Unsupervised study of plethysmography signals through DTW clustering

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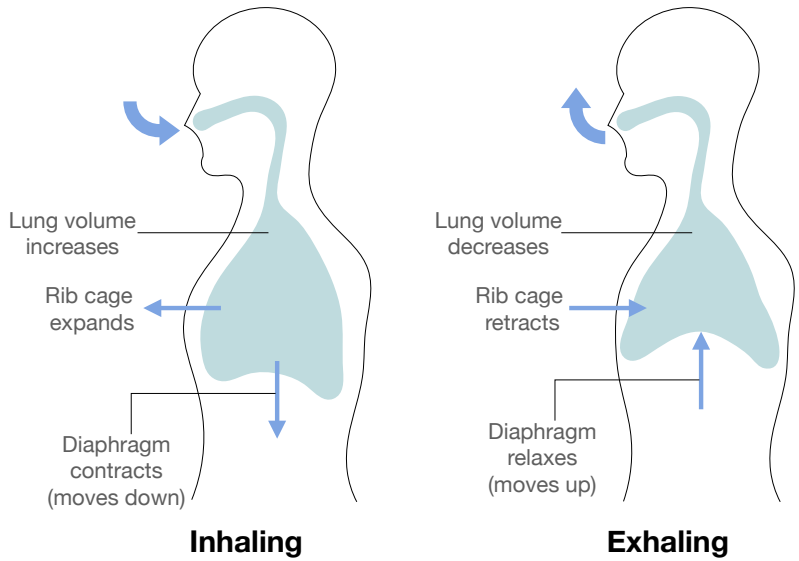
Motivations

Breathing: Process of moving air into and from the lungs.

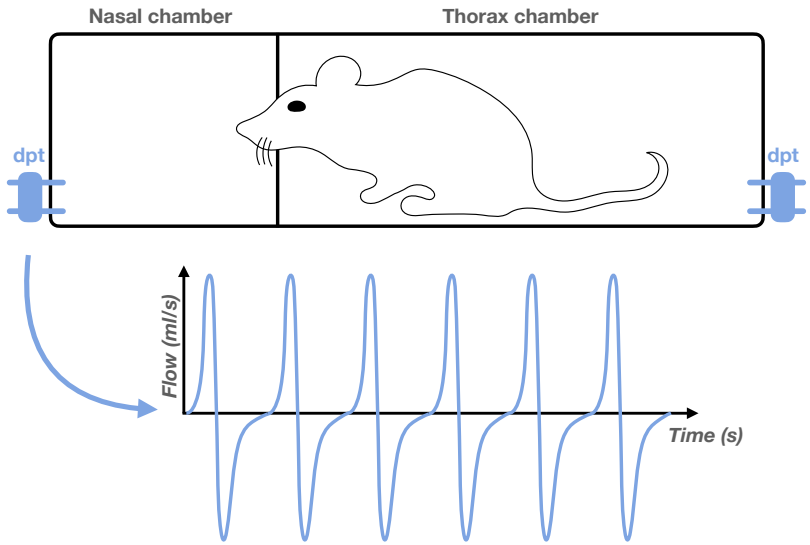


- Breathing involved reflexes (coughing, sneezing, etc) to protect the lung from the toxicity of the environment.
- Necessity of plethysmography for studying the breathing behavior (evolution of breathing over time)

Motivations

Plethysmography: measuring changes in volume within an organ.

Use of Double Chamber Plethysmograph to record nasal airflow.



Most studies rely on statistical analysis of breathing descriptors over long periods of time[1][2].

Problem: Breathing dynamics are hidden.

[1] Rob Hill et al. "Fentanyl depression of respiration: comparison with heroin and morphine". In: *British journal of pharmacology* 177.2 (2020), pp. 254–265.

[2] Samuel Mailhot-Larouche et al. "Assessment of respiratory function in conscious mice by double-chamber plethysmography". In: *Journal of visualized experiments: JoVE* 137 (2018).

Contributions

Work hypothesis:

- Breathing behavior is characterized by a small number of reflexes.
- Inhalation and exhalation are distinctive mechanisms.

