Diagnostic Feature Selection on Osteoporosis Clinical Data Using Genetic Algorithms

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Outline

- Osteoporosis
- Overview and motivation of the project
  - **Development of New Venn Prediction Methods for Osteoporosis Risk Assessment**
- Why Venn prediction?
- Collected data
- Feature selection with a Genetic Algorithm
- Conclusions and future work

Osteoporosis

- Osteoporosis is a metabolic bone disease in which the bones become more and more fragile, leading to an increased risk of fracture.
- In the European Union one person breaks a bone because of osteoporosis every fifteen seconds.
- Often the first apparent symptom of osteoporosis is a broken bone, which is why the condition is also known as "the silent crippler".
  - Early detection and treatment of osteoporosis can decrease the fracture risk of a person to a minimum.

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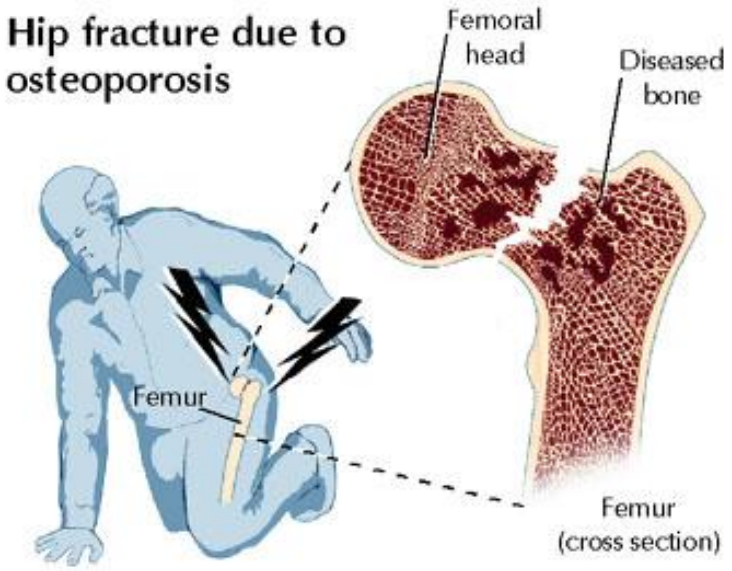

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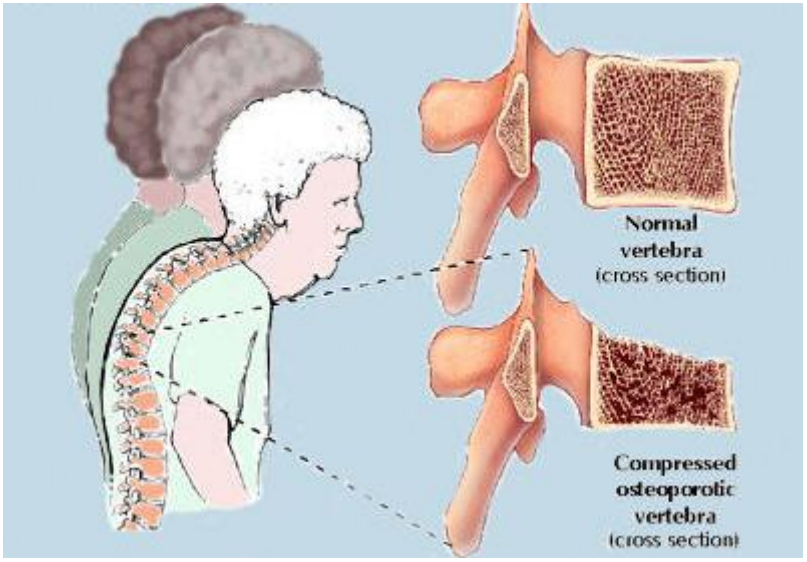
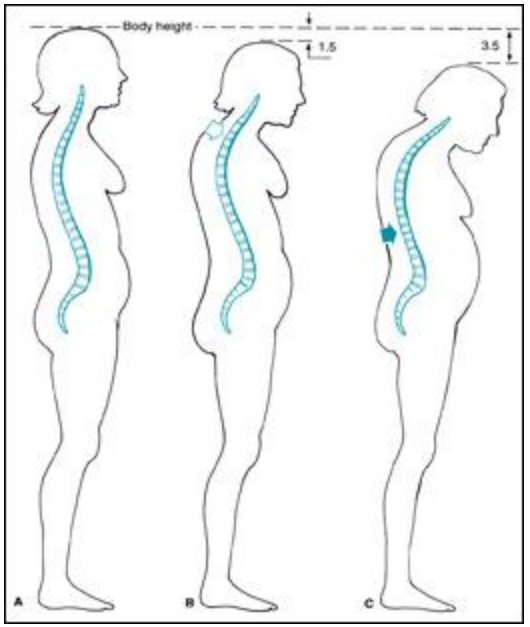
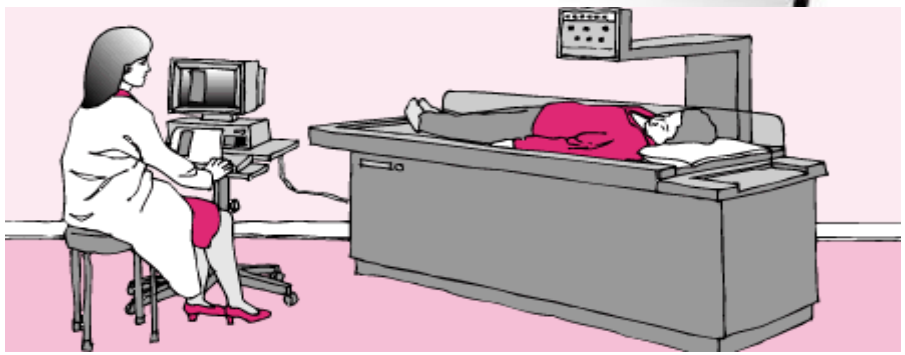




