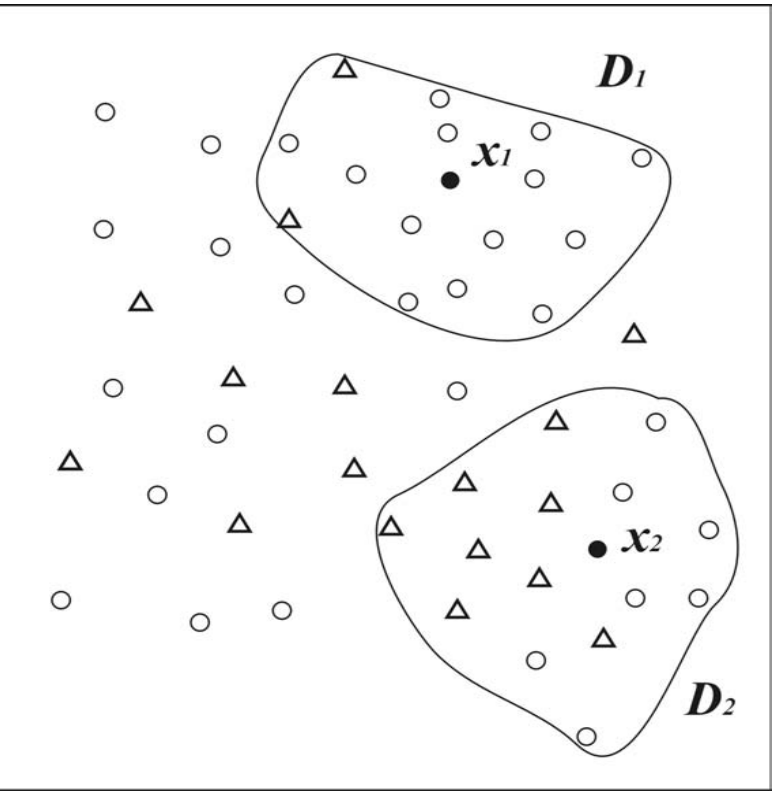


Global regression formulas versus local RK-KBNN

(A case study on GFR renal function evaluation)

Model	Neurons or rules	RMSE	MAE	Std
Jelliffe71	–	9.13	7.21	12.42
Mawer	–	11.01	8.09	13.34
Jelliffe73	–	7.84	5.90	9.66
Cockcroft-Gault	–	7.97	6.16	10.45
Hull	–	9.50	7.12	12.43
Bjorasson	–	10.29	7.83	12.07
Gates	–	7.49	5.62	9.92
Walser	–	7.36	5.58	10.19
MDRD	–	7.76	5.87	9.27
MLP	12	8.44	5.74	9.06
ANFIS	36	7.43	5.46	8.97
DENFIS	34	7.24	5.27	8.67
RBF	32	7.18	5.39	9.36
Local RK- KBNN	17	6.86	5.07	8.55

5. Transductive ("Personalised") Modelling



● – a new data vector
○ – a sample from *D*
Δ – a sample from *M*

• A transductive model is created on a sub-set of neighbouring data to each input vector. A new data vector is situated at the centre of such a sub-set (here illustrated with two of them – $\boldsymbol{x}_1$ and $\boldsymbol{x}_2$), and is surrounded by a fixed number of nearest data samples selected from the training data *D* and generated from an existing model *M (Vapniak)*

• The principle is: " What is good for my neigbors will be good for me"

Problems of the personalised modelling

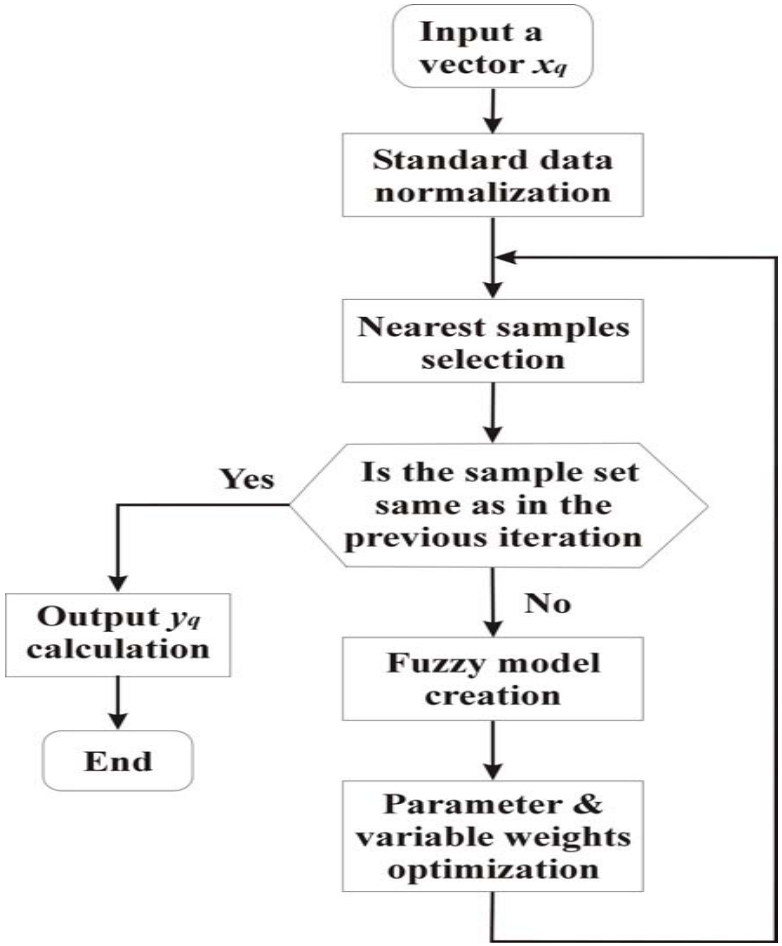
- Defining a correct number of neighbours – K. Is "the more – the better" principle held here?
- Defining appropriate number of features (variables)
- Defining appropriate "personalised" models, e.g. k-NN, MLR, MLP, SVM,…
- Defining the distance measure, e.g. Euclidean distance, Hamming distance, Cosine distance, etc.

Comparative Analysis of Global, Local and Personalised Modelling on the DLBCL Gene Expression Case Study

Model/ InpVar	Induct global MLR	Induct Global SVM	Induct Local ECF	Trans WKNN K=8	Trans WKN K=26 P_{thr}=0.5	Trans MLR K=8	Trans MLR k=26	Trans SVM K=8	Trans SVM k=26	Trans ECF K=8	Trans ECF k=26
1 var: IPI	73 (87,58	73 (87,58)	46 (0,100)	50 (87,8)	73 (87,56)	50 (87,8)	73 (87,58)	46 (100,0)	73 (87,58	61 (63,58)	46 (0,100
11 var: 11 genes	79 (91,65	83 (88,78)	86 (88,84)	74 (91,54	73 (93,47)	66 (66,65	78 (81,73	76 (91,58	78 (91,62	78 (81,73	83 (91,73
12var: IPI+ 11g.	82 (83,81	86 (90,81)	**88 (83, 92)**	77 (90,62	76 (100,50 Pthr=0.4: 77% (73,81) Pthr=.45, 82% (97,65)	57 (60,54	79 (80,77	77 (93,58	84 (93,73	75 (83,65	77 (87,65

Transductive Neuro Fuzzy Inference with Weighted Data Normalisation - TWNFI

(Q.Song and N.Kasabov, IEEE Tr FS, December 2005, and Neural Networks, 2005)



After the nearest samples are selected for an input vector **x,** the samples are clustered using ECM.