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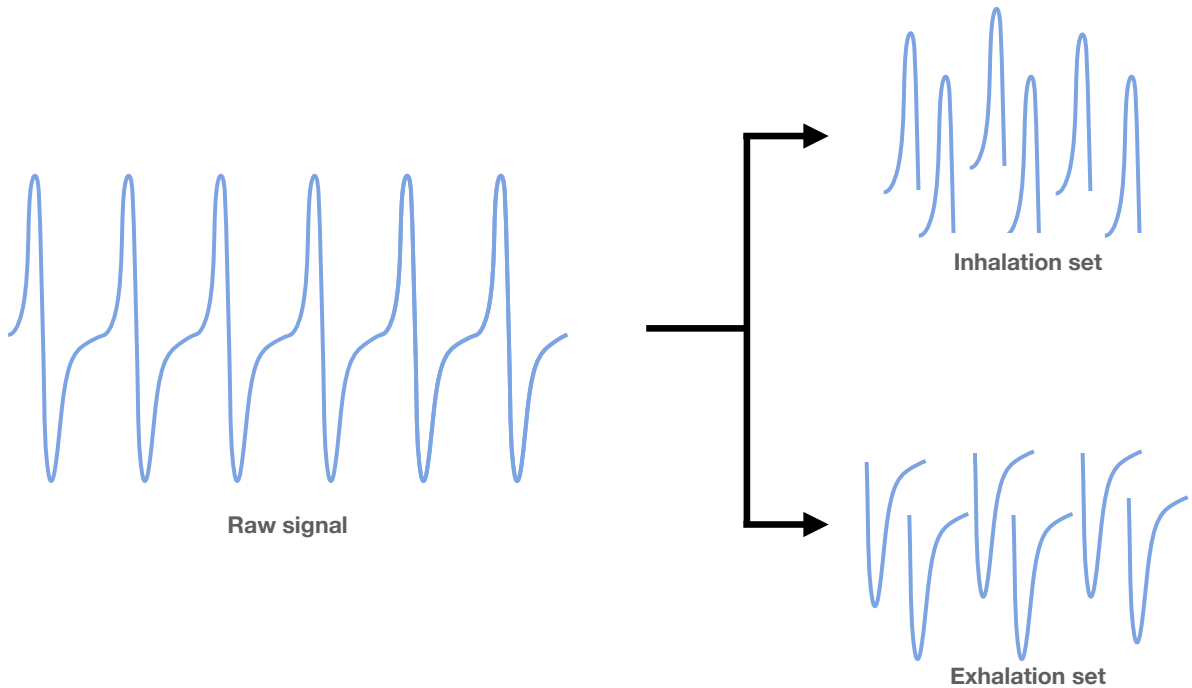
- Inhalation and exhalation are distinctive mechanisms.

Contributions:

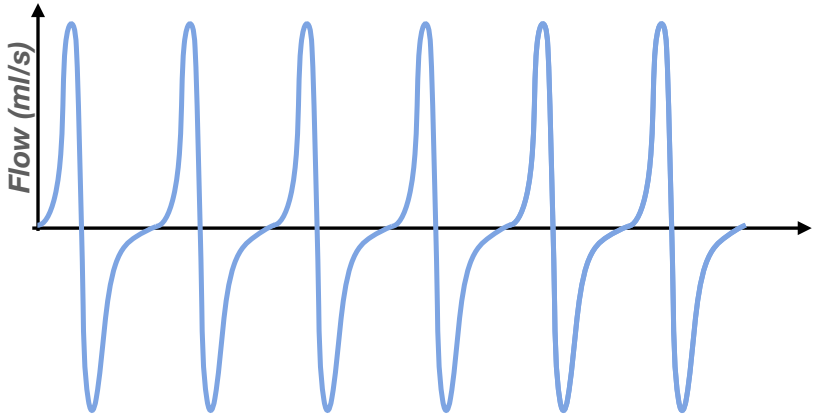
- New algorithm to extract inhalation/exhalation sequences.
- Detection and representation of most typical inhalation/exhalation sequences.
- A signal symbolic representation.