Osteoporosis Detection

- Today's clinical routine is based on:
  - Dual Energy X-Ray Absorptiometry (DEXA) scan



T-score Value	Coding
≤ - 2.5	3 (Osteoporosis)
-2.5 – -1.5	2 (Osteopenia)
-1.5 – 0	1 (poor osteopenia)
≥ 0	0 (normal)

Overview of the Project

- Title: **Development of New Venn Prediction Methods for Osteoporosis Risk Assessment**
- Funded by the **European Regional Development Fund and the Cyprus Government through the Cyprus Research Promotion Foundation**
- Total budget: €163,144
- Partners

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Royal Holloway University of London

ΔΗΜΟΚΡΙΤΕΙΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΡΑΚΗΣ

CYPRUS SOCIETY AGAINST OSTEOPOROSIS AND MYOSKELETAL DISEASES

Overview of the Project

- Main objectives:
  - Development of new Venn Prediction techniques based on **Neural Networks** and **Support Vector Machines**
  - The application of these techniques to the problem of osteoporosis risk assessment
  - Development of a **risk assessment tool** for helping clinicians identify people that should undergo further testing

Motivation

- Classical Machine Learning techniques do not provide any indication about the likelihood of their predictions
- Therefore, most existing Medical Decision Support systems just output the most likely diagnosis of a new patient, without any other information
- This is a major drawback in a medical setting
  - A physician would need to know how reliable each output is
- The aim of this project is to overcome this problem with the use of a novel framework, called **Venn Prediction**, that provides **Probability Intervals**, which are **guaranteed** to contain **well-calibrated probabilities**

Motivation

- Venn Prediction will be applied to the problem of **assessing osteoporosis risk**
  - Helping clinicians identify people that should undergo further testing (DEXA scan)
- The resulting decision support tool will provide probabilistic intervals that will be much more informative than a plain yes or no output

Project Outline

- Data collection
  - Questionnaire containing osteoporosis risk factors
  - The data can be used in the future for the assessment of fracture risk
- Algorithm development
  - Development of new Venn Predictors
- Analysis of the collected data with AI techniques
  - Identification of the most important risk factors
- Algorithm application to the collected data
- Development of risk assessment system
- Pilot application and evaluation of the system

Experimental Demonstration of Venn Prediction (with Neural Networks)

- Two medical datasets
  - *Mammographic Mass*: discrimination between benign and malignant mammographic masses. 961 cases: 516 benign and 445 malignant.
  - *Pima Indians Diabetes*: forecasting the onset of diabetes mellitus in a high-risk population of Pima Indians. 768 cases: 500 positive and 268 negative.
- The NNs were trained with the scaled conjugate gradient algorithm minimizing cross-entropy error
  - Their outputs can be interpreted as probabilities
- Comparison between original NN and NN-VP

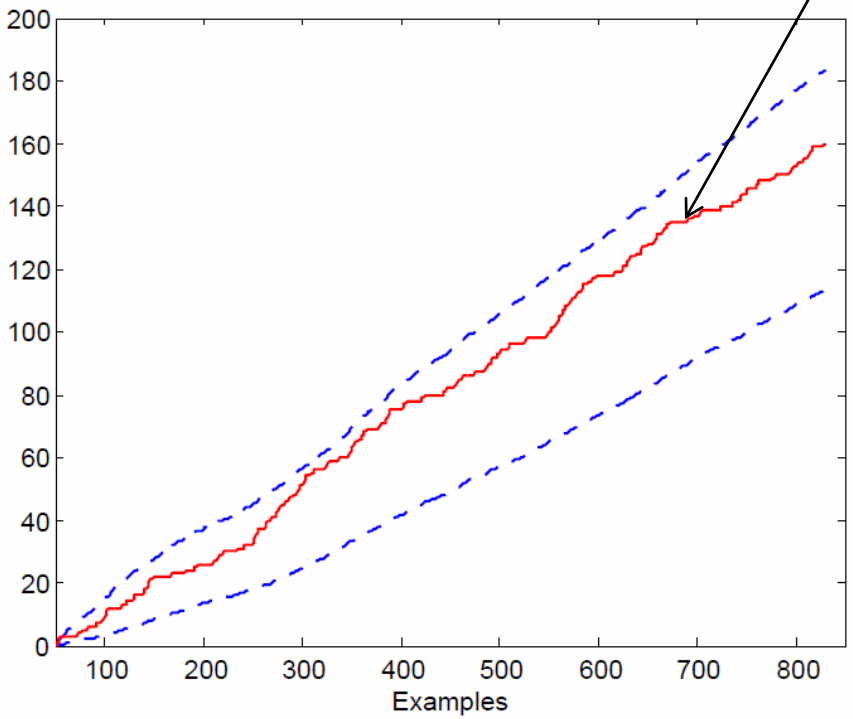
On-line Experiments

- Start with an initial training set containing 50 examples
- Predict each subsequent example
- After prediction each new example is added to the training set (with its true classification) for predicting the next examples

