Towards a Signal-Based Analysis of Karyotyping

Decision Support for Chromosomal Anomaly Detection

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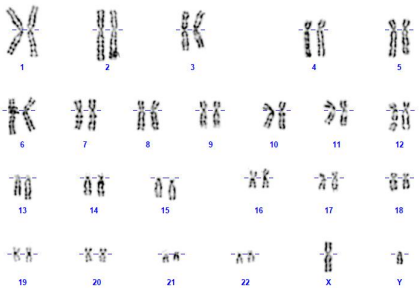
General context

- Karyotyping is a reference method in cytogenetics.
- Used to detect chromosomal abnormalities.
- Analysis is mostly visual, expert-driven, and manual.



Example of a human karyotype

Limitations of the current approach

- Time-consuming and costly analysis.
- High biological and technical variability.
- Strong dependence on operator expertise.

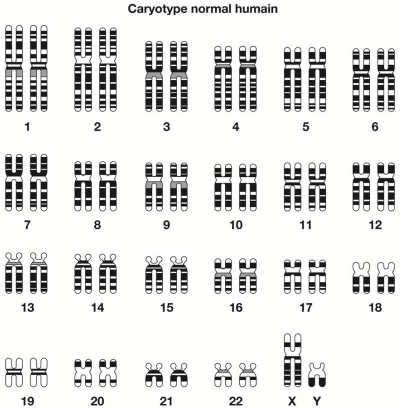
General idea of the PhD

Transforming a visual analysis into a quantitative approach

- Changing the data representation.
- Objectifying chromosome comparison.
- Assisting diagnosis without replacing the expert.

What is a karyotype?

- Ordered representation of a cells chromosomes.
- Chromosomes arranged into homologous pairs.
- Analysis of both structure and number.



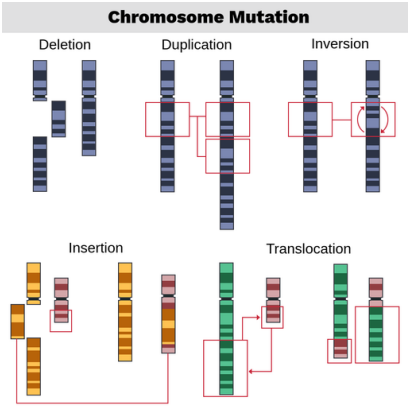
Metaphase

- Stage of mitosis.
- Chromosomes are highly condensed.
- Required condition for observation.

Example of a metaphase

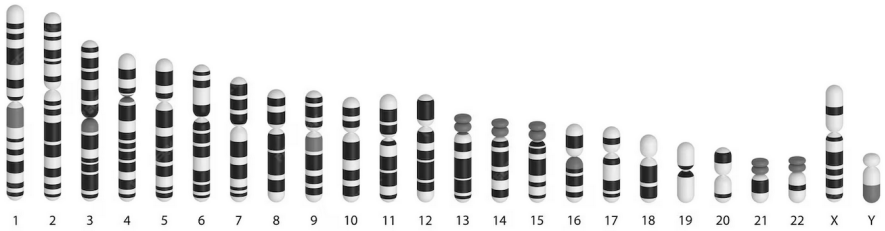
Chromosomal abnormalities

- Numerical abnormalities (trisomy, monosomy).
- Structural abnormalities (deletions, duplications, translocations, inversions, insertions).



Chromosome signatures

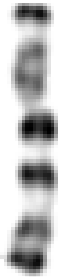
- Each chromosome has a specific organization.
- GTG banding forms a longitudinal signature.
- Basis for identification and diagnosis.

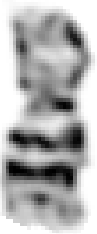


Human chromosome ideogram

Experimental variability

- Variability due to sample preparation.
- Influence of environmental conditions.
- Example: weather $\rightarrow$ dye behavior.