A fuzzy rule is created/derived for each cluster:

R_l :If x_1 is F_{l1} and x_2 is F_{l2} and … x_P is F_{lP}, then y is G_l,

where F_{lj} and Gl are fuzzy sets defined by Gaussian type membership functions.

Input variable weights w_j and fuzzy rule parameters are optimized through the steepest descent algorithm.

$$f(\boldsymbol{x}_i) = \frac{\sum_{l=1}^{M} \frac{n_l}{\delta_l^2} \prod_{j=1}^{P} \alpha_{lj} \exp\left[-\frac{w_j^2 (x_{ij} - m_{lj})^2}{2\sigma_{lj}^2}\right]}{\sum_{l=1}^{M} \frac{1}{\delta_l^2} \prod_{j=1}^{P} \alpha_{lj} \exp\left[-\frac{w_j^2 (x_{ij} - m_{lj})^2}{2\sigma_{lj}^2}\right]}$$

Comparative analysis of Global, Local and Personalised modelling on the case study o GFR renal function evaluation

Model	Neurons or rules	Testing RMSE	Testing MAE	Weights of input variables					
				Age w1	Sex w2	SCr w3	Surea w4	Race w5	Salb w6
MDRD	—	7.74	5.88	1	1	1	1	1	1
MLP	12	8.44	5.75	1	1	1	1	1	1
ANFIS	36	7.49	5.48	1	1	1	1	1	1
DENFIS	27	7.29	5.29	1	1	1	1	1	1
TNFI	**6.8 (average)**	**7.31**	**5.30**	**1**	**1**	**1**	**1**	**1**	**1**
TWNFI (patent)	**6.8 (average)**	**7.11**	**5.16**	**0.89**	**0.71**	**1**	**0.92**	**0.31**	**0.56**

A GFR exemplar personalised model of a patient obtained with the use of the TWNFI

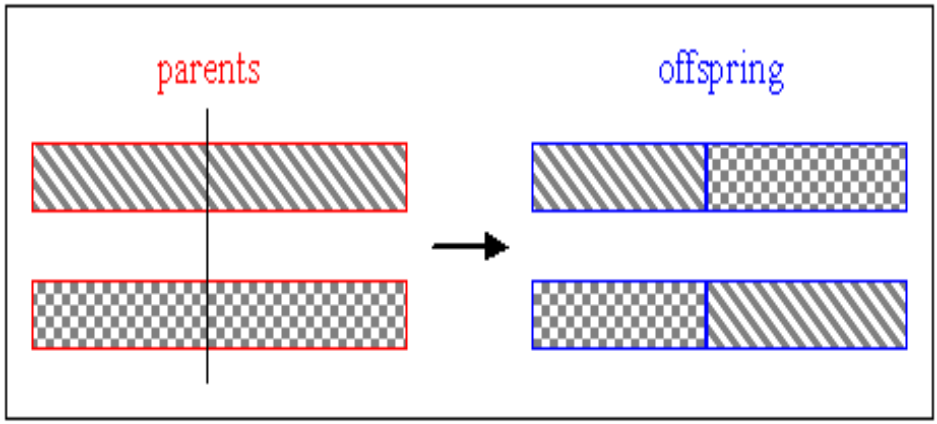
Input variables	Age 58.9	Sex Female	SCr 0.28	Surea 28.4	Face White	Salb 38
Weights of input variables (TWNFI)	0.91	0.73	1	0.82	0.52	0.46
Results	GFR (desired) 18.0		MDRD 14.9		**TWRBF 16.6**	

6. Evolutionary Computation for the Optimisation of Local Models

Evolutionary computation.

Terminology:

- *Gene*
- *Chromosome*
- *Population*
- *Crossover*
- *Mutation*
- *Fitness function*
- *Selection*



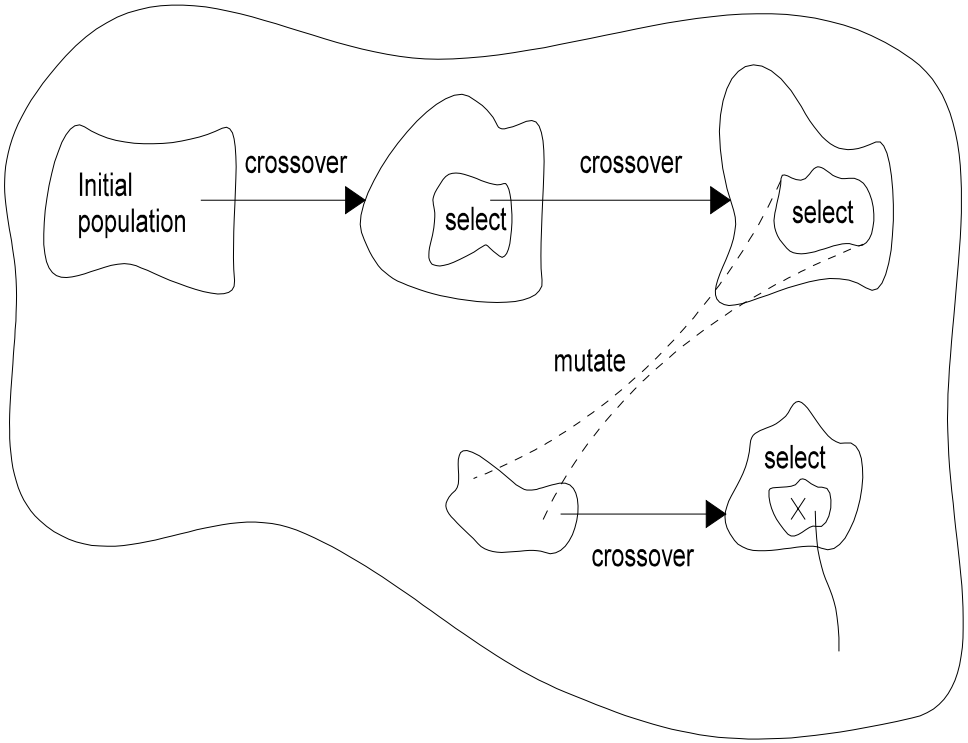
Genetic Algorithms (GA)

1. Initialize population of possible solutions

2. WHILE a criterion for termination is not reached DO
   {
   2a. Crossover two specimens ("mother and father") and generate new individuals;
   2b. Select the most promising ones, according to a fitness function;
   2c. Development (if at all);
   2d. Possible mutation (rare) }
   }