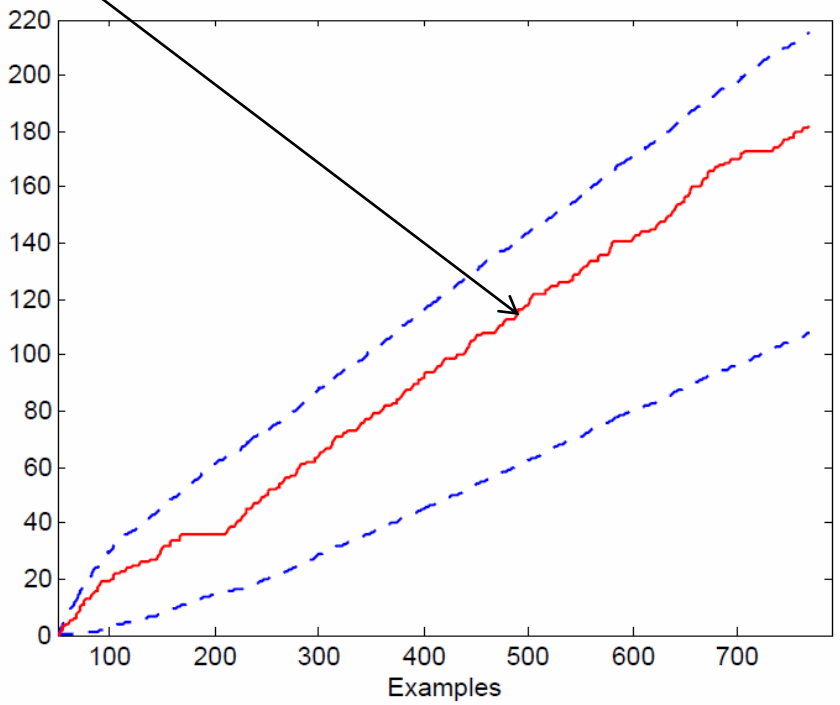
On-line Experiments: NN-VP

Cumulative Error Curve

$$E_n = \sum_{i=1}^{n} err_i$$



(a) Mammographic Mass

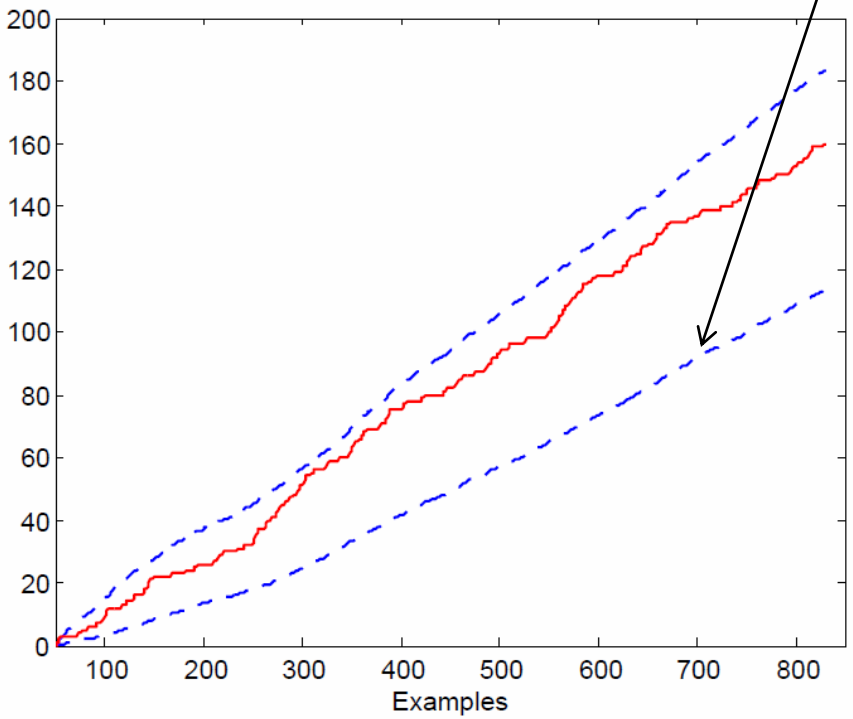


(b) Pima Indians Diabetes

On-line Experiments: NN-VP

Cumulative Lower Error Probability Curve

$$LEP_n = \sum_{i=1}^{n} 1 - U(\hat{y}_i)$$