Chromosome 7 from the same patient under different culture conditions

Consequence

Not all observed variations are biological

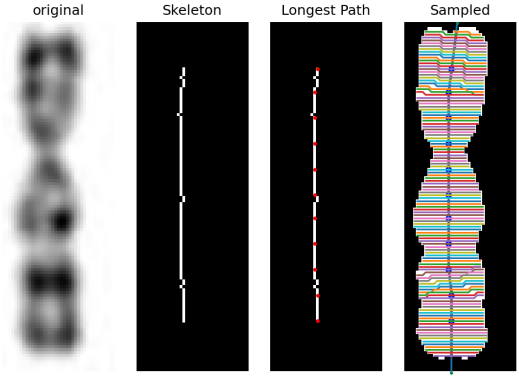
- Need for robust methods.
- Variability must be accounted for in the analysis.

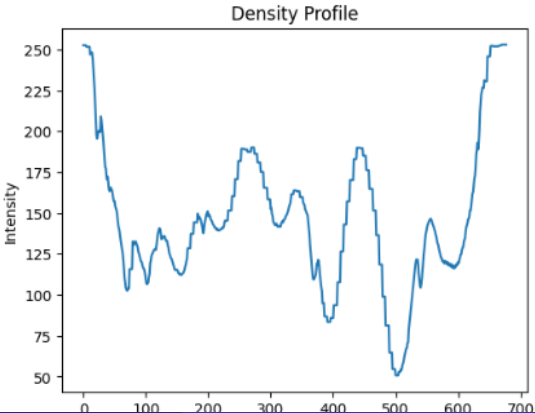
Data extraction

- Data obtained from industrial binary files.
- Automatic chromosome extraction.
- Organization by chromosomal class.

Central axis and profile

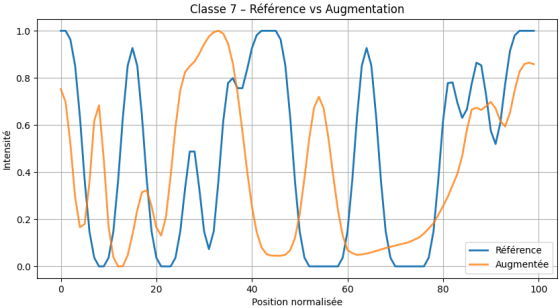
- Segmentation and skeletonization.
- Extraction of the central axis.
- Intensity sampling along the axis.

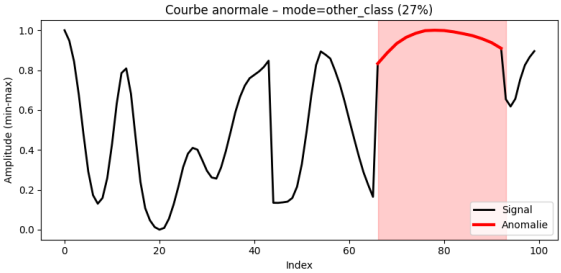




Data simulation

- Generation of synthetic profiles.
- Controlled deformations and noise.
- Testing method robustness.





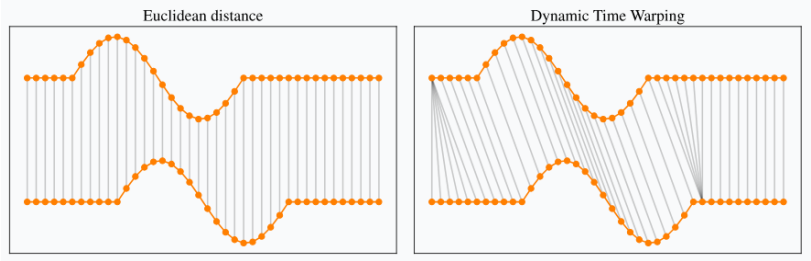
Comparing biological profiles

- Local shifts.
- Stretching / compression effects.
- Limitations of classical distances.

Why DTW?