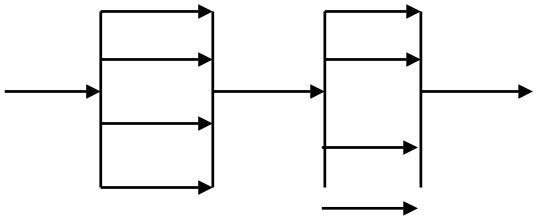
GA

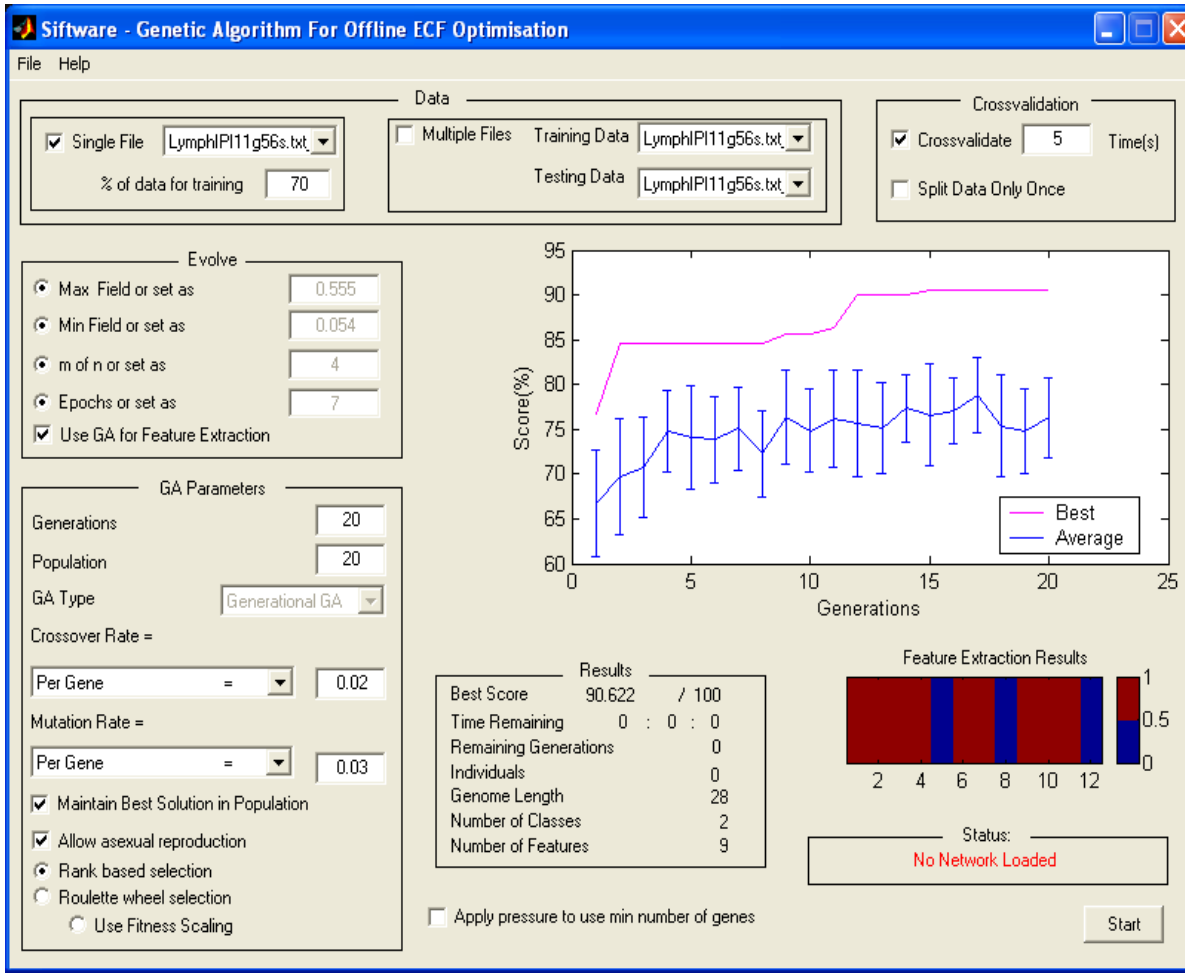
- Many individuals are evolved simultaneously on the same data through a GA method
- A chromosome represents each individual
- Individuals are evaluated and the best one is selected for a further development
- Mutation



GA feature and parameter optimisation of local ECOS in NeuCom and SIFTWARE

- Optimizing the parameters of the model and the input features
- A chromosome contains as "genes" all model parameters and input features
- Replication of individual ECOS systems and selection of:
  - The best one
  - The best *m* averaged, etc



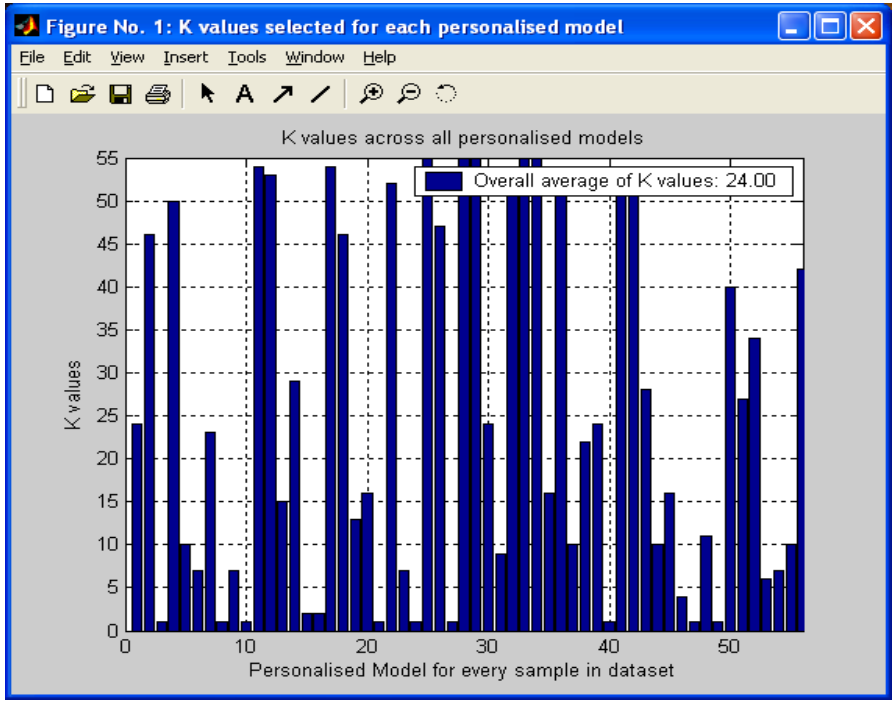


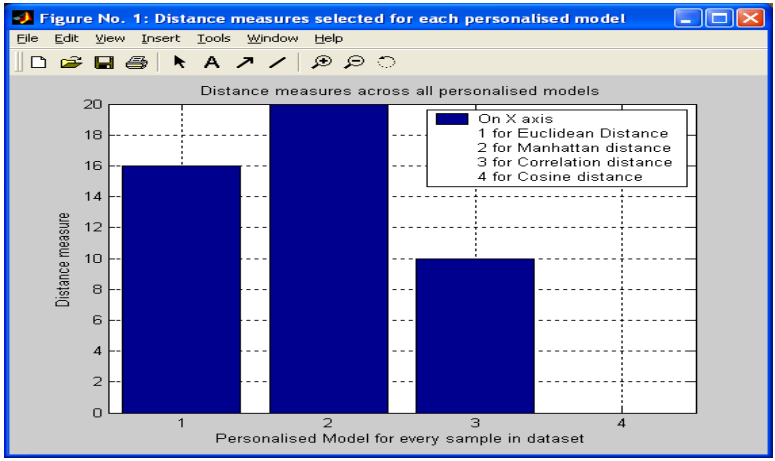
GA feature and parameter optimisation of personalised models

Optimising the number of neighbours K, the distance measure, and the model type

(N.Mohan and N.Kasabov, IJCNN, IEEE Press, 2005)