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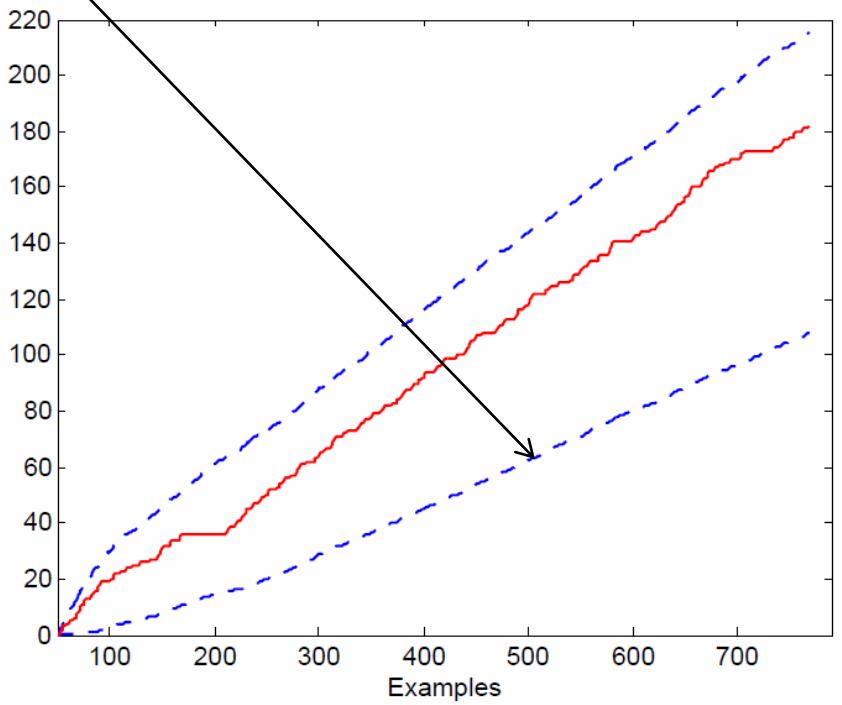
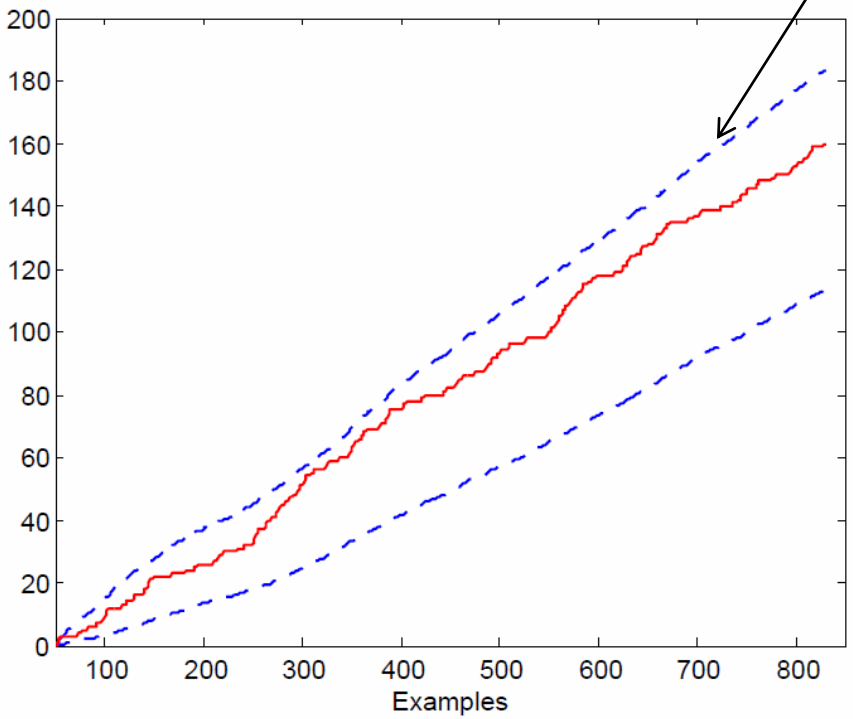


(b) Pima Indians Diabetes

On-line Experiments: NN-VP

Cumulative Upper Error Probability Curve

$$UEP_n = \sum_{i=1}^{n} 1 - L(\hat{y}_i)$$



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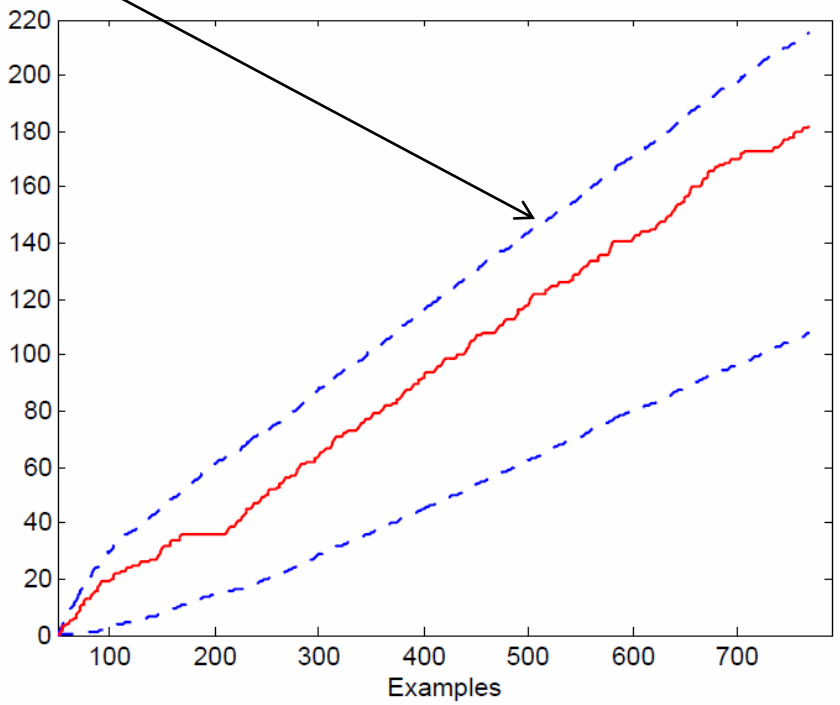
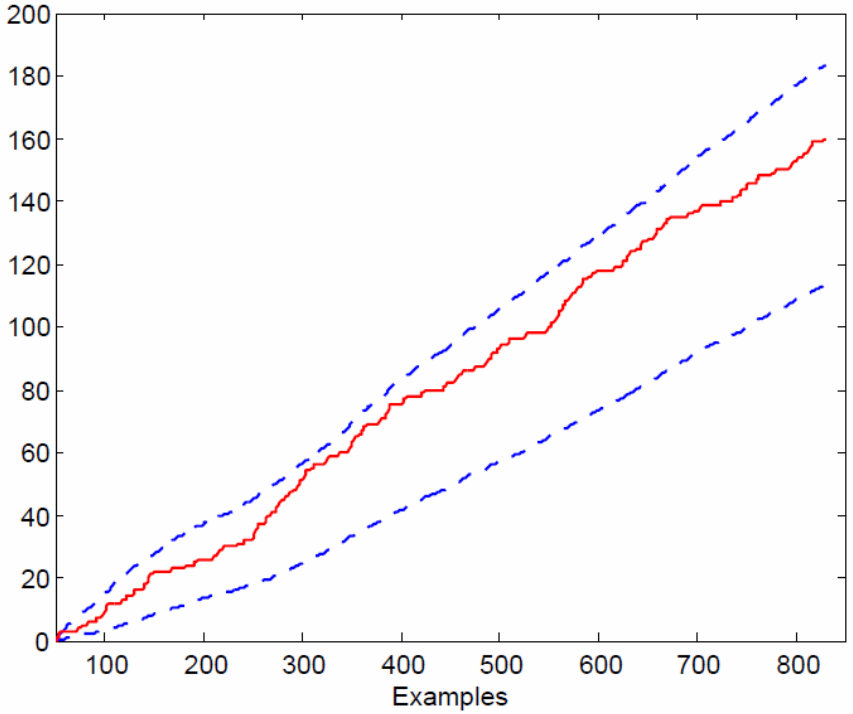


