university of groningen

University of Cyprus

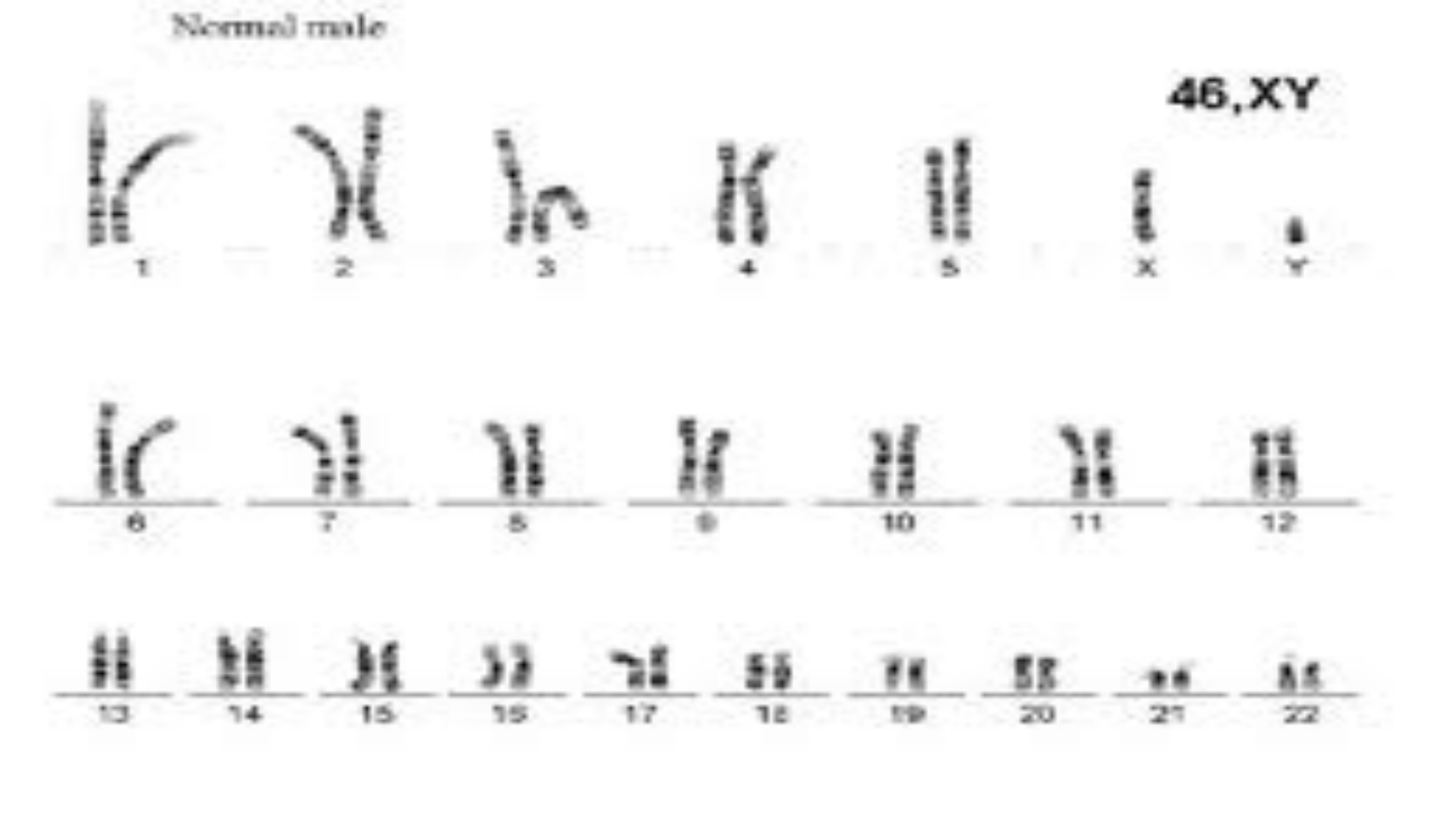
Non-invasive prenatal diagnosis of aneuploidy

Andreas Neocleous, Sep. 2015

university of groningen

University of Cyprus

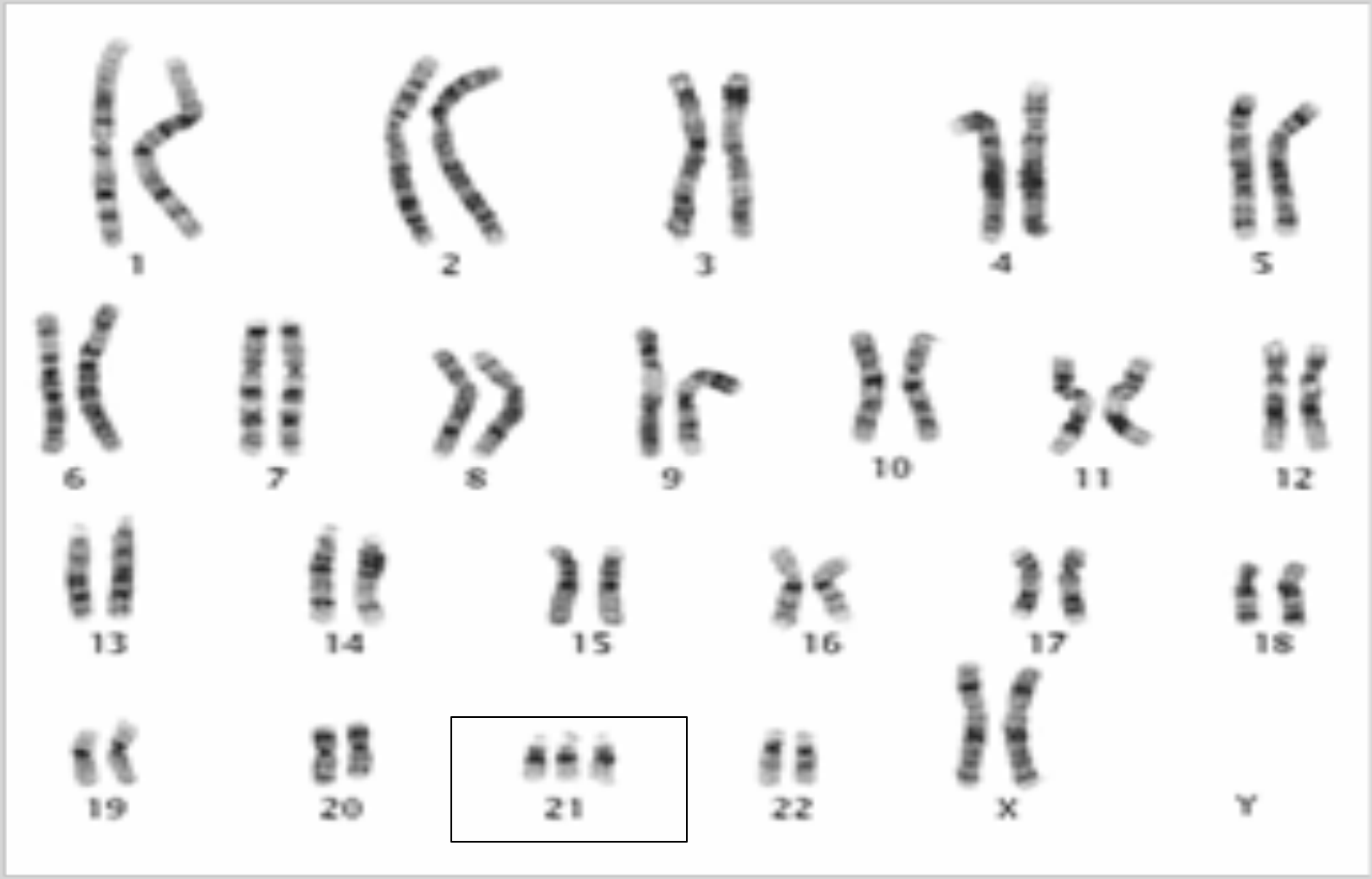
Euploidy (=normal case: 2 copies of each chromosome)



university of groningen

University of Cyprus

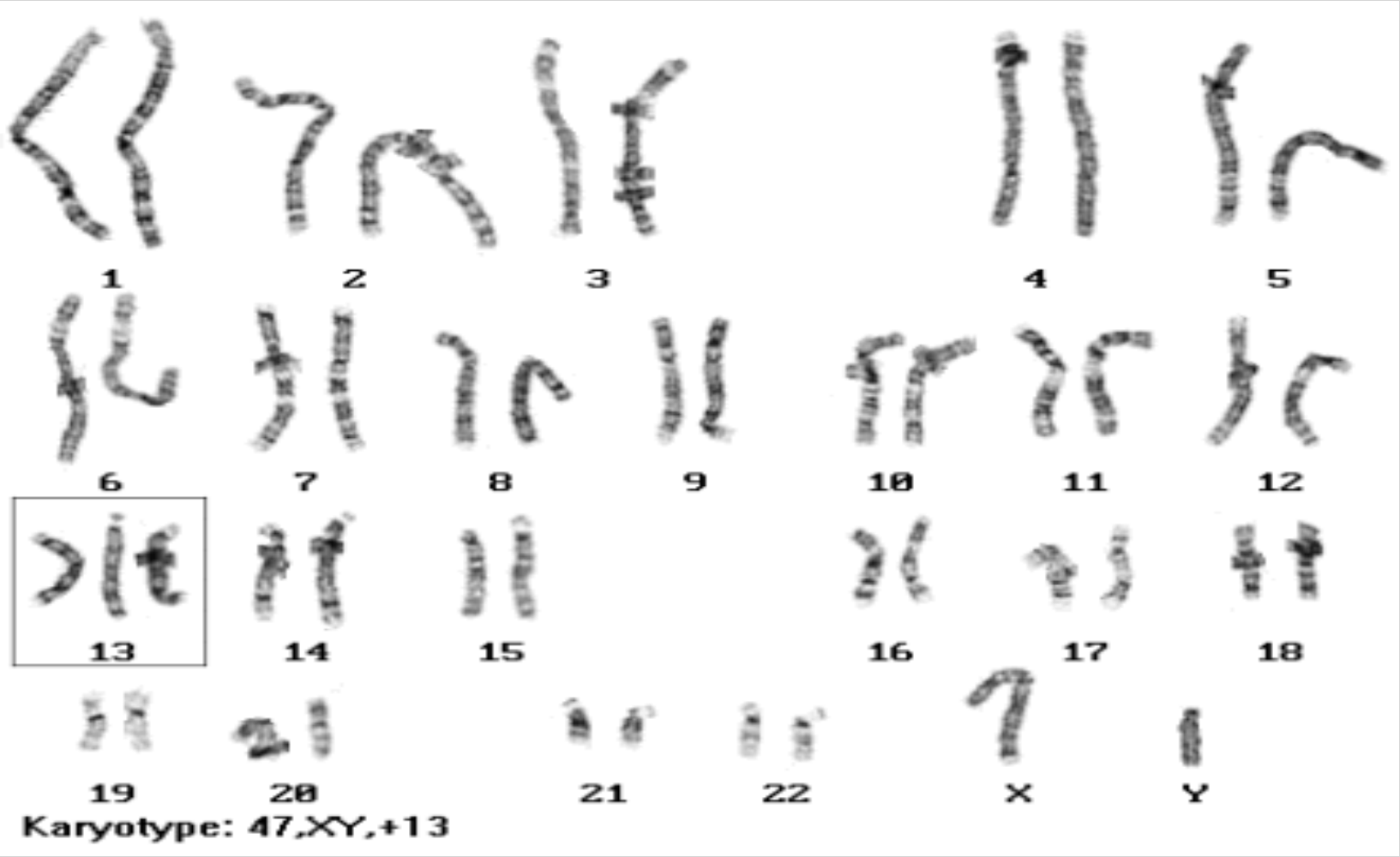
Aneuploidy (=chromosome abnormality), here: trisomy 21)