Align before comparing

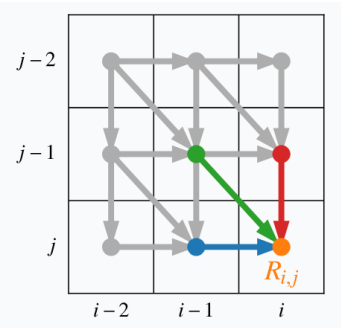
- Tolerance to local deformations.
- Preservation of band ordering.

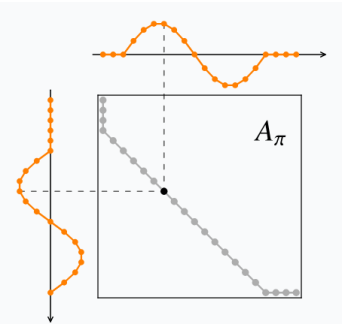


DTW: mathematical formulation

$$\mathrm{DTW}(x, y) = \min_{p} \sum_{(i,j)\in p} (x_i - y_j)^2$$

- Monotonic alignment path.
- Dynamic programming.

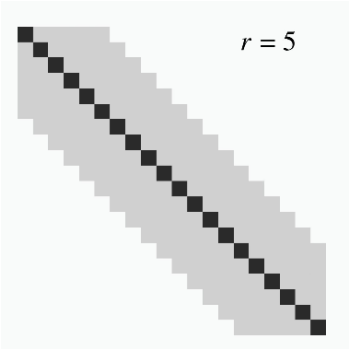




Sakoe–Chiba constraint

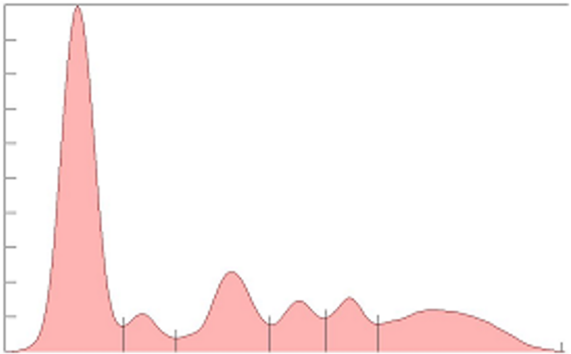
$$|i - j| \leq r$$

- Limitation of unrealistic alignments.
- Improved biological coherence.



DTW on simple data (PEP)

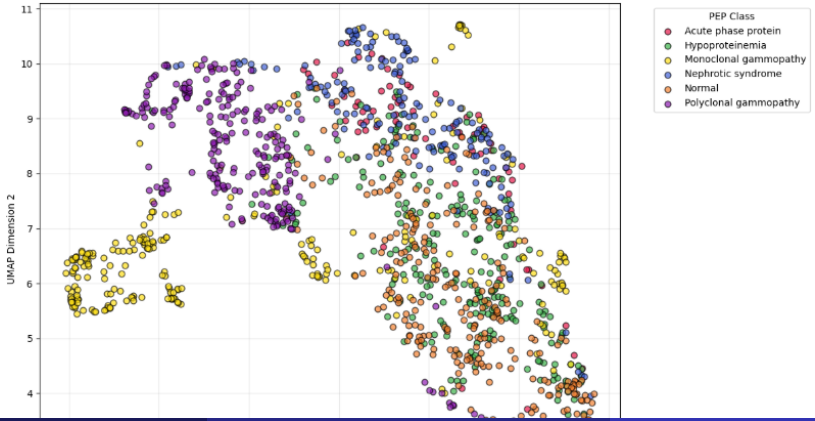
- Simple 1D profiles.
- Intuitive illustration of DTW.
- Validation of expected behavior.



Example of a PEP

UMAP visualization

- Profile projection.
- Natural clustering.
- Exploratory tool.



Towards a normality score

- Learning normal variability.
- Quantifying deviation from normality.
- One-class approach.

Conclusion

- Reformulating karyotyping as signal analysis.
- DTW as a central comparison tool.
- Towards robust and interpretable diagnostic support.

Thank you for your attention