(b) Pima Indians Diabetes

On-line Experiments: NN-VP

- Both plots confirm that the probability intervals are well-calibrated



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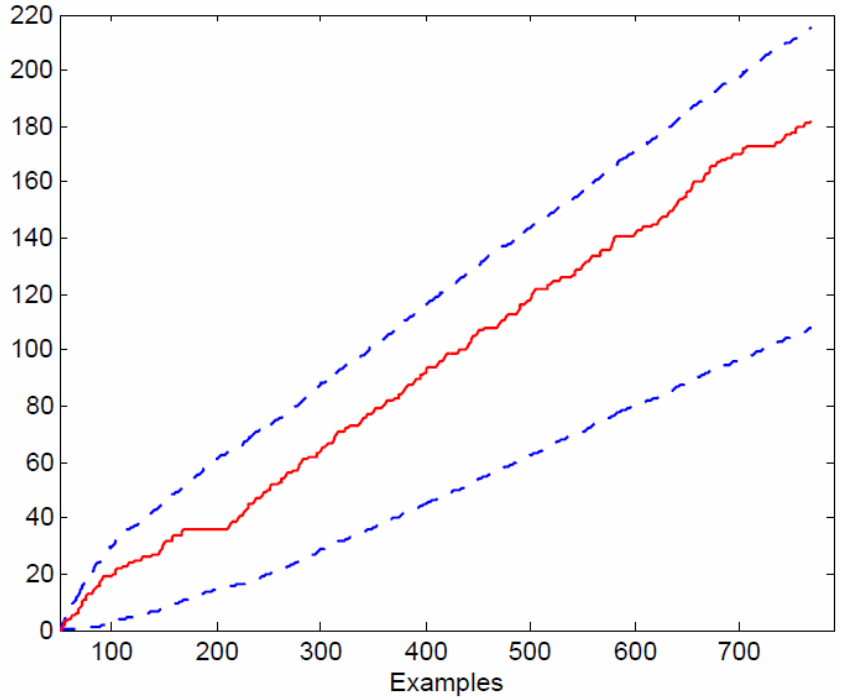
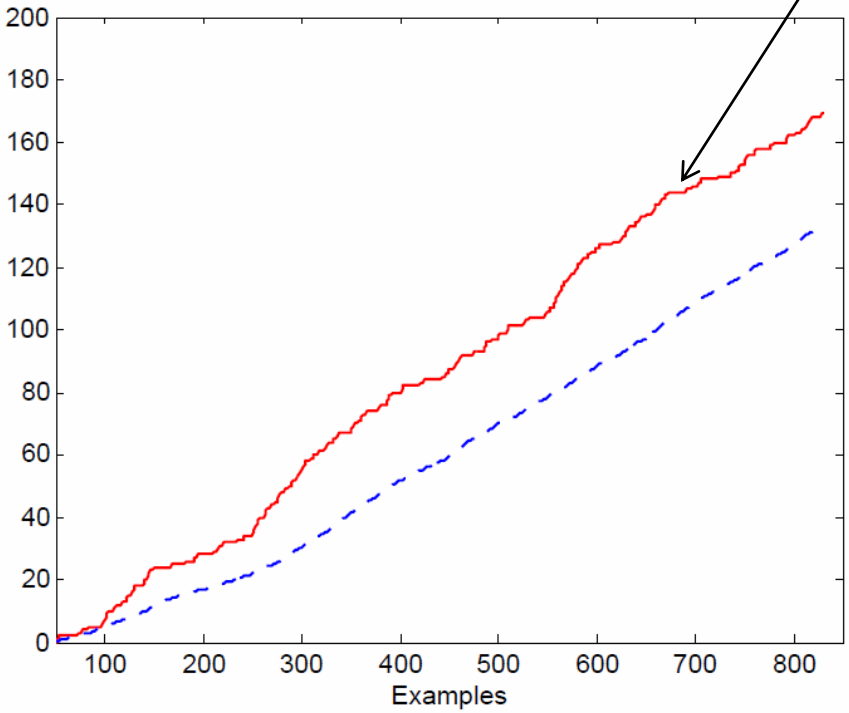