university of groningen

University of Cyprus

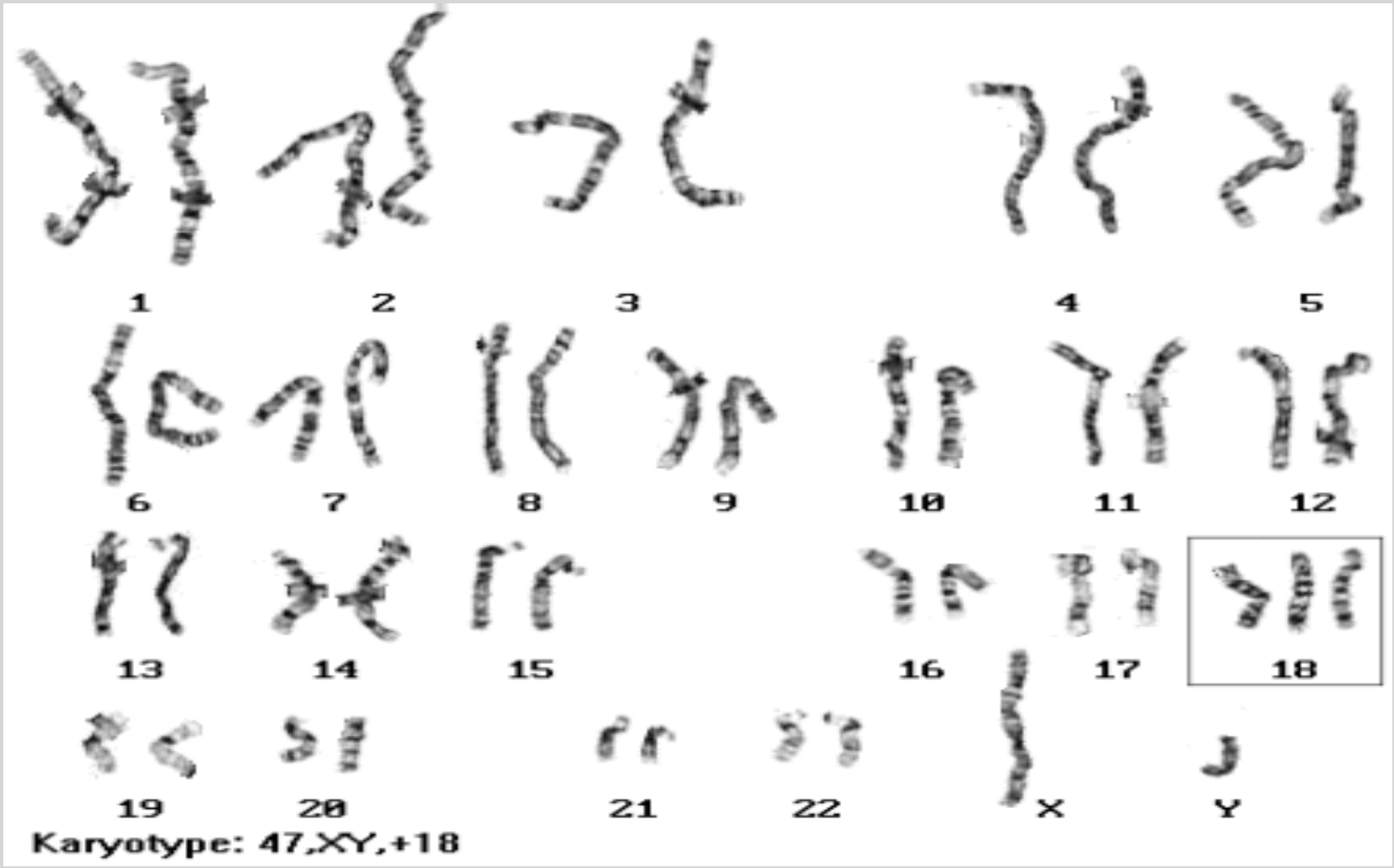
Aneuploidy: here – trisomy 13



university of groningen

University of Cyprus

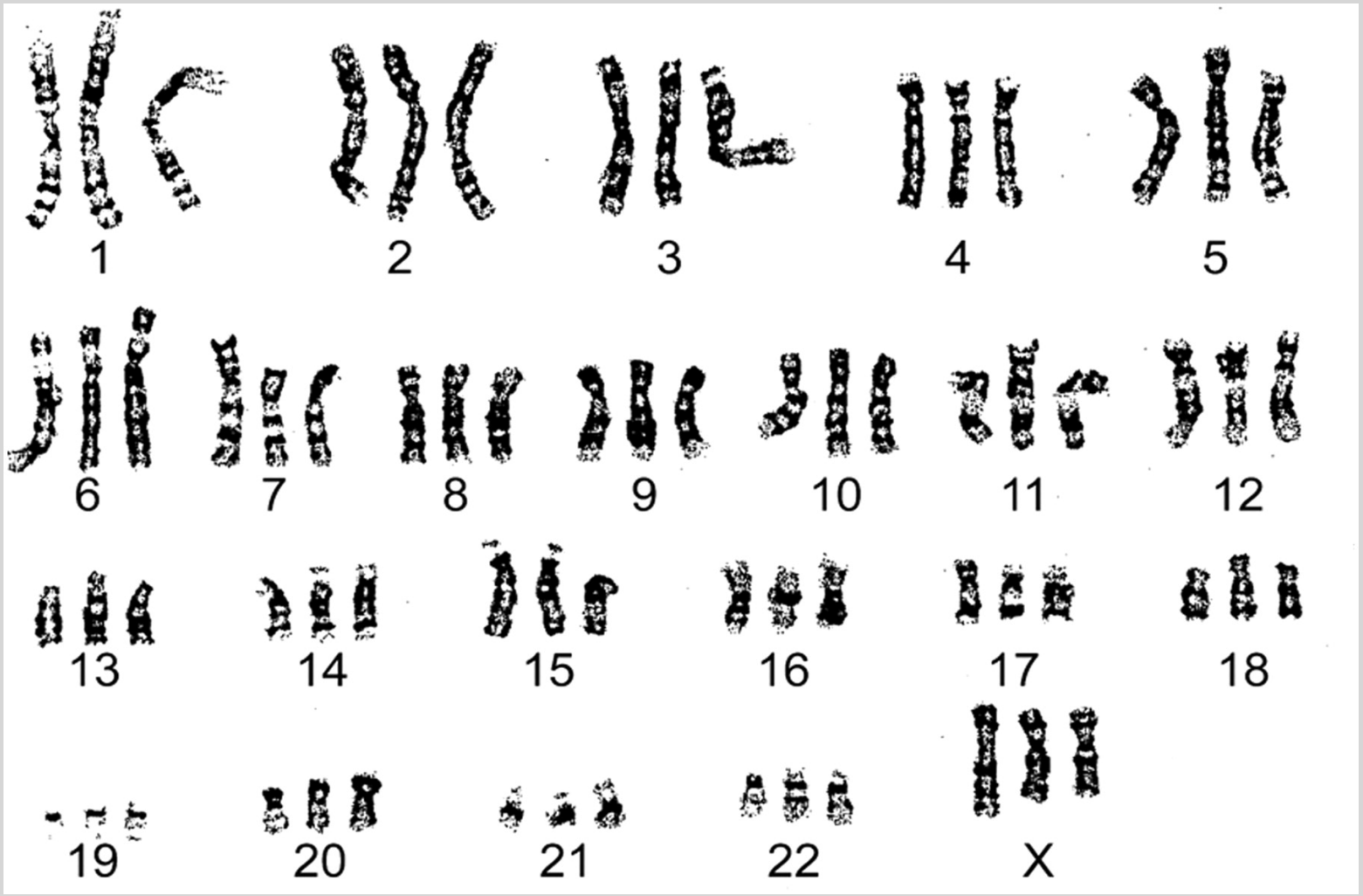
Aneuploidy: here – trisomy 18



university of groningen

University of Cyprus

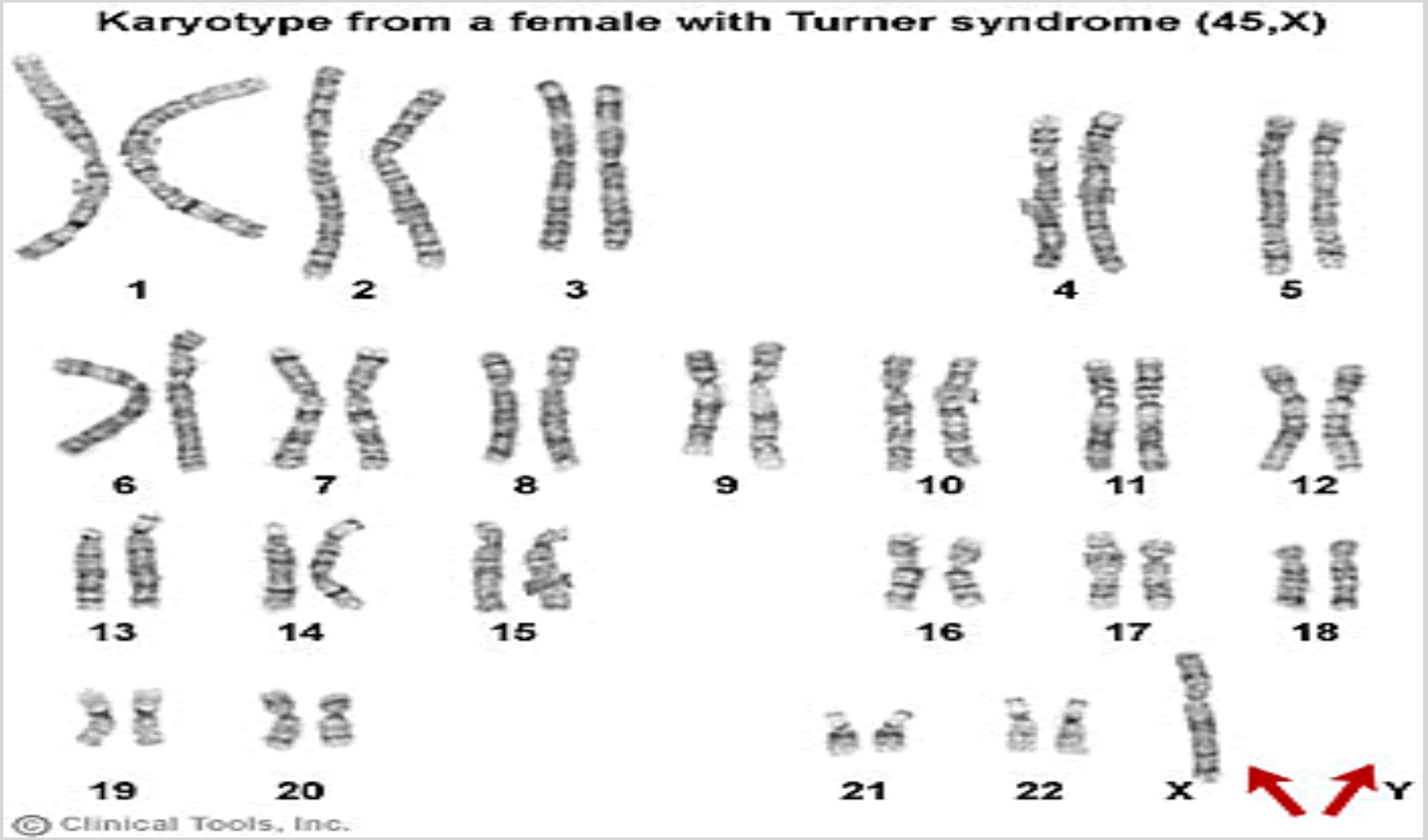
Aneuploidy: here – triploidy