Inhalation/exhalation extraction

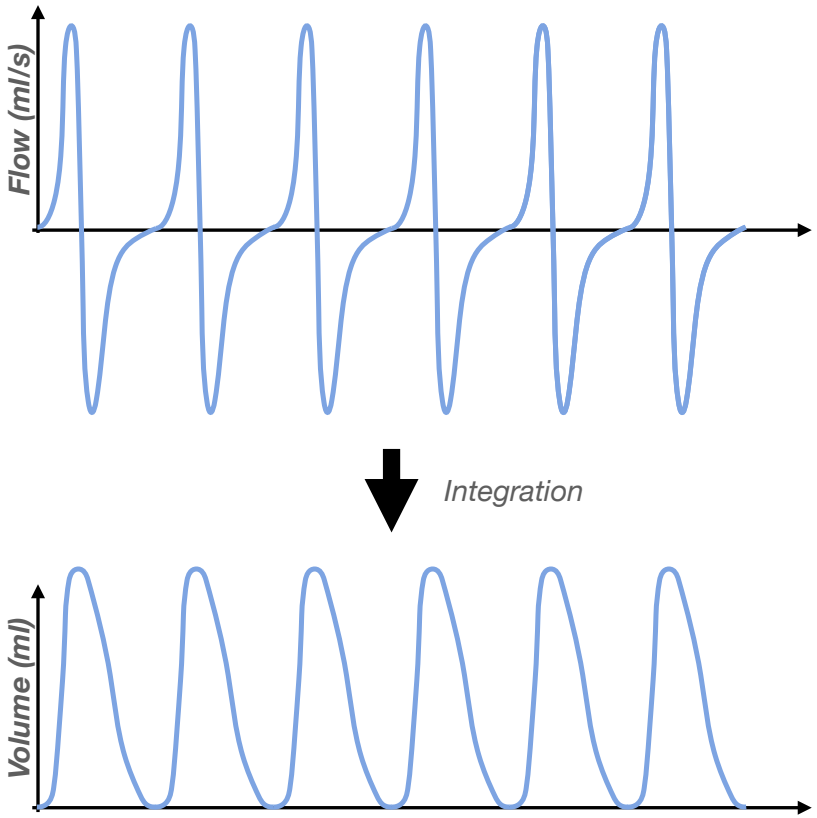
Objective : Transforming a nasal airflow signal in a set of inhalation sequences and a set of exhalation sequences.