(b) Pima Indians Diabetes

On-line Experiments: Conventional NN

Cumulative Error Curve

$$E_n = \sum_{i=1}^{n} err_i$$



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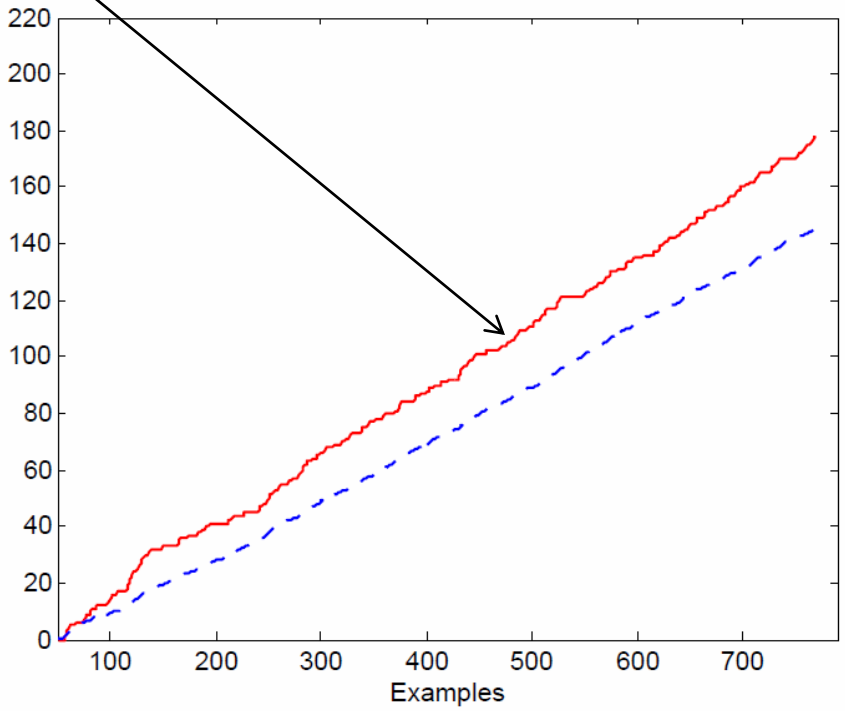
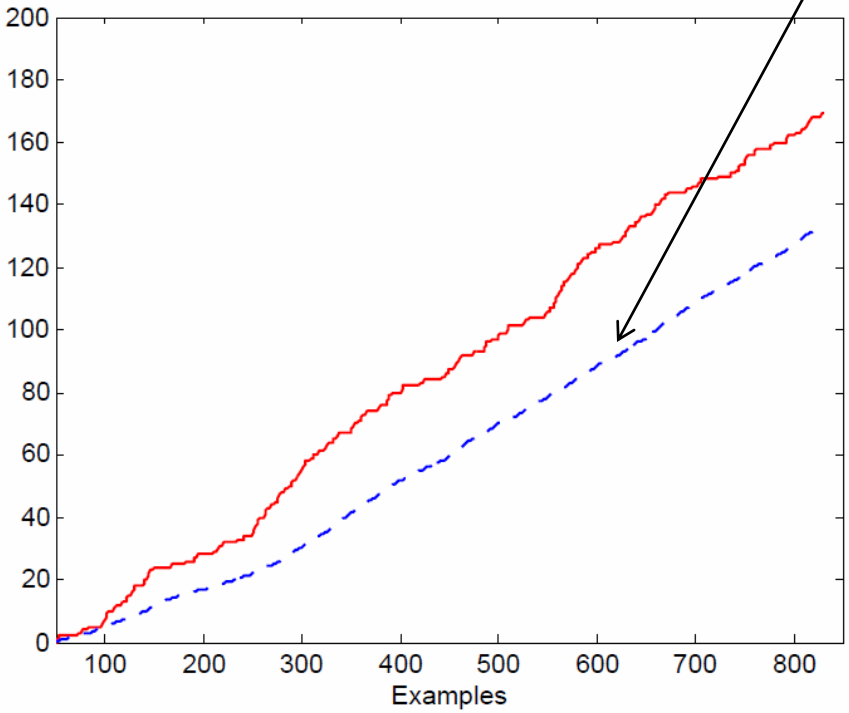