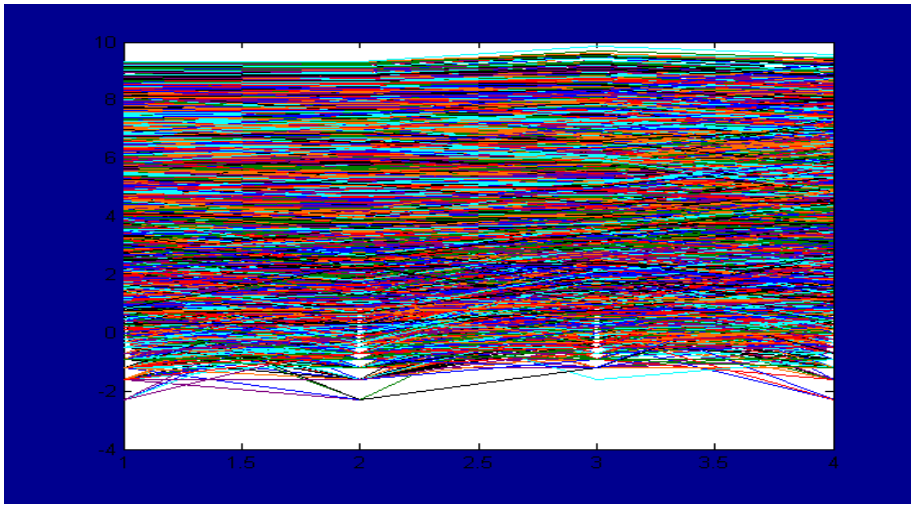
a)

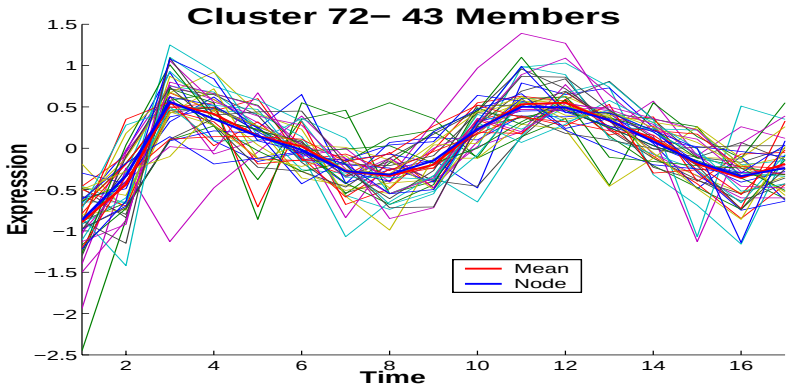




7. Gene regulatory network (GRN) modeling and discovery

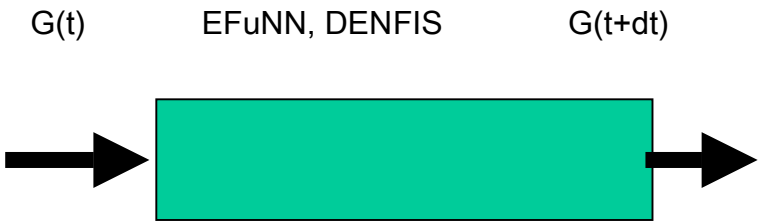
- Genes that share similar functions usually show similar gene expression profiles and cluster together
- Different clustering techniques:
  - Exact clusters vs fuzzy clusters
  - Pre-defined number of clusters or evolving
  - Batch vs on-line
  - Using different similarity or correlation measure
- Case study:
  - Leukemia cell line U937 (experiments done at the NCI, NIH, Frederick, USA, Dr Dimitrov's lab)
  - Two different clones of the same cell line treated with retinoic Acid
  - 12,680 genes expressed over time points
  - 4 time points (the MINUS clone, the cell died) and
  - 6 time points (PLUS cell line, cancer)





ECOS for GRN modeling

(Kasabov and Dimitrov, ICONIP 2002, IEEE Press, 2002)



- On-line, incremental learning of GRN
- Adding new inputs/outputs (new genes)
- The rule nodes capture clusters of input genes that are related to the output genes
- Rules can be extracted that explain the relationship between G(t) and G(t+dt), e.g.:
- EFUNN rules:

IF g1 (t) is High (0.87) and g2(t) is Low (0.9)

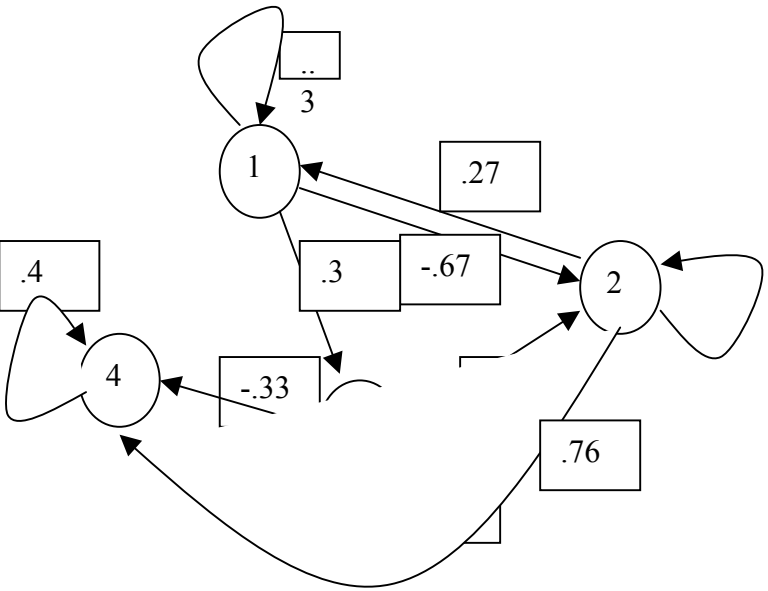
THEN g1 (t+dt) is High (0.6) and g4 (t+dt) is Low

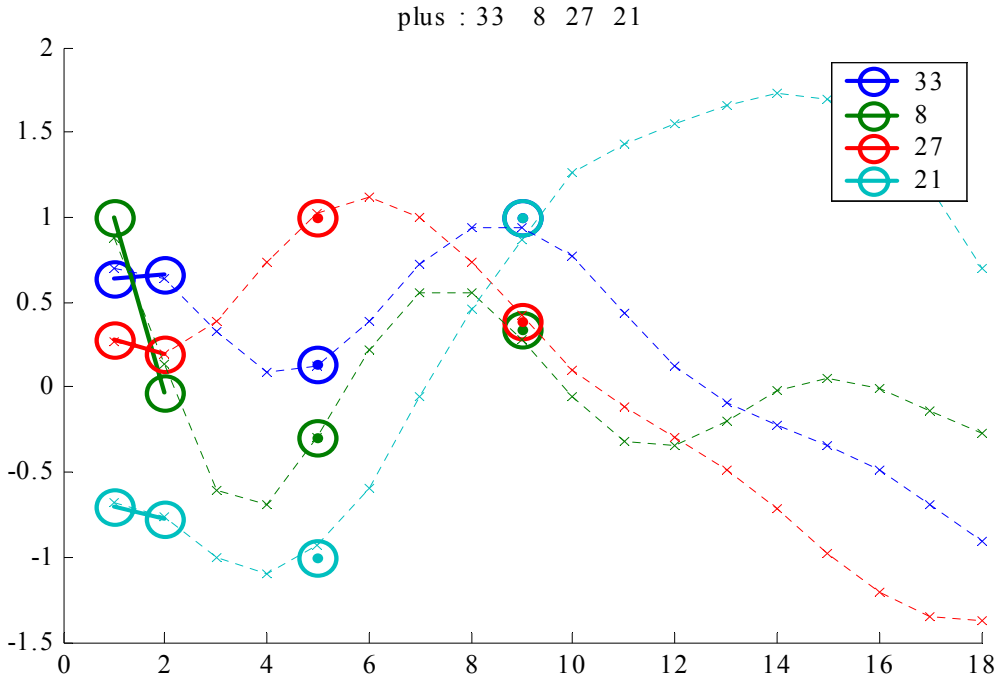
- DENFIS rules:

IF g1(t) is (0.63 0.70 0.76) and g2 (t) is (0.71 0.77 0.84) and
g3 (t) is (0.71 0.77 0.84) and g4 (t) is (0.59 0.66 0.72)
THEN g1(t) = 1.84 - 1.26 X1 - 1.22X2 + 0.58X3 - 0.03 X4

Using GRN models to predict the expression of genes in a future time

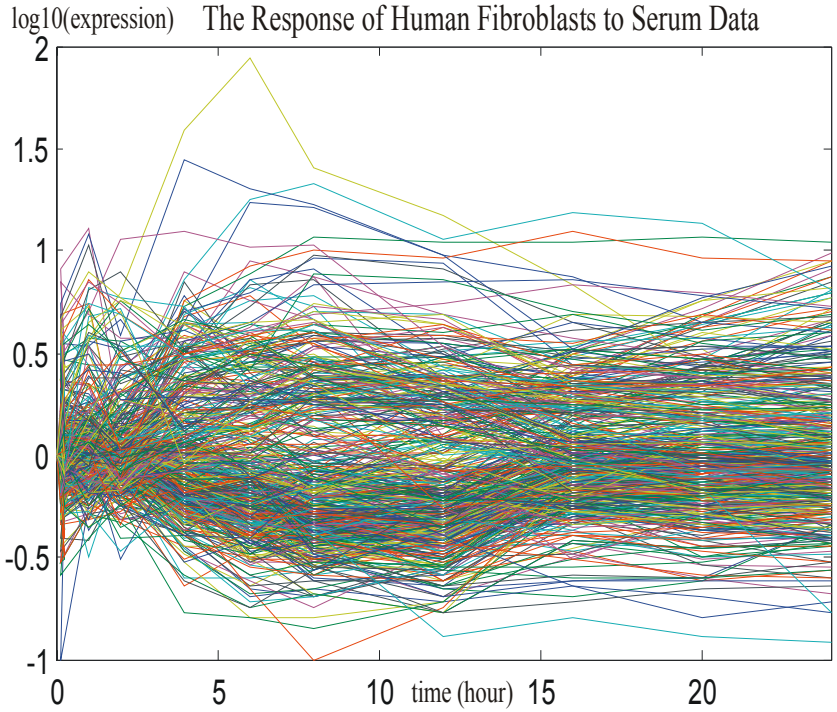
(Zeke Chan, N. Kasabov, I. Sidorov and D.Dimitrov, IEEE Tr CBBI, 2005) .

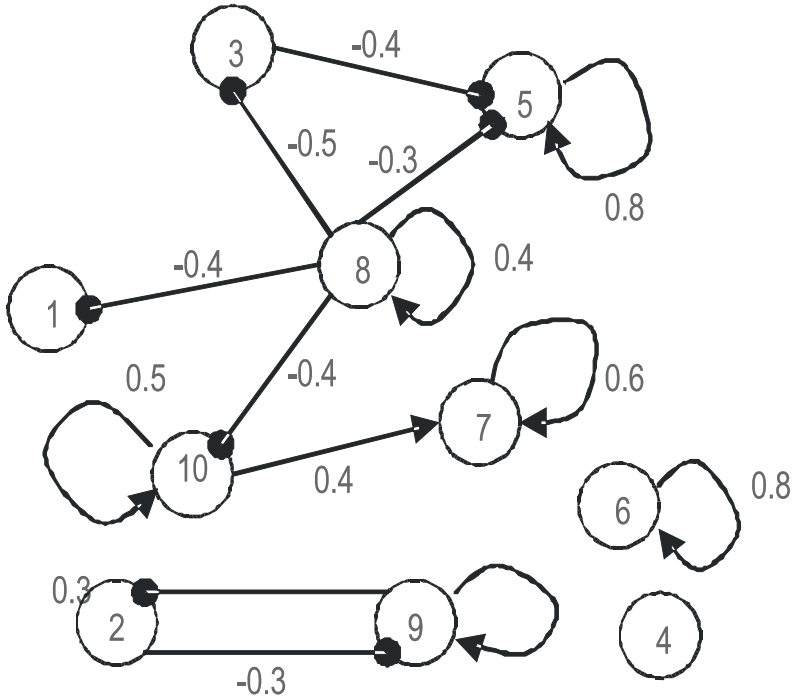




Example of a GRN derived from gene expression time course data

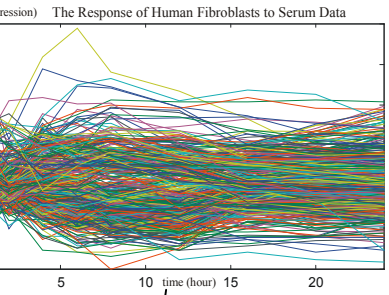
(Chan, Collins and Kasabov, JBCB, 2005)





GNetXP methodology and software

(Chan, Collins and Kasabov, JBCB, 2005)

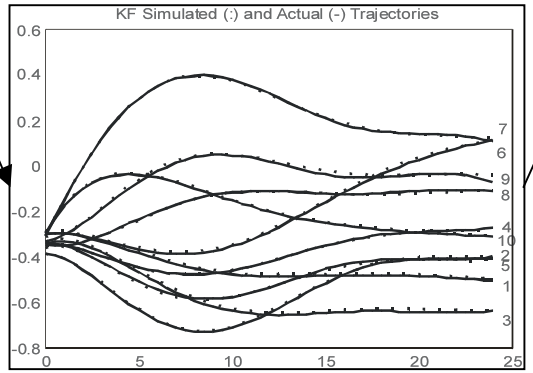


Trajectory

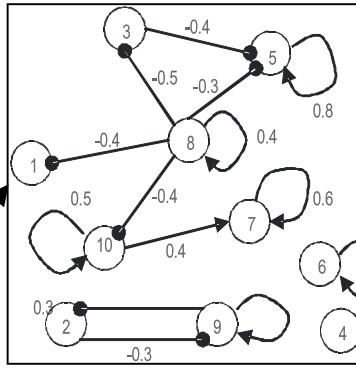
idx	Key Genes in the cluster
1	p57 Kip2
2	CDK1, E2F2; HMG CoA reductase, IPPisomerase, Farnesyl-DFT
3	p27 Kip1; Asparagine synthesase; Squalene epoxidase, Cyp51
4	P18
5	/
6	/
7	HEF1, ATF3 transcription factor
8	Interleukin 1ß, Interleukin 6, ID2, ID3,Interleukin 8, VEGF, Plasminogen activator inhibitor type 1 and Metallothionein 1ß; VEGF; Plasminogen activator inhibitor; metalloproteinases type 1
9	CyclinB, Cdc28; metalloproteinases
10	CyclinA, CyclinD1 Cdc2, Madp2, Wee1-like protein kinase, TGFβ and CENP-f; c-FOS, JUNB, MAPK1; Metallothionein 1A, Flap endonuclease; metalloproteinases 1