university of groningen

University of Cyprus

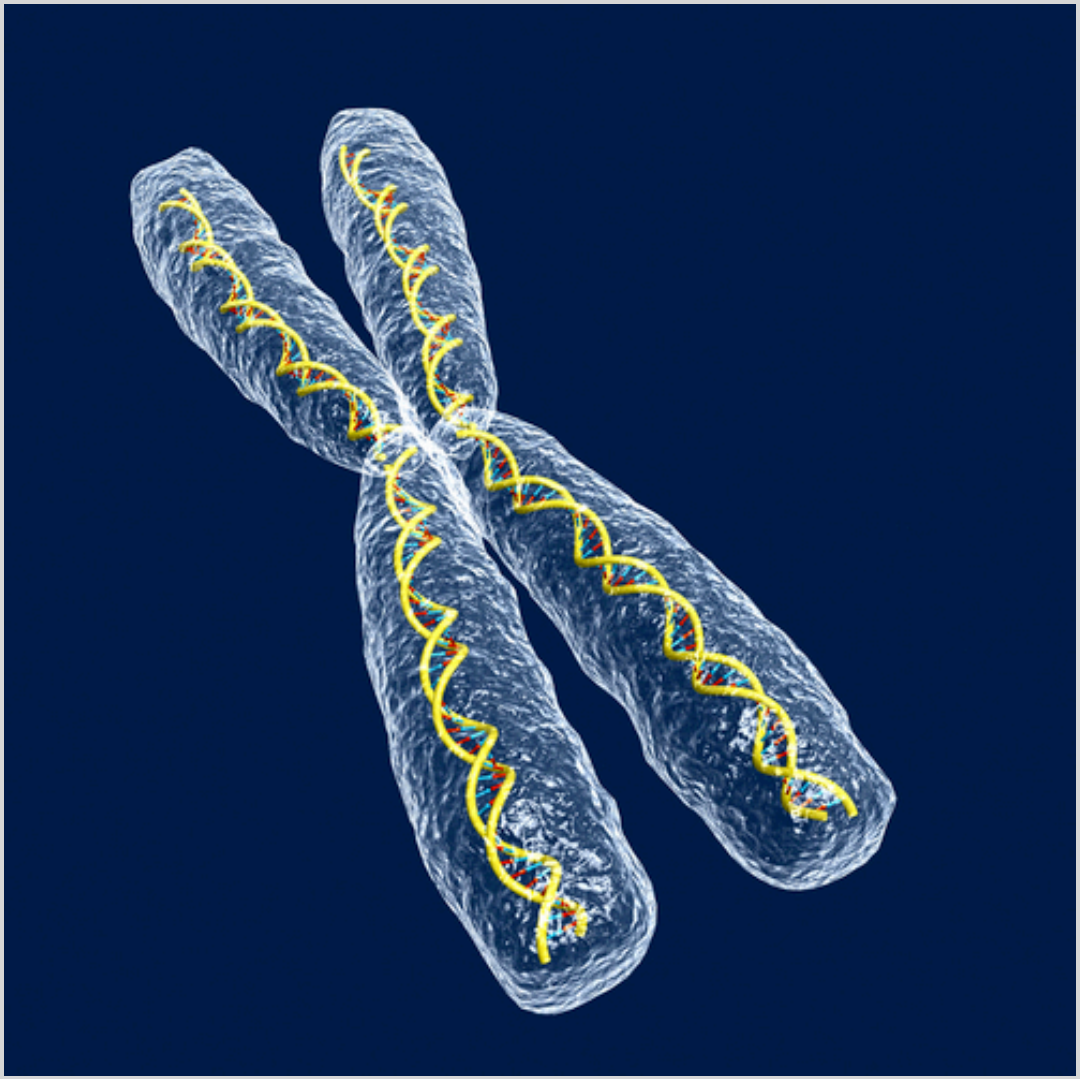
Aneuploidy: here – Turner



university of groningen

University of Cyprus

Chromosome structure



university of groningen

University of Cyprus

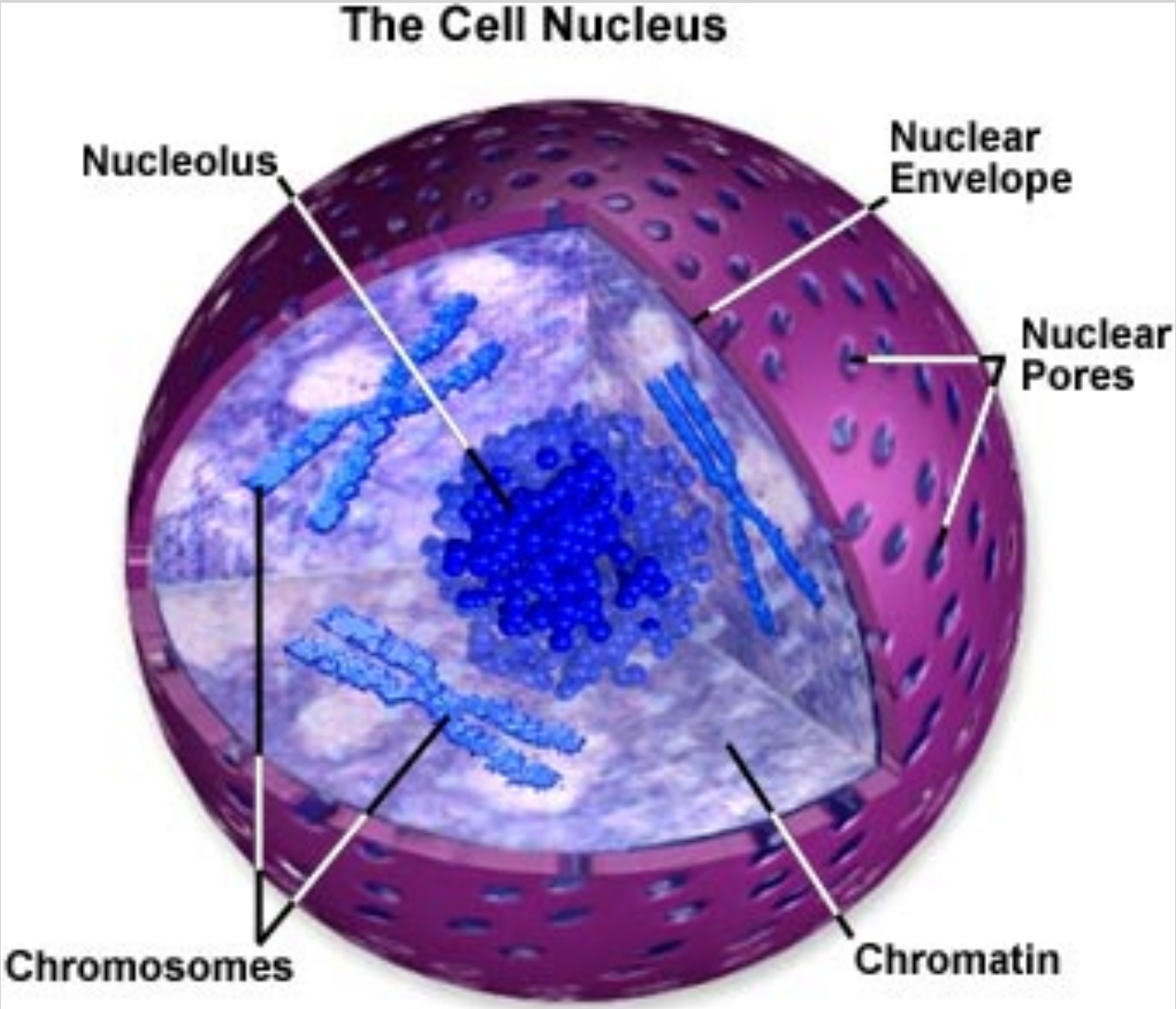
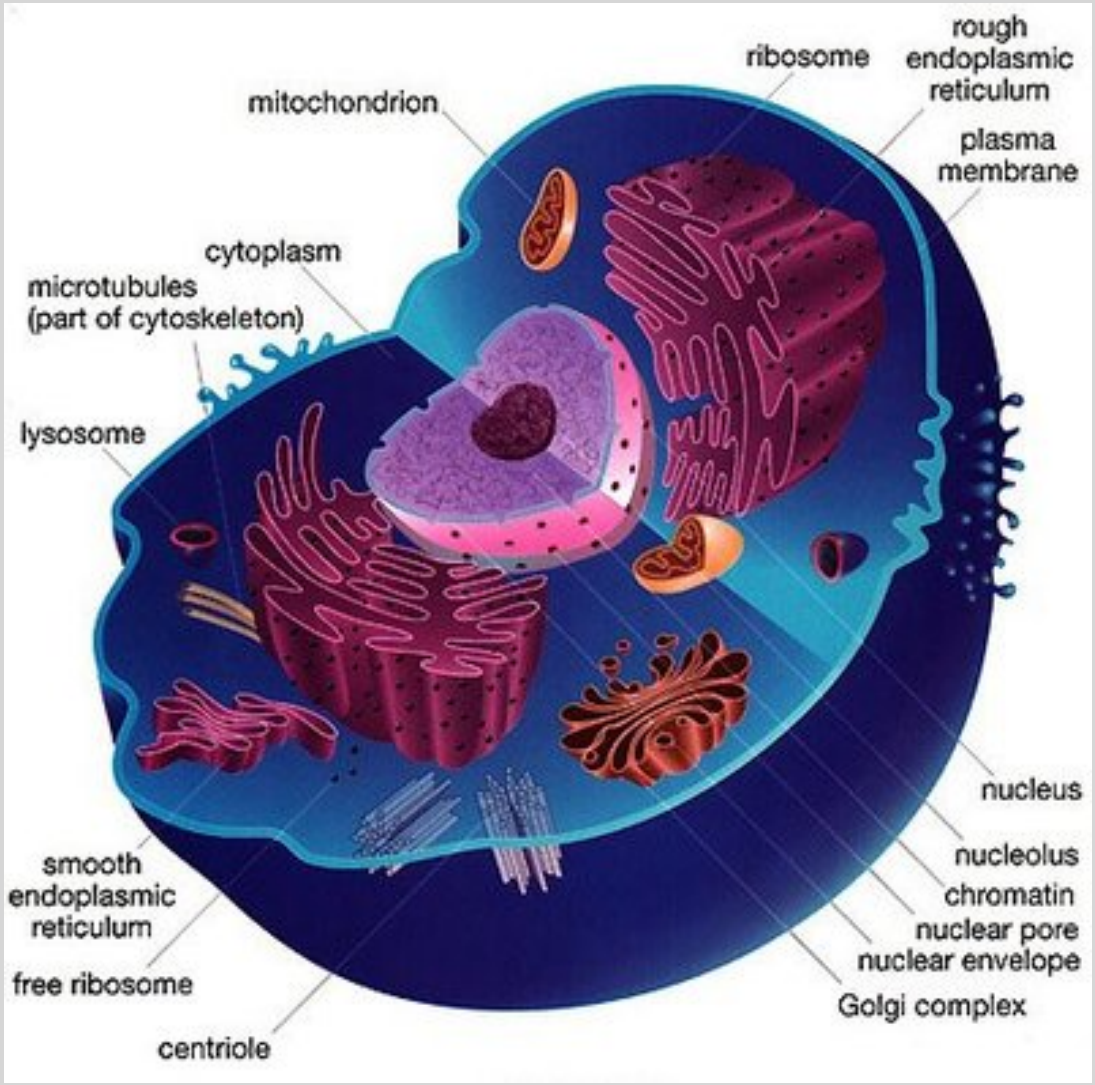


Figure 1

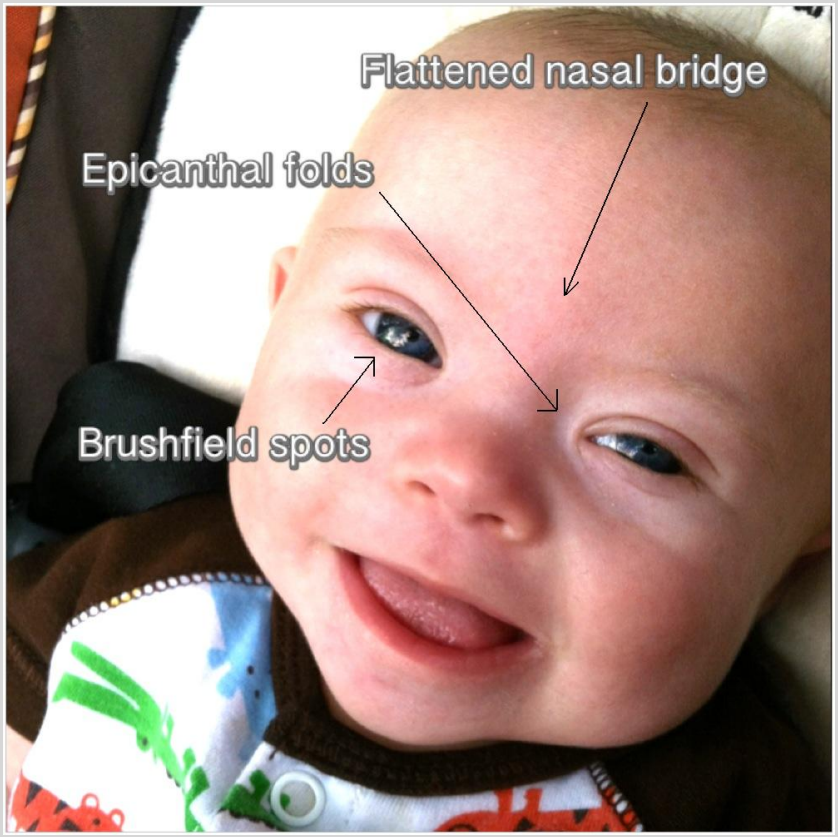