(b) Pima Indians Diabetes

On-line Experiments: Conventional NN

Cumulative Error Probability Curve

$$EP_n = \sum_{i=1}^{n} |\hat{y}_i - \hat{p}_i|$$



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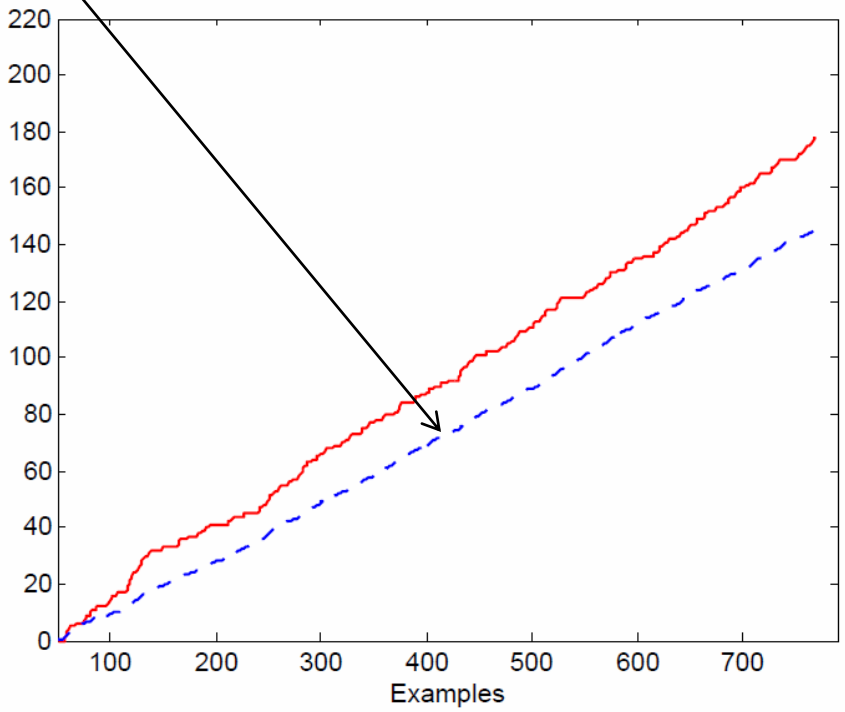
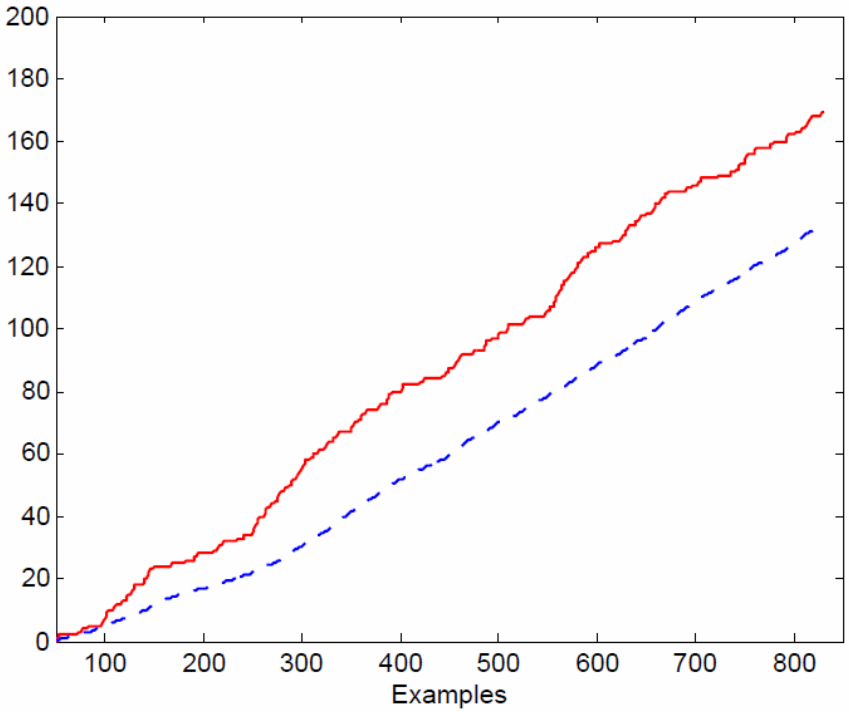


(b) Pima Indians Diabetes

On-line Experiments: Conventional NN

- The p-values of obtaining the resulting total number of errors given the probabilities produced by the ANN were 0.000179 and 0.000548 respectively (extremely unlikely!)



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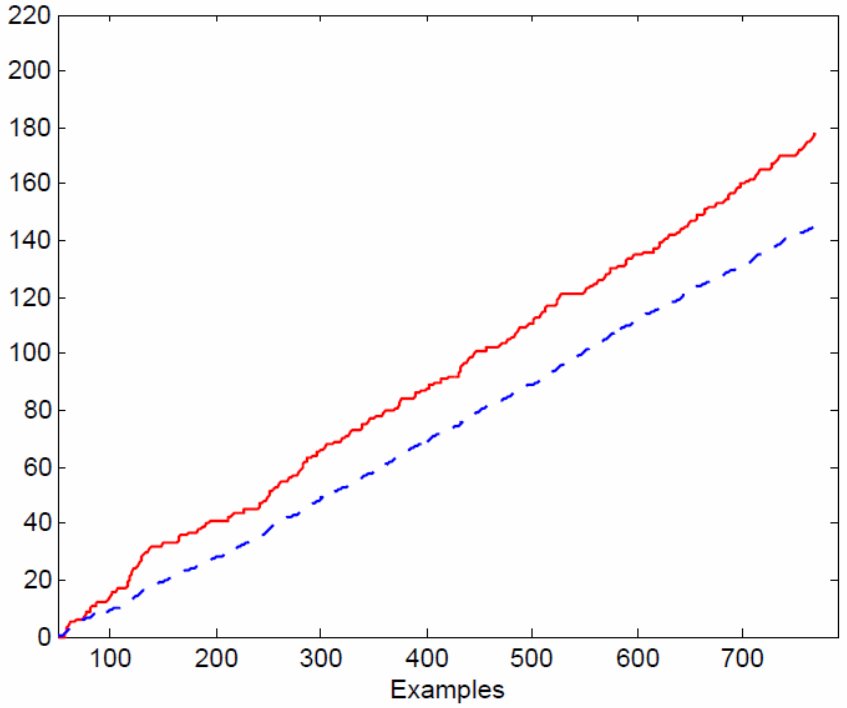