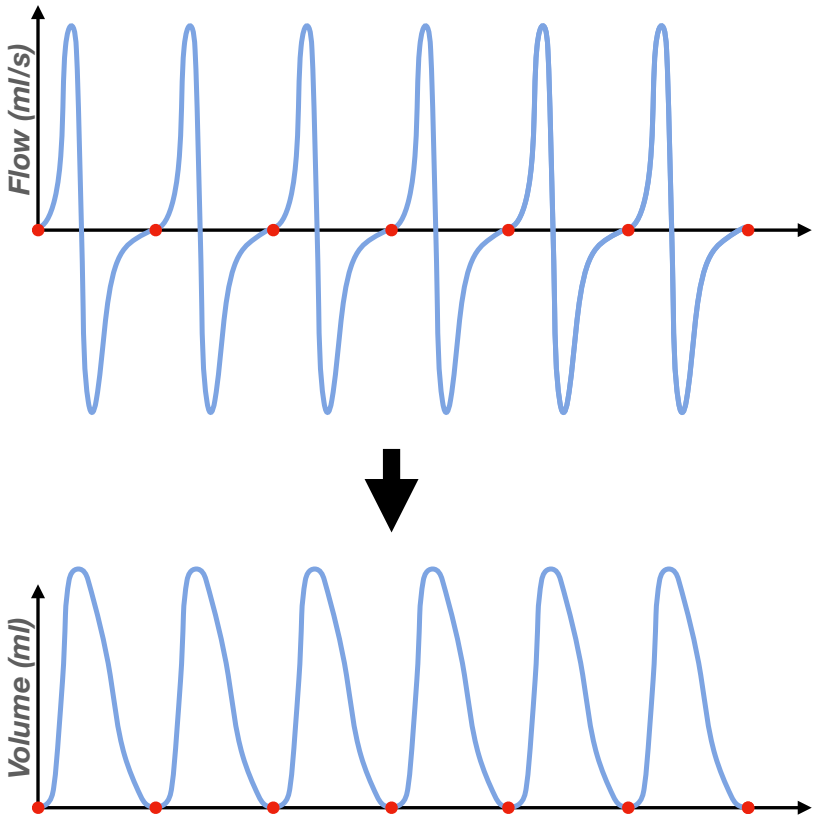
Inhalation/exhalation extraction



Inhalation/exhalation extraction

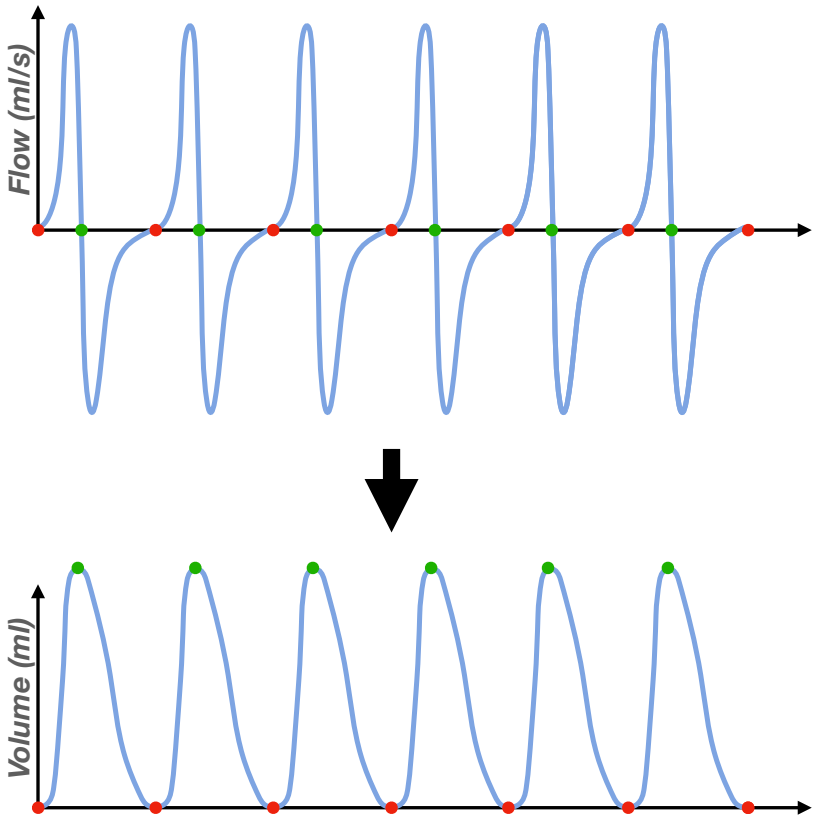