university of groningen

University of Cyprus

Human cell



Down syndrome (trisomy 21)



university of groningen

University of Cyprus

Patau syndrome (trisomy 13)

university of groningen

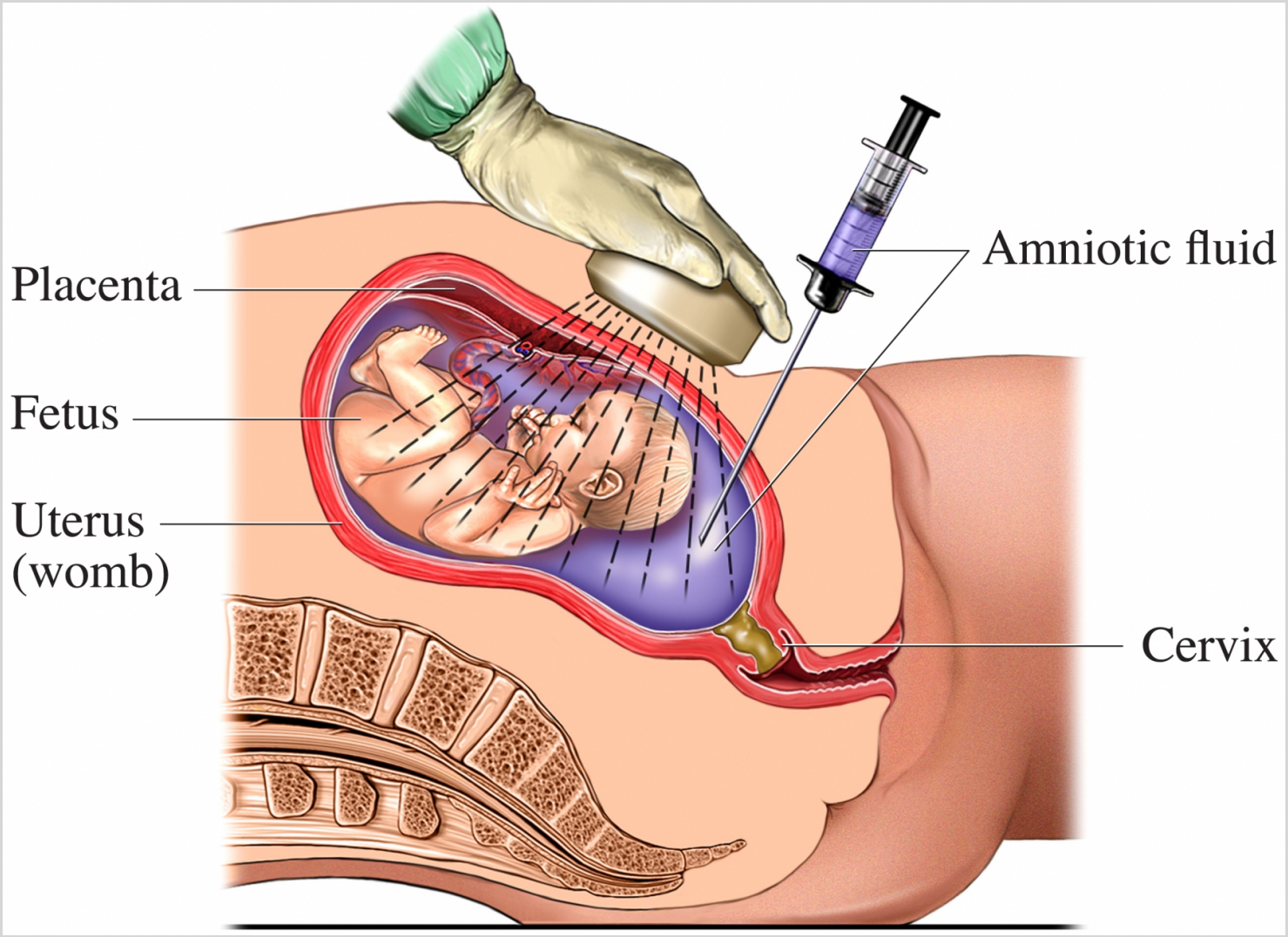
University of Cyprus

Edwards syndrome (trisomy 18)

university of groningen

University of Cyprus

Amniocentesis (taking amniotic fluid)