(b) Pima Indians Diabetes

Data (Standalone Information 1)

- Age
- Weight
- Height
- Sex
  - Male
  - Female
- Menstruation
  - Starting Age
  - Ending Age
- Number of pregnancies
- Smoking
  - Now
    - Years of Smoking
    - Cigarettes per day
  - In the past
    - Years of Smoking
    - Cigarettes per day
    - Never
- Alcohol (units/day)
- Caffeine (coffees per day)
- History of previous fracture
  - Yes/No
  - When
- Area of previous fracture
  - Hip
  - Spine
  - Wrist
- Type of fracture
  - High Energy
  - Low Energy
- Exercise more than 30 minutes, 3 times a week
- History of osteoporosis or fracture of the hip in parent

Data (Standalone Information 2)

- Family history of osteoporosis or another bone condition
- Loss of height more than 3 cm
- Kyphosis
- End of menstrual bleeding for more than 12 months for any reason except pregnancy
- Suffer from rheumatoid arthritis
- History of secondary osteoporosis
- Breastfeeding
- Avoid milk and other dairy products
- Men: Incompetence or lack of sexual desire or other symptoms associated with low testosterone levels
- Diarrhea due to chronic bowel disease
  - Yes
    - Condition
  - No
- Receive cortisone
  - Yes
    - Dosage
    - Reason
  - No
- Taking thyroxin
  - Yes
    - For how long
    - Reason
  - No
- Receive estrogen

Data (Previous conditions or surgeries)

- Neurogenic anorexia
- Malabsorption syndrome
- Chronic liver diseases
- Inflammatory bowel diseases
- Transplantation
- Chronic renal failure
- Prolonged immobilization
- Cushing's syndrome
- Epilepsy
- Insulin Dependent P. D
- Ovariectomy before menopause
- Chronic gastrointestinal disorders
- Disease of Paget's Disease
- Hyperthyroidism
- Parathyroid gland disease
  - Yes
    - Which
  - No

Data (Previous/current medicine or treatments)

- Steroids (prednisone, cortisone, etc.)
- Thyroxin
- Anticonvulsants (for seizures, epilepsy)
- Diuretics (Lasix)
- Heparin
- Chemotherapy

- Earlier treatment of osteoporosis (Yes/No)
  - Duration
  - Type of treatment
    - Alendronati 'Fosamax' or 'Fosavance'
    - Risedronati 'Actonel'
    - Zoledronati 'Aclasta' or 'Zomeda'
    - Raloxifeni 'Evista'
    - Strontio 'Protelos'
    - Parathormoni 'Forsteo'
    - Denosoymapi 'Prolia'
    - Kalsitonini 'Miacalcic'
    - Calcium + Vitamin D
    - Calcium
  - Dosage per day

Data (Bone density measurements)

- Lumbar Vertebrae
  - T-Score
  - Z-Score
- Hip
  - T-Score
  - Z-Score
- Neck
  - T-Score
  - Z-Score

Feature Selection with GA and NN

- A Genetic Algorithm together with a Neural Network approach was used to select the best feature subset (out of 33 features)
- Data collected at the Orthopedic Surgery Department of Alexandroupolis University Hospital
  - 589 cases
  - Random division: 80% for training and 20% for testing
- The GA chromosome encoded the inputs and the number of hidden units of the NN
- Fitness function:

$$f = \frac{MSE_p}{< MSE_t >} + \frac{I}{N} + \frac{H}{64}$$

Results

#Exp.	#Gen.	MSEp	I	Features	H
1	1	$1.63 \cdot 10^{-4}$	15	1 3 7 8 10 11 13 15 17 20 23 24 28 30 32	2
1	17	$1.43 \cdot 10^{-4}$	5	2 6 7 10 25	2
1	29	$1.37 \cdot 10^{-4}$	3	3 7 10	1
1	49	$1.37 \cdot 10^{-6}$	2	7 10	1
2	1	$1.85 \cdot 10^{-6}$	12	3 7 8 10 14 15 16 18 23 25 28 32	6
2	19	$1.65 \cdot 10^{-6}$	2	7 10	1

Conclusion

- Our final objective is to develop a medical decision support tool for assessing the probability of a person having osteoporosis.
- The Venn prediction framework, which is being used, provides probabilistic intervals that are guaranteed to contain well calibrated probabilities up to statistical fluctuations
  - Thus providing reliable decision support, which is of paramount importance in a medical setting
- In the particular work a GA was used in conjunction with NN for finding the best feature subset
- Future work
  - Further analysis with other feature subset selection techniques
  - Extension of the dataset
  - Analysis of the findings with doctors

Acknowledgments

- This work was supported by the European Regional Development Fund and the Cyprus Government through the Cyprus Research Promotion Foundation "ΔΕΣΜΗ 2009-2010" research contract ΤΠΕ/OPIZO/0609(BIE)/24 ("Development of New Venn Prediction Methods for Osteoporosis Risk Assessment").

Thank you for listening