Inhalation/exhalation extraction



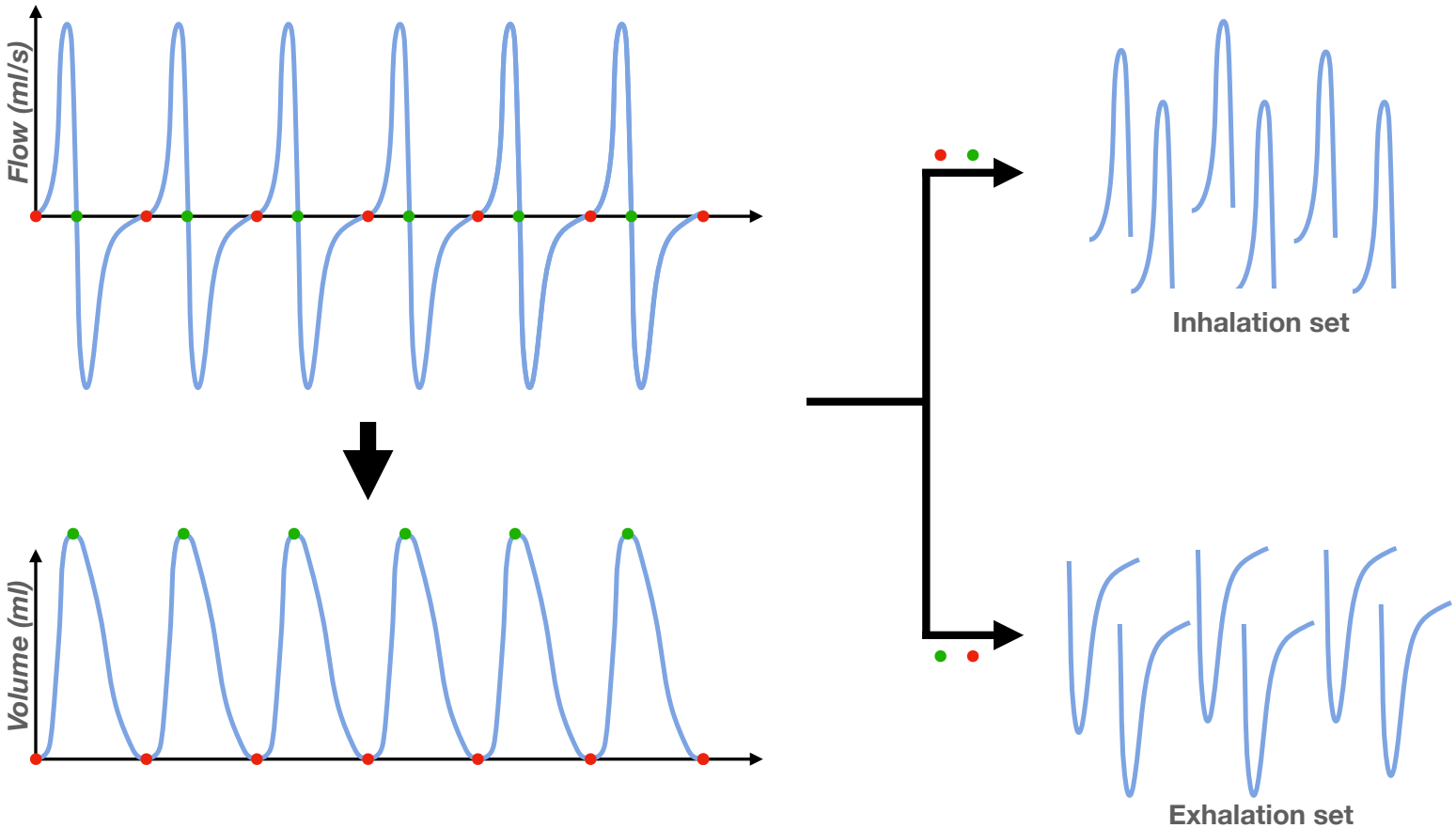
Volume local minima correspond to inhalation starts