university of groningen

University of Cyprus

Amniocentesis

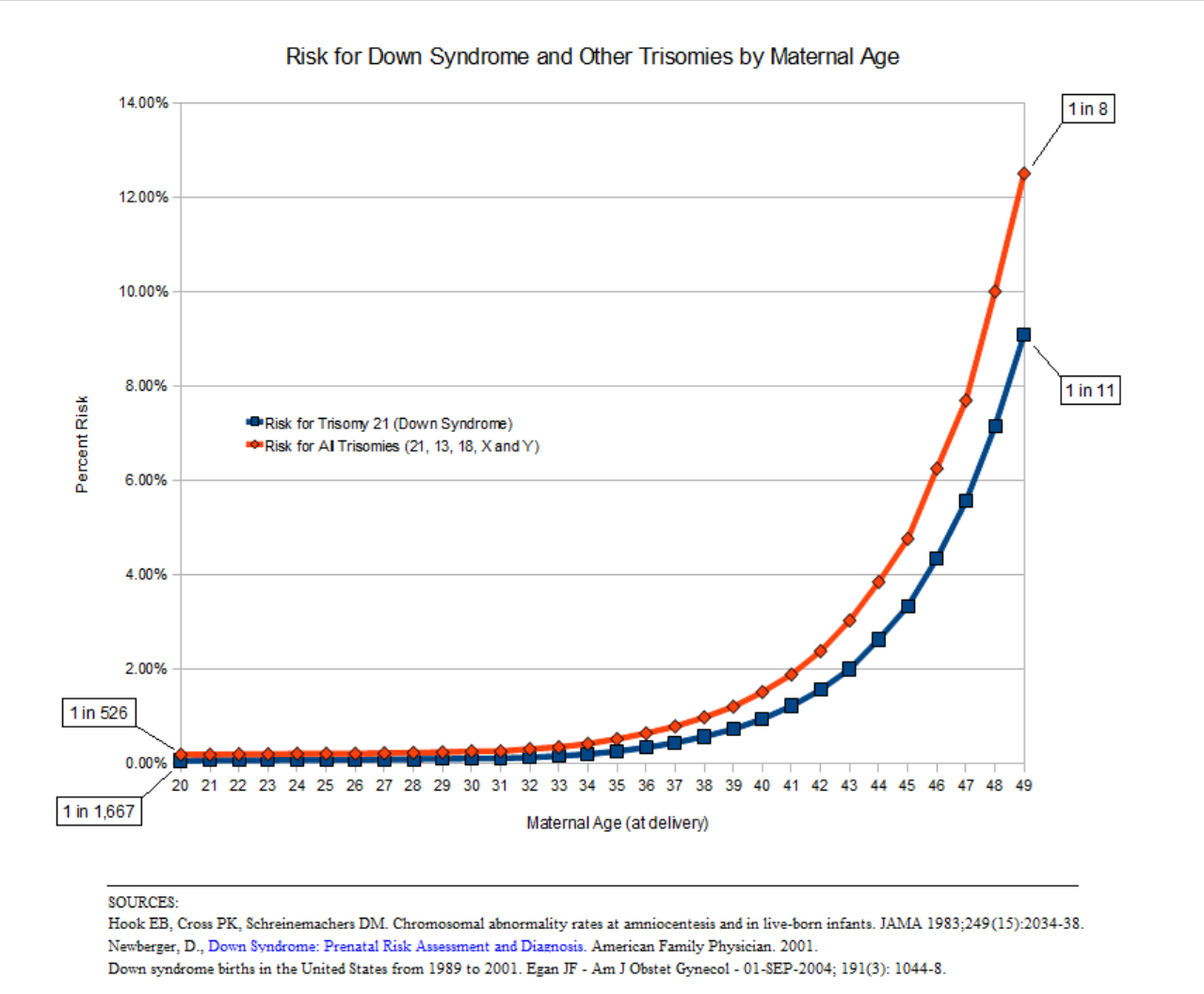
Drawbacks:

- invasive test
- fetal miscarriage risk ~ 3%
- infection risk
- expensive

university of groningen

University of Cyprus

Amniocentesis 1980-90



SOURCES:

Hook EB, Cross PK, Schreinemachers DM. Chromosomal abnormality rates at amniocentesis and in live-born infants. JAMA 1983;249(15):2034-38.

Newberger, D., Down Syndrome: Prenatal Risk Assessment and Diagnosis. American Family Physician. 2001.

Down syndrome births in the United States from 1989 to 2001. Egan JF - Am J Obstet Gynecol - 01-SEP-2004; 191(3): 1044-8.

Prenatal examination

- Maternal and fetal physiological characteristics
- Ultrasonographic fetal screening

university of groningen

University of Cyprus

Maternal physiological characteristics (features)

- Age
- Heart rate
- Weight
- Smoking
- Parity
- Diabetes
- PAPP-A (Protein Coding gene)
- b-hCG (glycoprotein hormone)

Other:

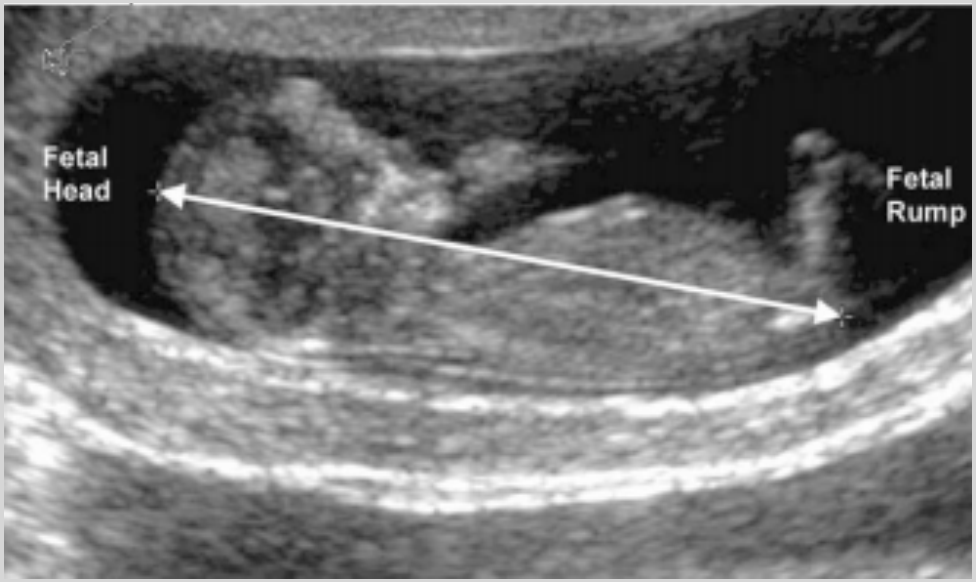
- Conception
- History of previous aneuploidy

Fetal physiological characteristics (features)

- Heart rate
- Crown rump length (CRL)
- Nuchal translucency (NT)
- Nasal bone
- Tricuspid flow
- Ductus venosus flow

Fetal physiological characteristics (features)

- Heart rate
- **Crown rump length (CRL)**
- Nuchal translucency (NT)
- Nasal bone
- Tricuspid flow
- Ductus venosus flow

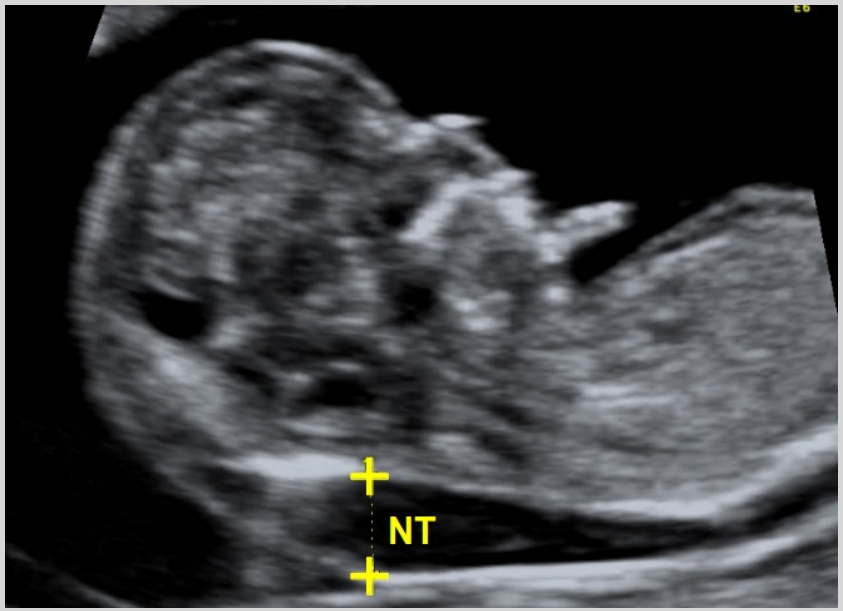


university of groningen

University of Cyprus

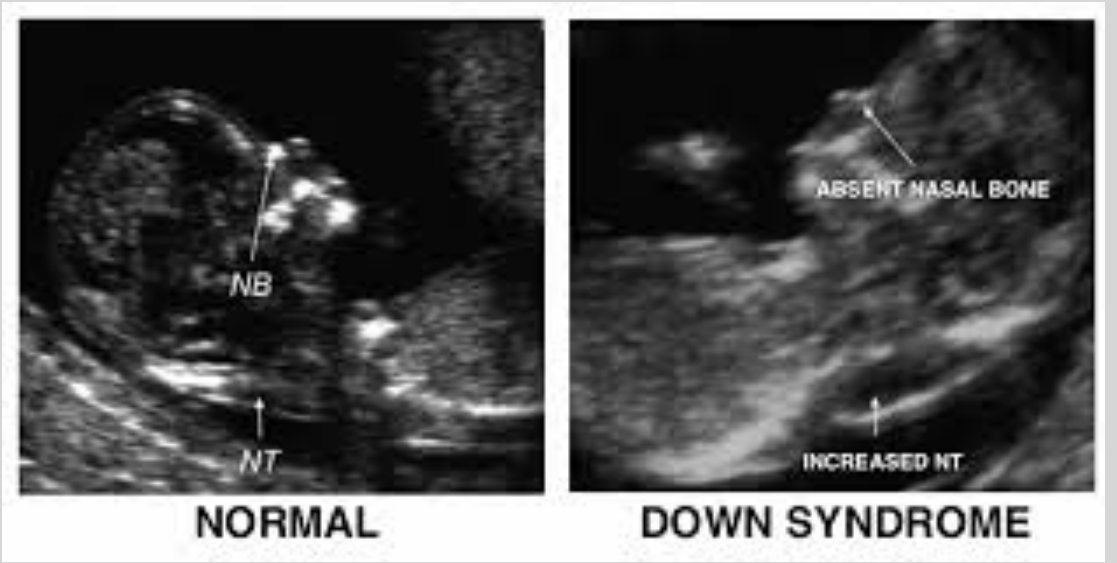
Fetal physiological characteristics

- Heart rate
- Crown rump length (CRL)
- **Nuchal translucency (NT)**
- Nasal bone
- Tricuspid flow
- Ductus venosus flow