key genes in each cluster

Representative trajectories from the clusters

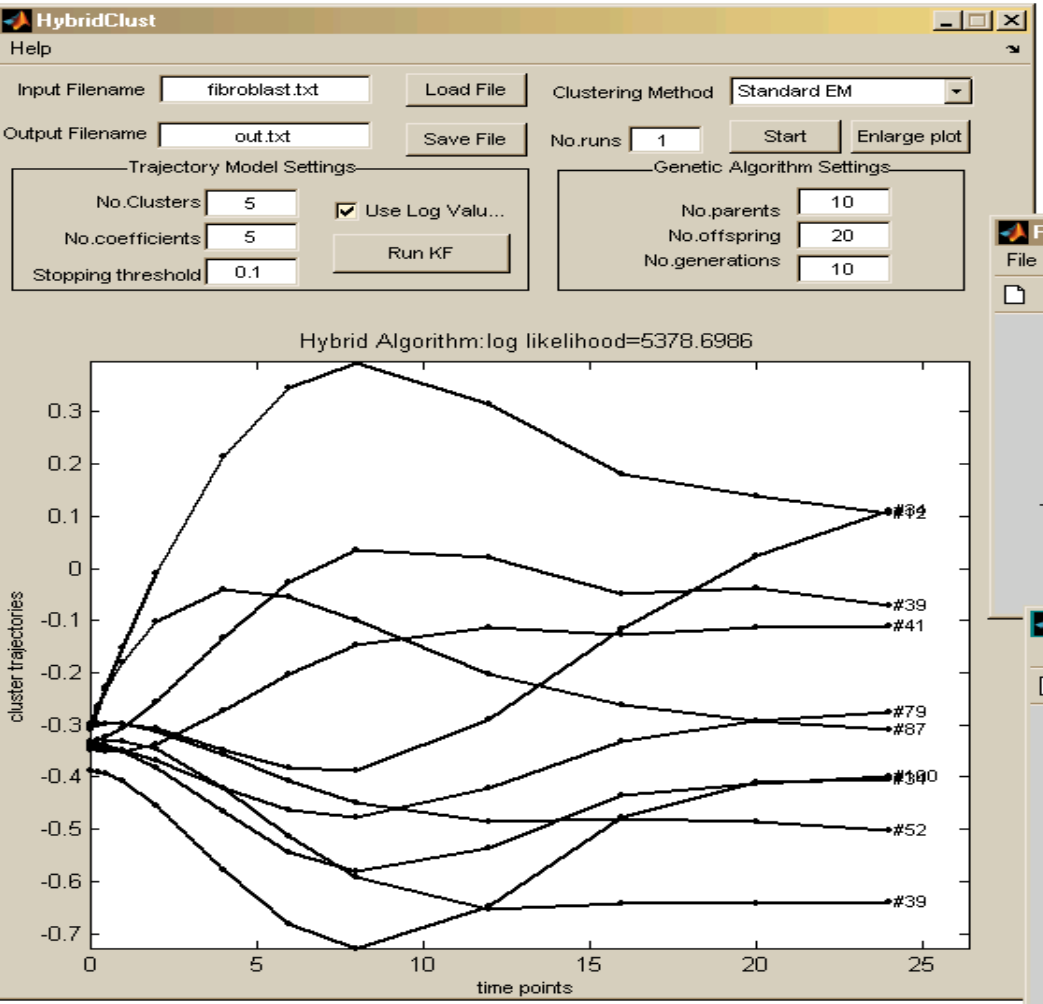


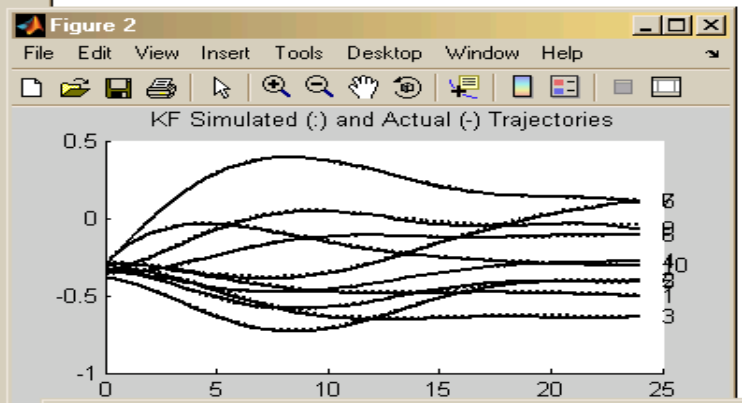
Stage 2: GRN extraction

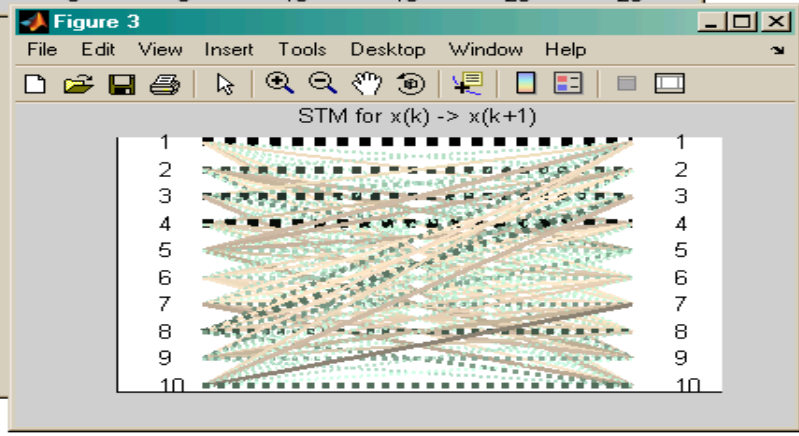


The GNetXP software system

(license available from KEDRI, www.kedri.info)





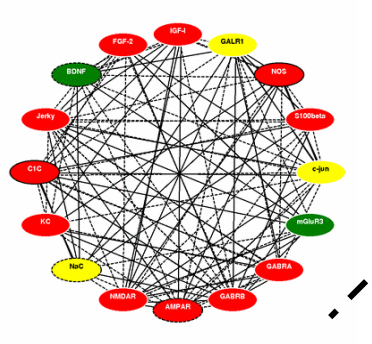


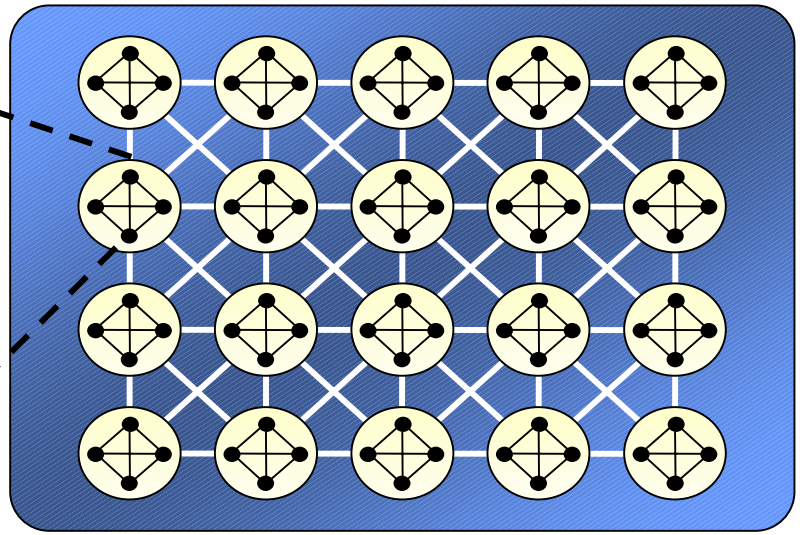
Computational Neurogenetic Modelling: GRN within neurons as part of a SNN

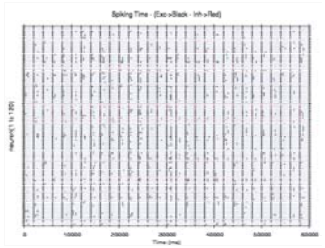
(L.Benuskova, S.Wysoski, N.Kasabov, IJCNN05 – IEEE Press, 2005, ICANN05- LNCS 3697 Springer, 2005