Inhalation/exhalation extraction

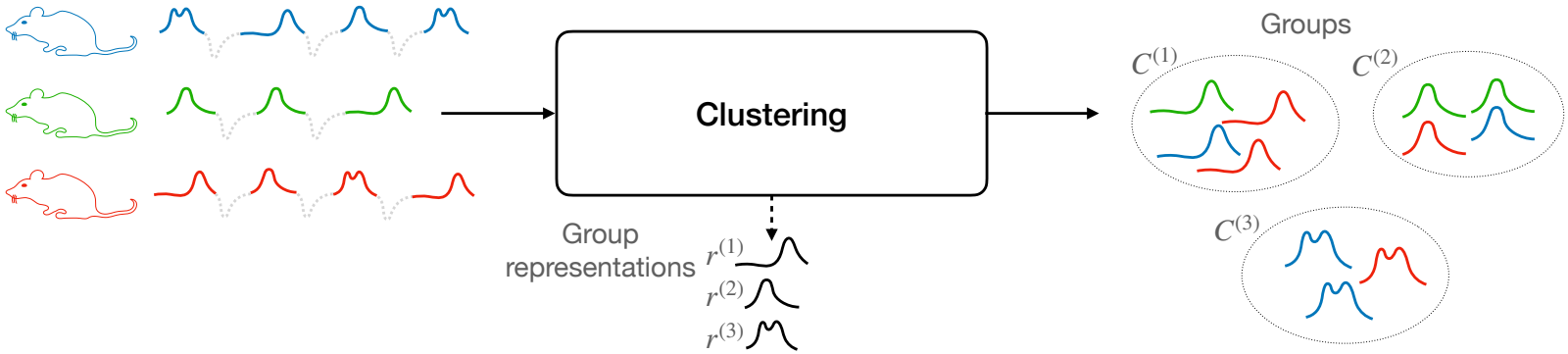


Volume local maxima correspond to exhalation starts

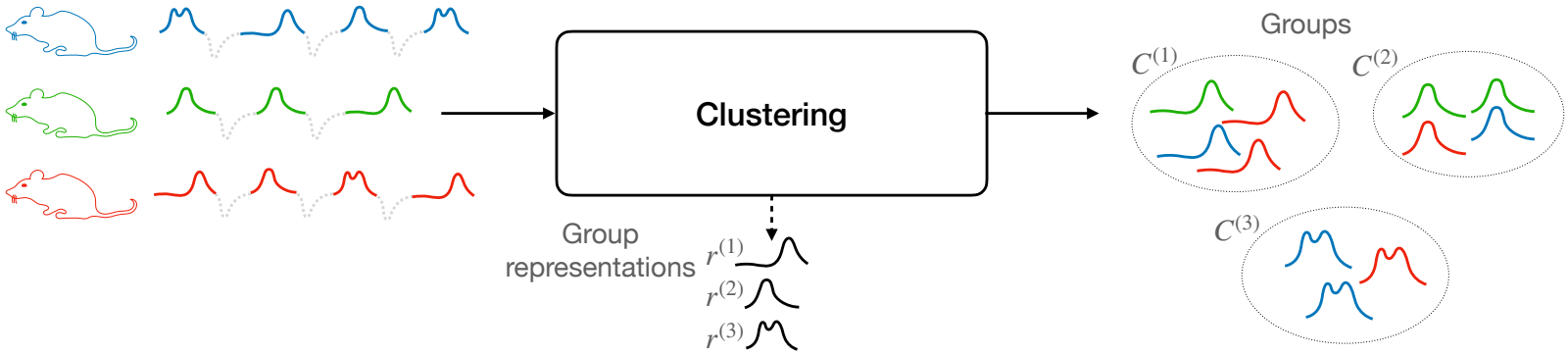
Inhalation/exhalation extraction



Reference sequence computation



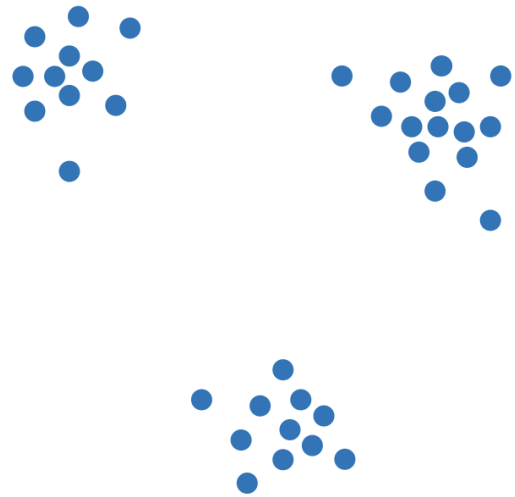
Reference sequence computation



Inter-individual variability:

Clustering algorithm: K-Means

- K-Means algorithm partitions a dataset in K groups where each observation belongs to the group of its closest centroid.
- Centroids are barycenters of the groups, and they are computed iteratively.