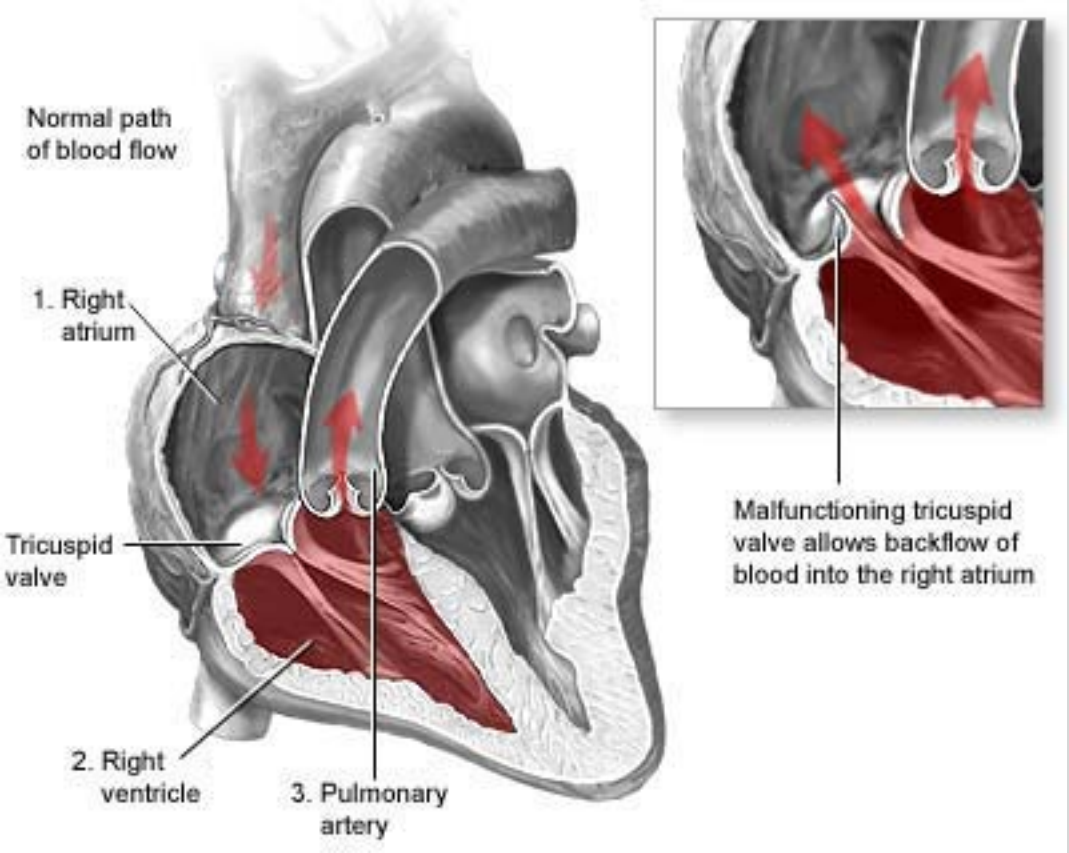
Fetal physiological characteristics

- Heart rate
- Crown rump length (CRL)
- Nuchal translucency
- **Nasal bone**
- Tricuspid flow
- Ductus venosus flow



Fetal physiological characteristics

- Heart rate
- Crown rump length (CRL)
- Nuchal translucency
- Nasal bone
- **Tricuspid flow**
- Ductus venosus flow



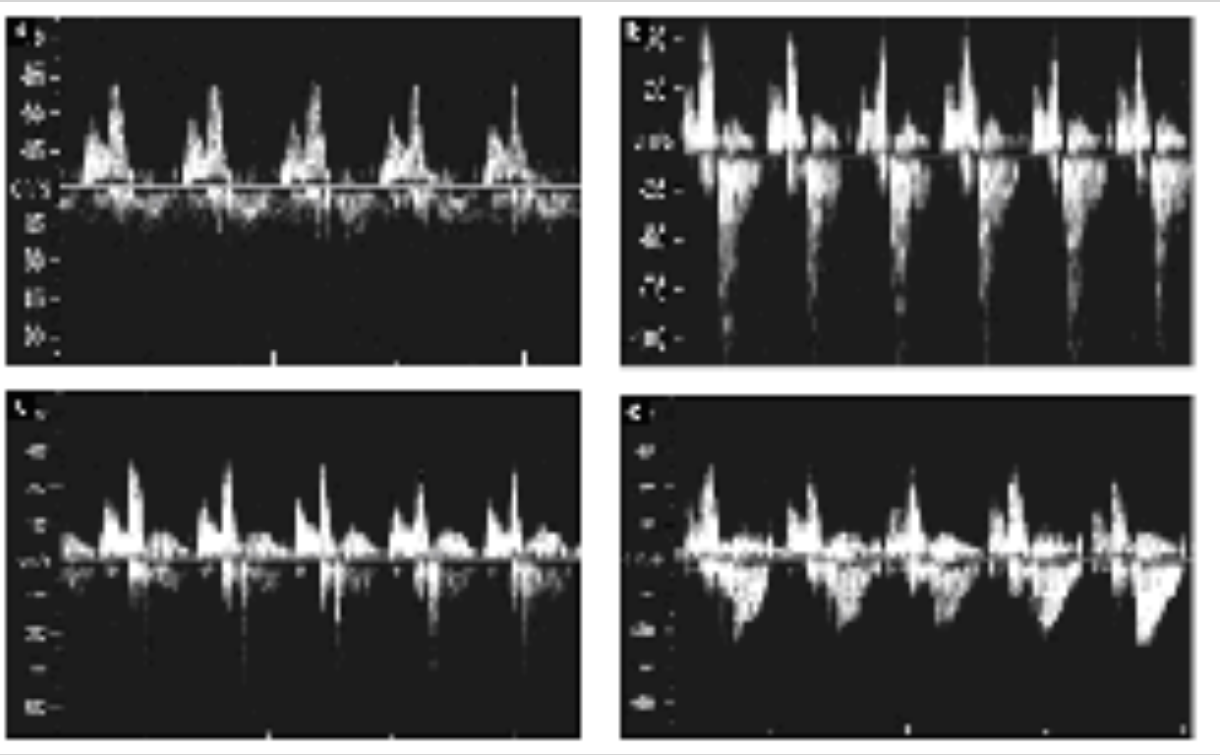
Fetal physiological characteristics

- Heart rate
- Crown rump length (CRL)
- Nuchal translucency
- Nasal bone
- **Tricuspid flow**
- Ductus venosus flow