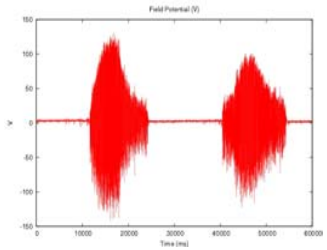
CNGM as a SNN

GRN

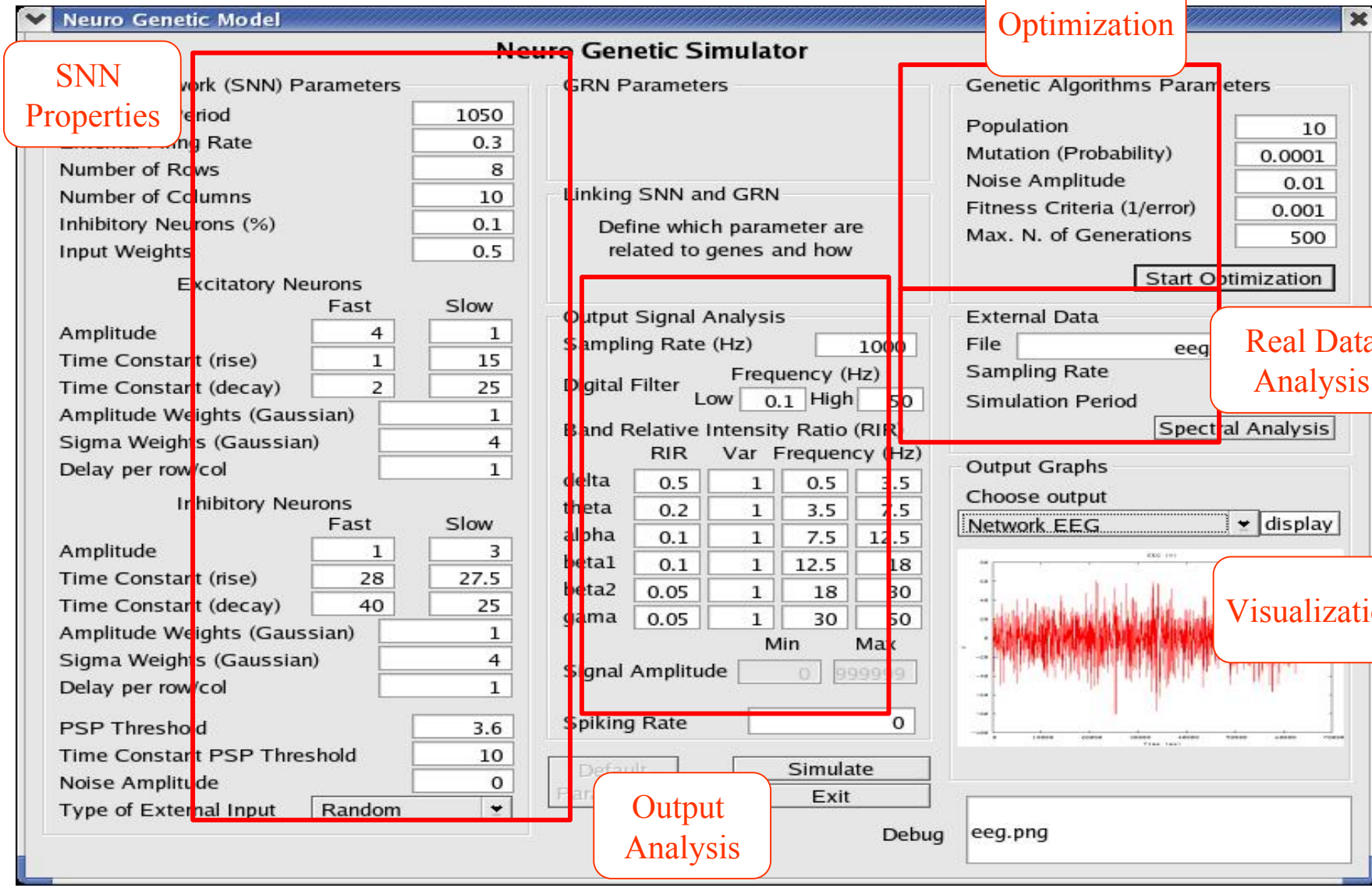








CNG Simulator *(Licence available from KEDRI, www.kedri.info)*



8. Conclusions and further directions

- Advantages of local and personalised modelling:
  - More accurate
  - Better explanation
  - Different number of variables can be used

- Questions and problems for further research in local and personalised modelling
  - How many neighbouring data points D_j should be selected in a transductive reasoning (personalised modelling)? That is the problem of choosing K
  - How is "vicinity" measured
  - Choice of distance function
  - Transductive feature selection
  - Speed, when optimisation is needed

- How to combine different models – each of them giving a different perspective,
  i.e global, local and "personalised"?

- Computational neurogenetic modelling (CNGM)

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- Established March-June 2002.
- Funded by AUT, NERF (FRST), NZ industry.
- Appr. NZ$ 1mln pa
- 25 research staff and graduate students; 25 associated researchers
- Both fundamental and applied research (theory + practice)
- 95 publications in 2002-05
- 450 publications all together
- Multicultural environment (12 ethnical origins)
- Strong national and international collaboration:
- PEBL (www.pebl.co.nz);
- UA – BI, SCOPE project; EEE
- Middlemore hospital
- ViaLactia; FONTERRA
- RIKEN; KIT; Ritsumeikan
- UCBerkeley; NCI, NIH;
- TU Sofia-Plovdiv, BG

References …

N.Kasabov, Evolving Connectionist Systems: Methods and Applications in Bioinformatics, Brain Study and Intelligent Machines, Springer Verlag, 2002 (www.springer.de)

Kasabov, N., Evolving Fuzzy Neural Networks for Supervised/Unsupervised On-Line, Knowledge-Based Learning, IEEE Transactions on Systems, Man and Cybernetics, Part B: Cybernetics, Vol. 31, No. 6, December (2001) 902-918.

Q.Song and N.Kasabov, NFI: Transductive neuro-fuzzy inference method for personalized modelling, IEEE Transactions on Fuzzy Systems, vol.13, No.6, December, 2005

N.Moan, N.Kasabov, GA-parameter optimisation of the parameters of personalised models, proc. IJCNN, Montreal, 2005, IEEE Press.

N. Kasabov, Adaptation and Interaction in Dynamical Systems: Modelling and Rule Discovery Through Evolving Connectionist Systems, Applied Soft Computing, 2005.

Q. Song, N. Kasabov, T. Ma, M. Marshall, Integrating regression formulas and kernel functions into locally adaptive knowledge-based neural networks: a case study on renal function evaluation, Artificial Intelligence in Medicine, 2005

N. Kasabov, L. Benuskova L and Wysoski SG (2005) Computational neurogenetic modeling: integration of spiking neural networks, gene networks, and signal processing techniques. In: ICANN 2005, LNCS 3697, W. Duch et al (Eds), Springer-Verlag, Berlin Heidelberg, pp. 509-514.