Doppler flow profile

Normal

Abnormal

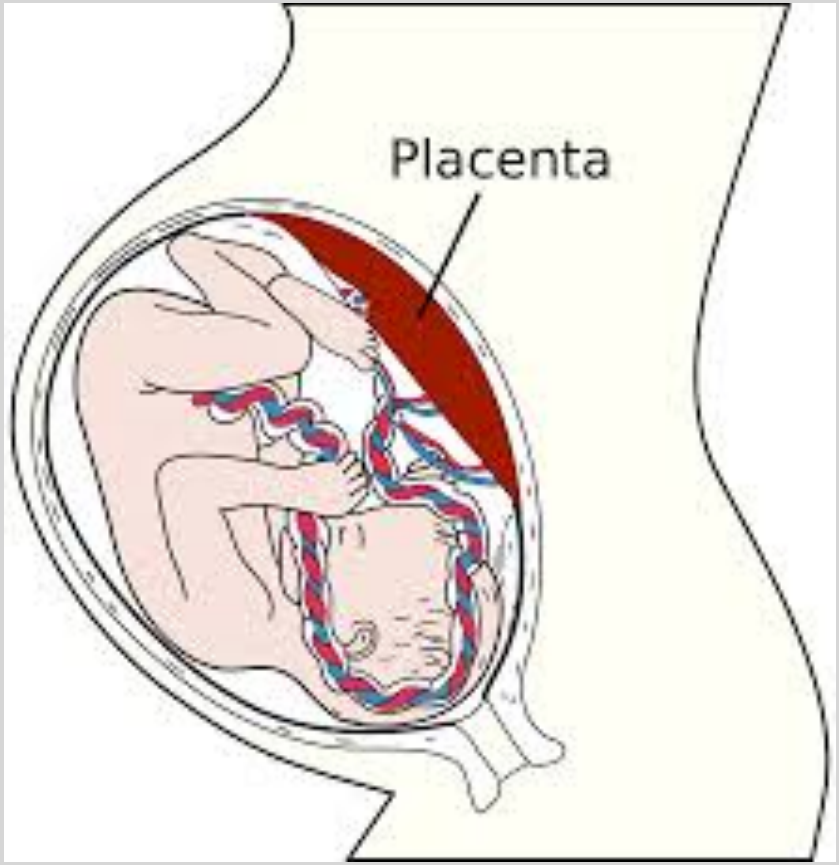


university of groningen

University of Cyprus

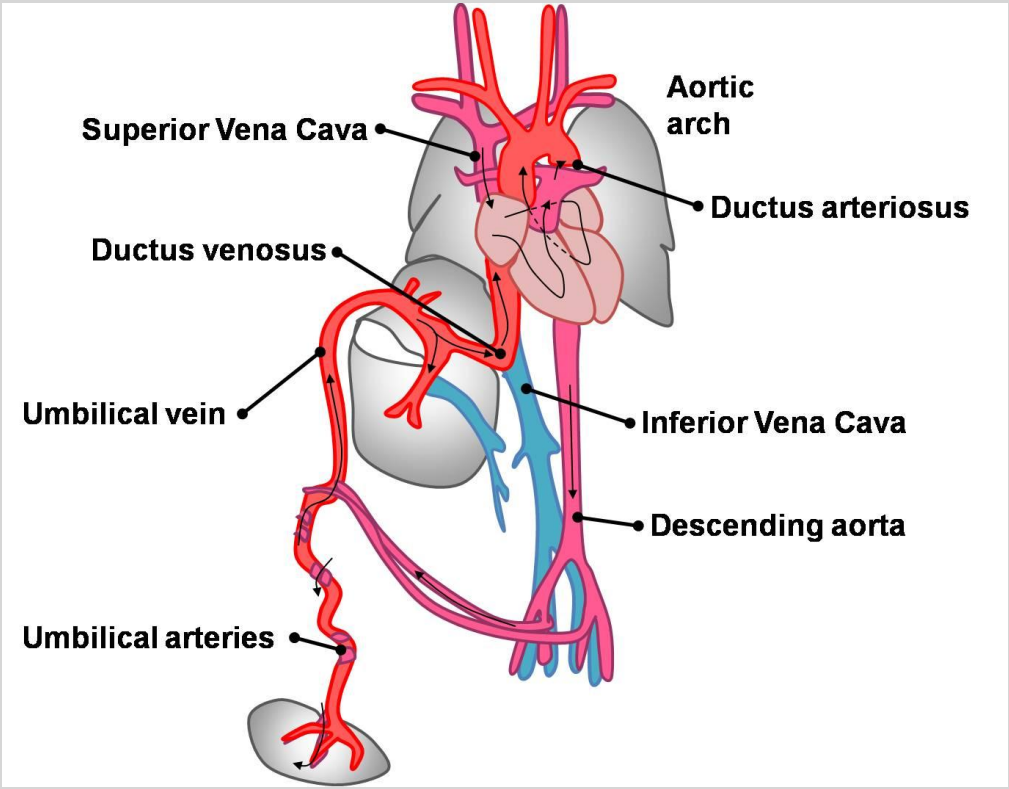
Fetal physiological characteristics

- Heart rate
- Crown rump length (CRL)
- Nuchal translucency
- Nasal bone
- Tricuspid flow
- **Ductus venosus flow**



Fetal physiological characteristics

- Heart rate
- Crown rump length (CRL)
- Nuchal translucency
- Nasal bone
- Tricuspid flow
- **Ductus venosus flow**



Data set

This is a highly imbalanced data set!

Euploidy: 29791
T21: 124
T13: 10
T18: 42
Triploidy: 14
Turner: 19

→

Euploidy: 29791
Aneuploidy: 209 (much smaller number!)

↓

Data reduction

(of the number of euploidy representatives)

↓

Euploidy: 200
Aneuploidy: 209

The two classes are now represented by equal numbers of representatives

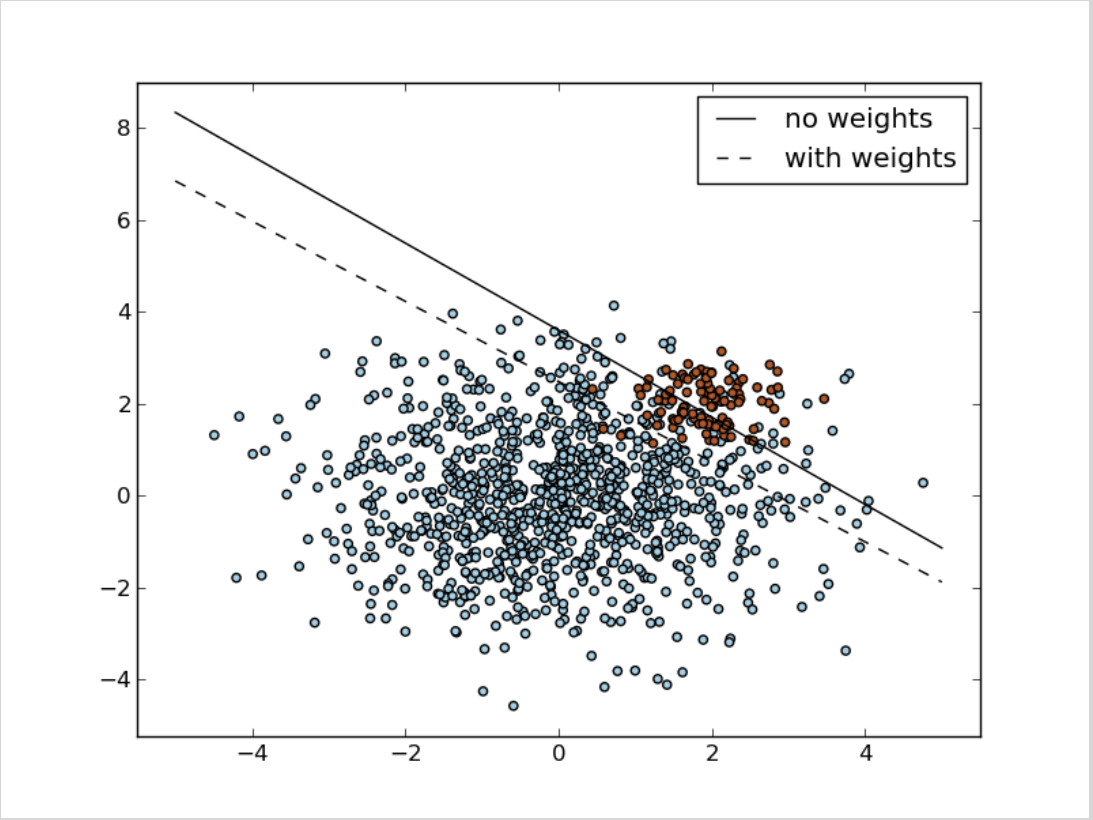
↓

Classifier

The problem of an imbalanced data set

Examples can be fond in:

- Telecommunications
- Web
- Finance-world
- Ecology
- Biology
- Medicine
- others



If the total number of misclassifications is minimized, the boundary will be pushed away from the large class and this will lead to many misclassifications of the smaller class that might be of higher interest (as in medicine)

The problem of an imbalanced data set

- Prior probabilities of different classes
- Biased towards the majority class
- Higher misclassification rate for the minority class

Ex: Naive Bayes classifier

$$p(C_k|\mathbf{x}) = \frac{p(C_k)\ p(\mathbf{x}|C_k)}{p(\mathbf{x})}.$$

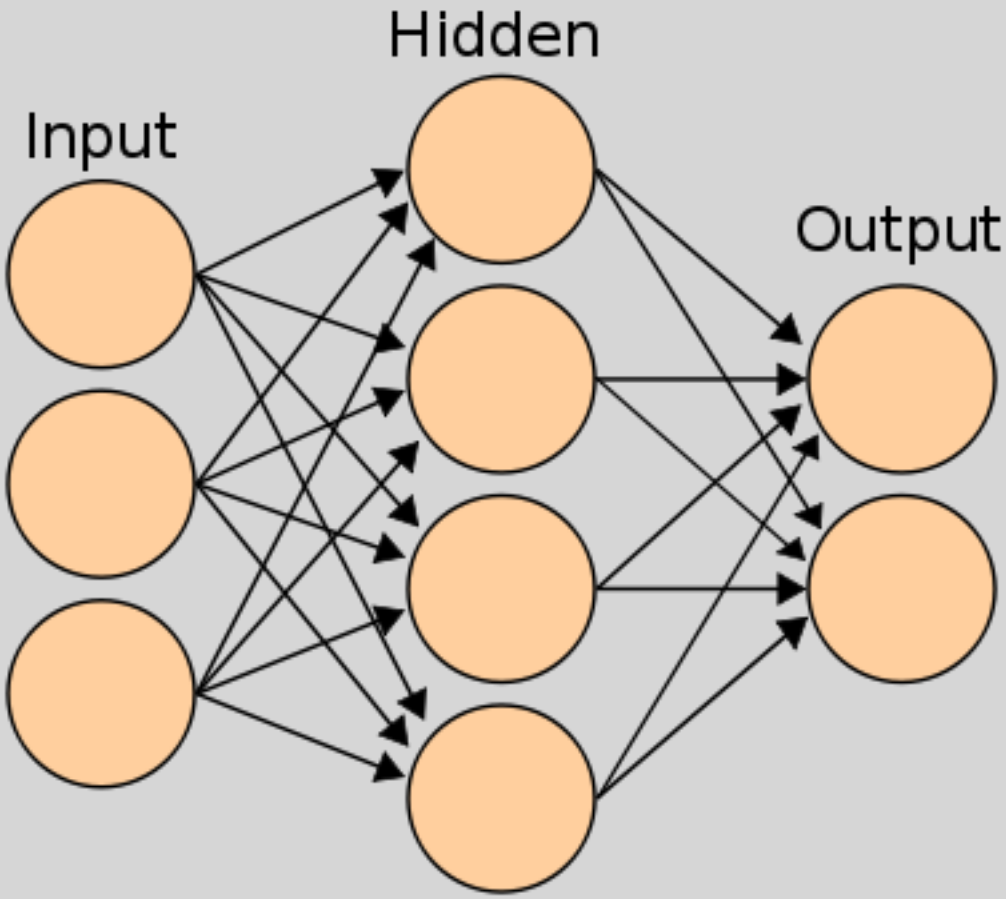
Solutions to the problem of an imbalanced data set