N. Kasabov, Bioinformatics: A Knowledge engineering approach, Int. Journal of Intelligent Systems, Willey Int., 2005

S. Pang, S. Ozawa and N. Kasabov, Incremental Linear Discriminant Analysis for Classification of Data Streams, IEEE Trans. SMC-B, vol. 35, No. 5, 2005, 905 – 914

L.Goh, N.Kasabov, An integrated feature selection and classification method to select minimum number of variables on the case study of gene expression data, J. of Bioinformatics and Computational Biology, Imperial College Press and World Sci. Publ., vol.3, N. 5, 2005

Z.Chan, N.Kasabov, An Efficient Greedy K-means Algorithm for Global Gene Trajectory clustering, Expert Systems with Applications: An International Journal (ISSN: 0957-4174). Special issue on Intelligent Bioinformatics Systems, December, 2005.

Z.Chan, N.Kasabov, A Two-Stage Methodology for Gene Regulatory Network Extraction from Time-Course Gene Expression Data, Expert Systems with Applications: An International Journal (ISSN: 0957-4174), Special issue on Intelligent Bioinformatics Systems, December, 2005.

Q. Song and N. Kasabov, TNFI: A Neuro-Fuzzy Inference Method for Transductive Reasoning, IEEE Transactions on Fuzzy Systems, 2005.

Chan and N.Kasabov, A Preliminary Study on Negative Correlation Learning via Correlation-Corrected Data (NCCD), Neural Processing Letters, Springer, 2005

M.R. Marshall, Q. Song, T.M. Ma, S. MacDonell, N.Kasabov, Evolving Connectionist System versus Algebraic Formulae for Prediction of Renal Function from Serum Creatinine, Kidney International, vol. 67 (2005), pp. 1944 – 1954

….References

Q. Song, T.M. Ma, N.Kasabov, Transductive Knowledge Based Fuzzy Inference System for Personalized Modelling, L.Wang and Y.Lin (eds): FSKD 2005, LNAI 3614, Springer-Verlag, Berlin- Heidelberg, 2005, pp. 528 – 535.

S. Chan, N.Kasabov and L.Collins, A hybrid genetic algorithm and expectation maximization method for global gene trajectory clustering, Journal of Bioinformatics and Computational Biology, Imperial College Press and World Scie. Publ., vol.3 No.5, 2005

N. Kasabov, Knowledge based neural networks for gene expression data analysis, modelling and profile discovery, Drug Discovery Today: BIOSILICO, vol. 2, No. 6, November 2004, pp. 253-261.

N. Kasabov, Z. S.H. Chan, Igor Sidorov and Dimiter Dimitrov, Gene Regulatory Network Discovery for Time Series Gene Expression Data – A Computational Intelligence Approach, Lecture Notes in Computer Science, Vol.3316, 2004, Springer Verlag, 1344-1353.

S. Chan and N.Kasabov, Efficient global clustering using the greedy elimination method, Electronic Letters, vol. 40, No. 25, 2004,

N. Kasabov and S. Pang, Transductive Support Vector Machines and Applications in Bioinformatics for Promoter Recognition, Neural Information Processing - Letters and Reviews 3(2), KAIST Press, pp.31-38., 2004

S. Ozawa, S. Pang and N. Kasabov, A Modified Incremental Principal Component Analysis for On-Line Learning of Feature Space and Classifier, Lecture Notes in Artificial Intelligence LNAI, Volume 3157, Springer-Verlag, Berlin, Heidelberg, 2004, 231 – 240.

S. Soltic, S.Pang, N.Kasabov, S. Worner and L.Peacock, Dynamic Neuro-fuzzy Inference and Statistical Models for Risk Analysis of Pest Insect Establishment, Lecture Notes of Computer Science, vol. 3316, Springer, 2004, 971-976.

Q. Song and N. Kasabov, TWRBF – Transductive RBF Neural Network with Weighted Data Normalization, Lecture Notes in Computer Science, Vol.3316, Springer Verlag, 2004, 633-640.

N. Kasabov and L. Benuskova, Computational Neurogenetics, International Journal of Theoretical and Computational Nanoscience, Vol. 1 (1) American Scientific Publisher, 2004, 47-61.

Z.Chan and N.Kasabov, Evolutionary computation for on-line and off-line parameter tuning of evolving fuzzy neural networks, Int. J. of Computational Intelligence and Applications, Imperial College Press, vol. 4, N.3, September 2004, 309-319

M. Futschik, M. Sullivan, A. Reeve, N. Kasabov, Prediction of clinical behaviour and treatment of cancers, Applied Bioinformatics, vol.3, 2003, 553-558

M. Futschik, A.Reeve, and Kasabov, N. Evolving connectionist systems for knowledge discovery from gene expression data of cancer tissue, Artificial Intelligence in Medicine, 28 (2003) 165-189

….References

N. Kasabov, Liang Goh and Mike Sullivan, *Integrated Prognostic Profiles: Combining Clinical and Gene Expression Information through Evolving Connectionist Approach,* Chapter 10, in: Bajic. V and Tan Tin Wee (eds), Information Processing and Living Systems, Imperial College Press, Singapore, 2005, 695-706.

N. Kasabov, Zeke Chan, Vishal Jain, Igor Sidorov and Dimiter Dimitrov, *Computational Modelling of Gene Regulatory Networks,* Chapter 8, in: Bajic., V and Tan Tin Wee (eds), Information Processing and Living Systems, Imperial College Press, Singapore, 2005, 673-686.

N.Kasabov, Z.Chan, Q.Song and D.Greer, Evolving neuro-fuzzy systems with evolutionary parameter self-optimisation, chapter in: *Do Adaptive Smart Systems exist?* Springer Verlag, Series Study in Fuzziness, vol.173, 2005

D. S Dimitrov, Igor A. Sidorov and Nikola Kasabov *Computational Biology,* in: M. Rieth and W. Sommers (eds) Handbook of Theoretical and Computational Nanotechnology, Vol. 1 (1) American Scientific Publisher, Chapter 21,2004

N. Kasabov and L. Benuskova, *Theoretical and Computational Models for Neuro-, Genetic-, and Neuro-Genetic Information Processing,* in: M. Rieth and W. Sommers (eds) Handbook of Theoretical and Computational Nanotechnology, Vol. 1 (1) American Scientific Publisher, Chapter 41, 2004

Kasabov, N. and D. Dimitrov, E*volving connectionist systems for gene regulatory network modelling and discovery,* chapter in: L.Wang and Rajapakse (eds) Advances in neuro-information processing, Springer Verlag, 2004

Kasabov, N. *Evolving Connectionist-based Decision Support Systems*, in: X.Yu, J.Kacprzyk (eds), Applied Decision Support with Soft Computing, series: Studies in Fuzziness and Soft Computing, vol. 124, Springer (2003).

Kasabov, N. *Decision support systems and expert systems*, in: M. Arbib (ed) Handbook of brain study and neural networks, MIT Press (2003).

Kasabov, N. *Brain-like functions in evolving connectionist systems for on-line, knowledge-based learning*, in: T. Kitamura (ed) What should be Computed to Understand and Model Brain Functions, FLSI Soft Computing Series, Volume 3, World Scientific (2001), 77-113.

Kasabov N., and G. Iliev, *A methodology and a system for adaptive speech recognition in a noisy environment based on adaptive noise cancellation and evolving fuzzy neural networks*, in: Neuro-Fuzzy Pattern Recognition, H. Bunke and A. Kandel, eds., World Scientific 2000, 179-203.

Kasabov, N., *Evolving and Evolutionary Connectionist Systems for On-Line Learning and Knowledge Engineering* in: Peter Sincak, Jan Vascak (eds) Quo Vadis Computational Intelligence? New Trends and Approaches in Computational Intelligence, Physica-Verlag, 2000, 361-369