- By data sampling
  - Under-sampling (of the larger class)
  - Over-sampling (of the smaller class)
- By algorithm modification
  - Adaptation of the learning method to class imbalance issues
- Cost-sensitive learning
  - Higher costs for the misclassification of the minority class

university of groningen

University of Cyprus

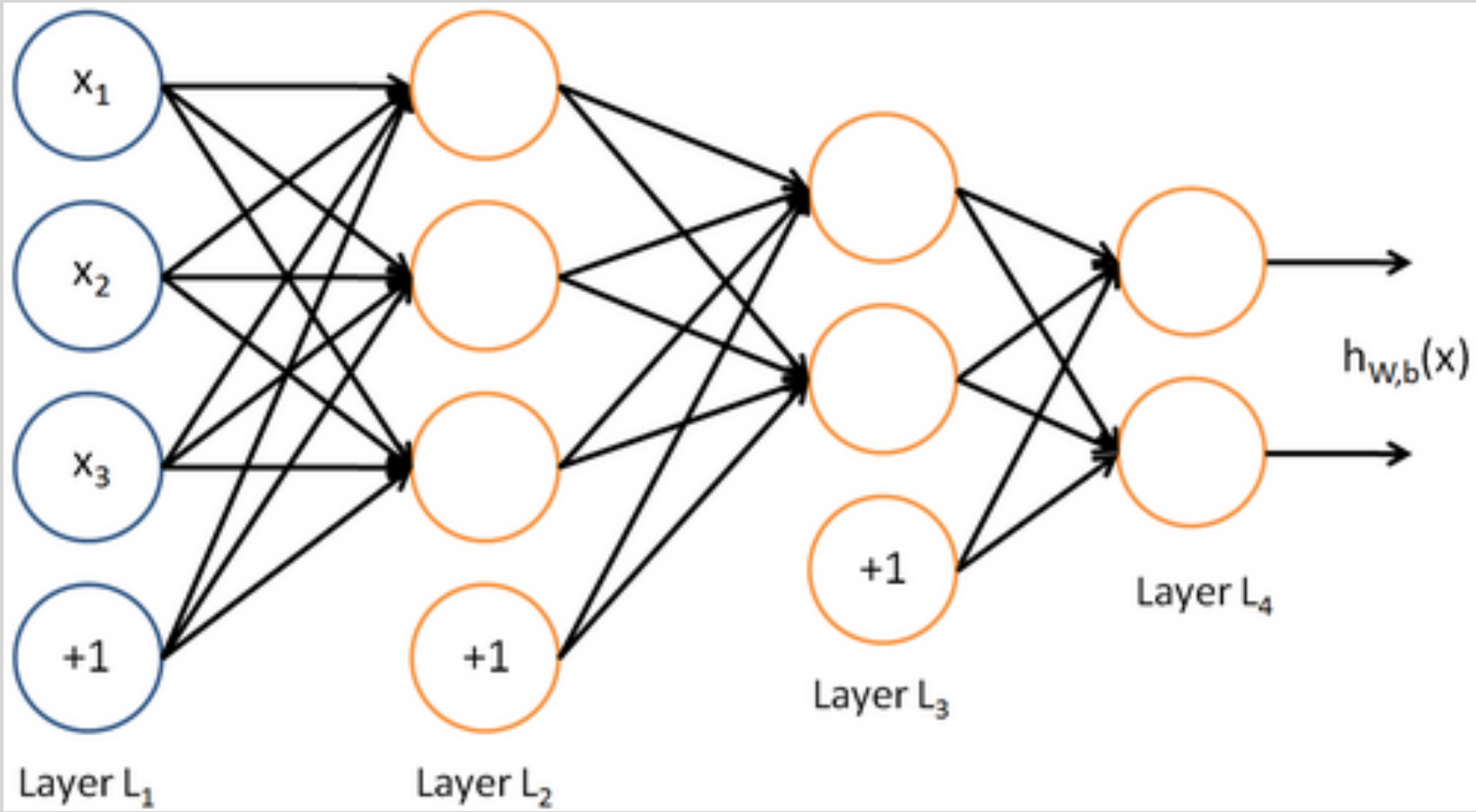
Neural networks



university of groningen

University of Cyprus

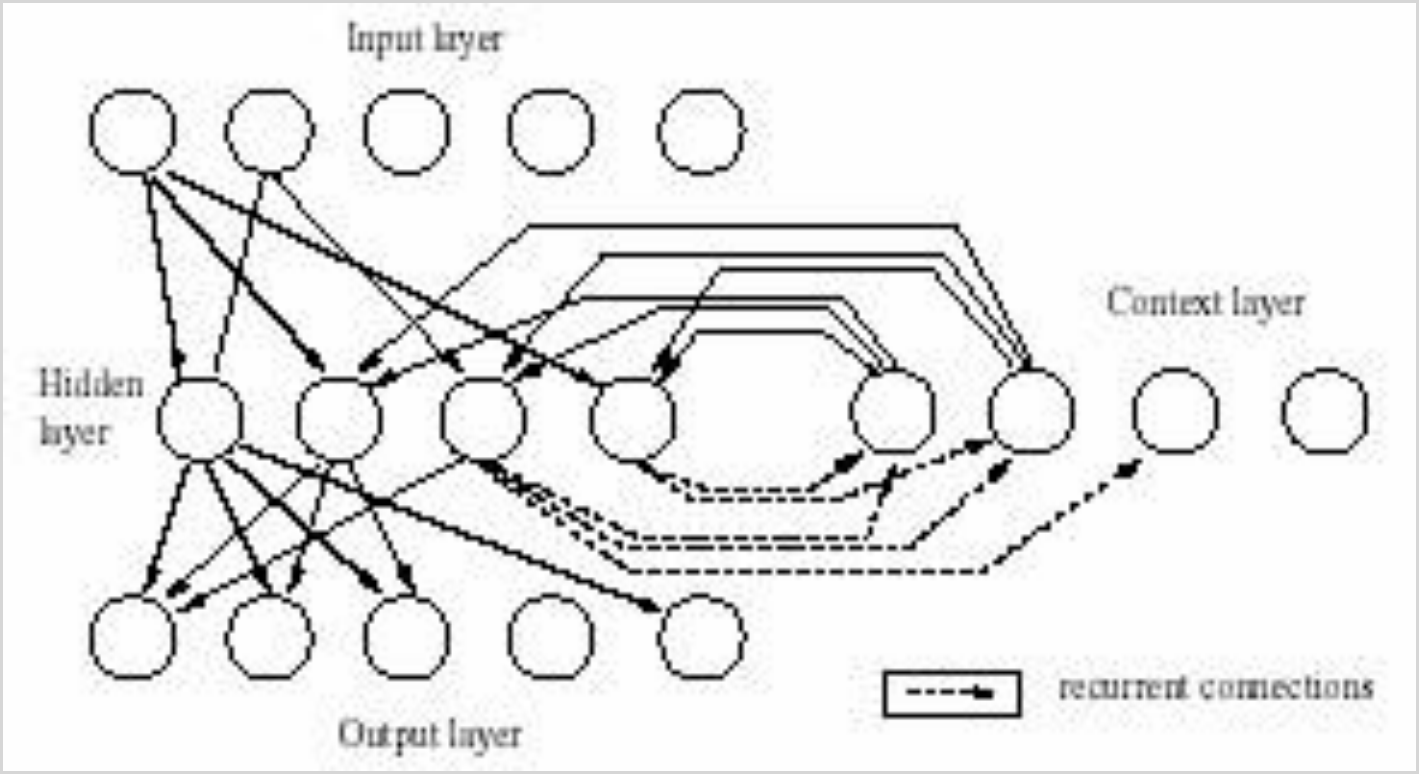
Neural networks



university of groningen

University of Cyprus

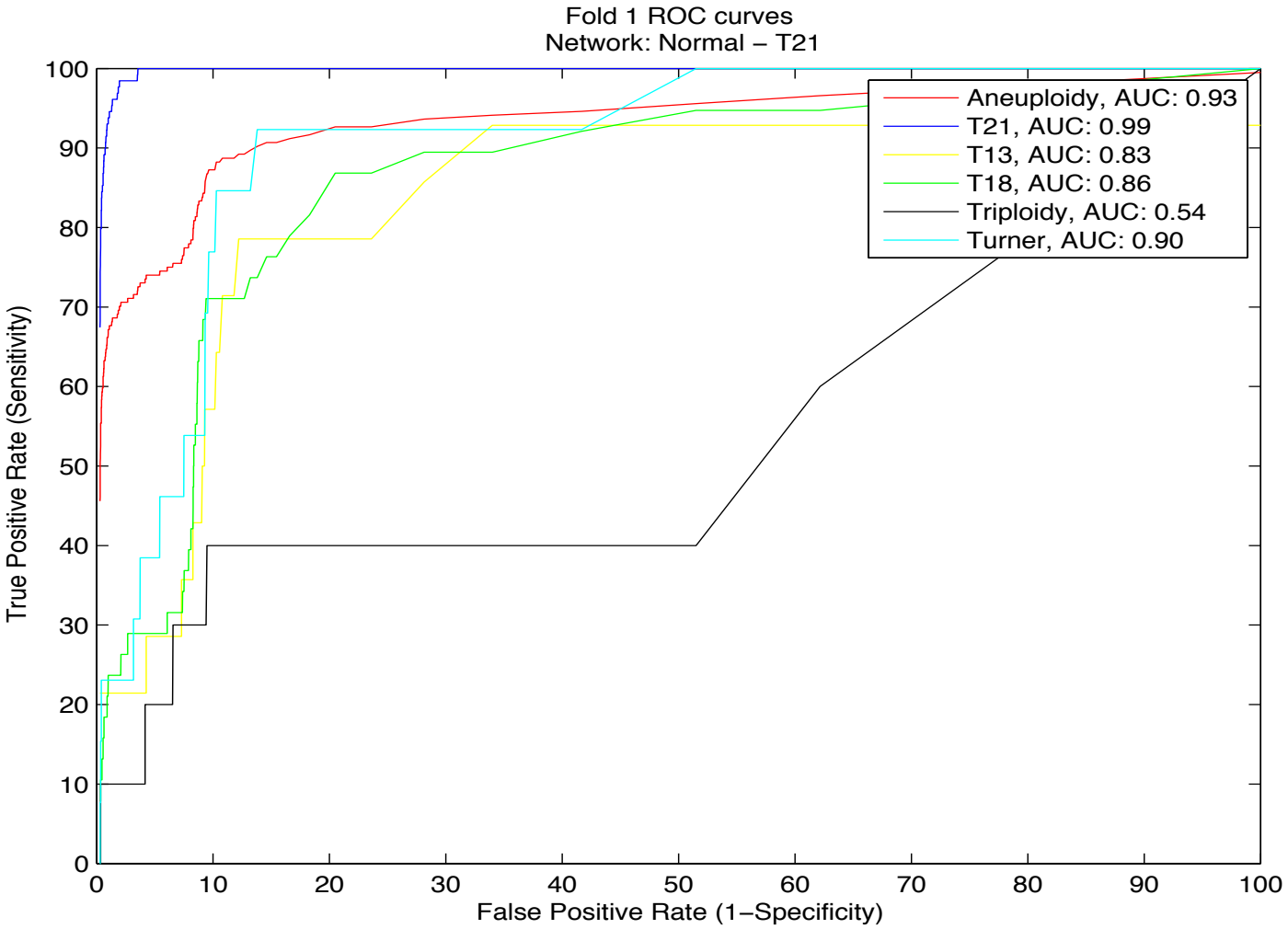
Neural networks



university of groningen

University of Cyprus

Results



Thank you!