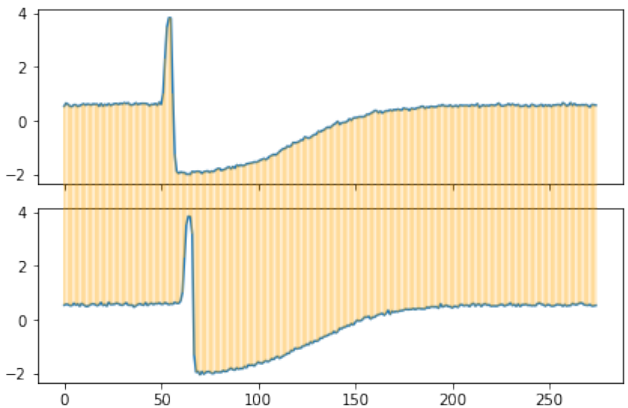
Remark: A centroid is a unique representative of its group.

Reference sequences are the centroids. They represent the most typical inhalation/exhalation sequences.
U

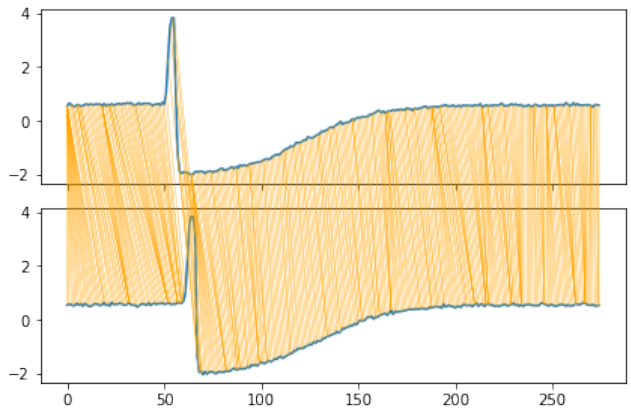
Measure of fit: Dynamic Time Warping (DTW)

Dynamic Time Warping[3]**:** it measures the similarities in shape between two time-series independently of time fluctuation.

DTW establishes an optimal alignment between time-series. Its value corresponds to the euclidean distance of the optimally aligned time-series.



Euclidean alignment

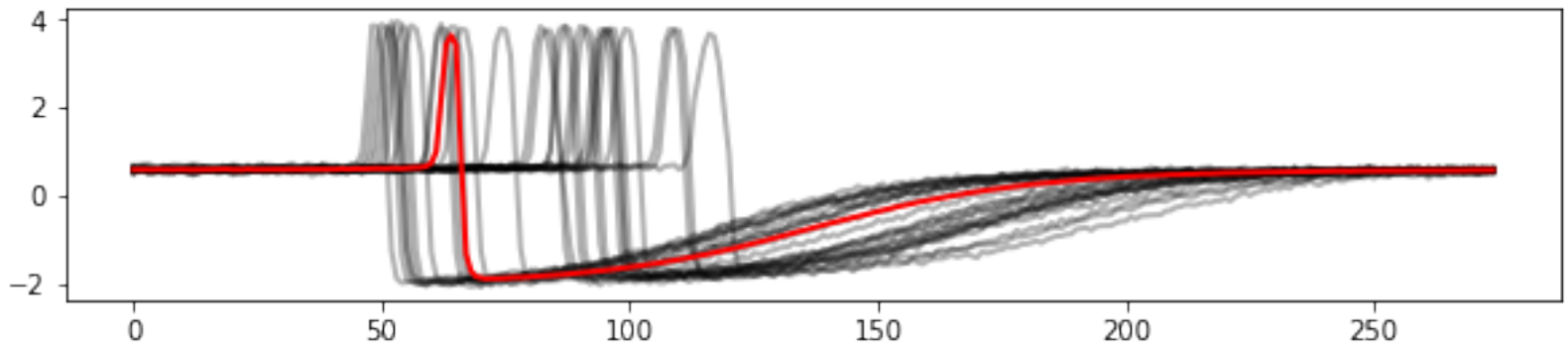


DTW alignment

Sakoe-Chiba constraint: the time difference between two aligned points cannot exceed a threshold.

[3] Donald J Berndt and James Clifford. "Using dynamic time warping to find patterns in time series.". In: *KDD workshop*. Vol. 10. 16. Seattle, WA, USA:. 1994, pp. 359–370.

Barycenter Computation

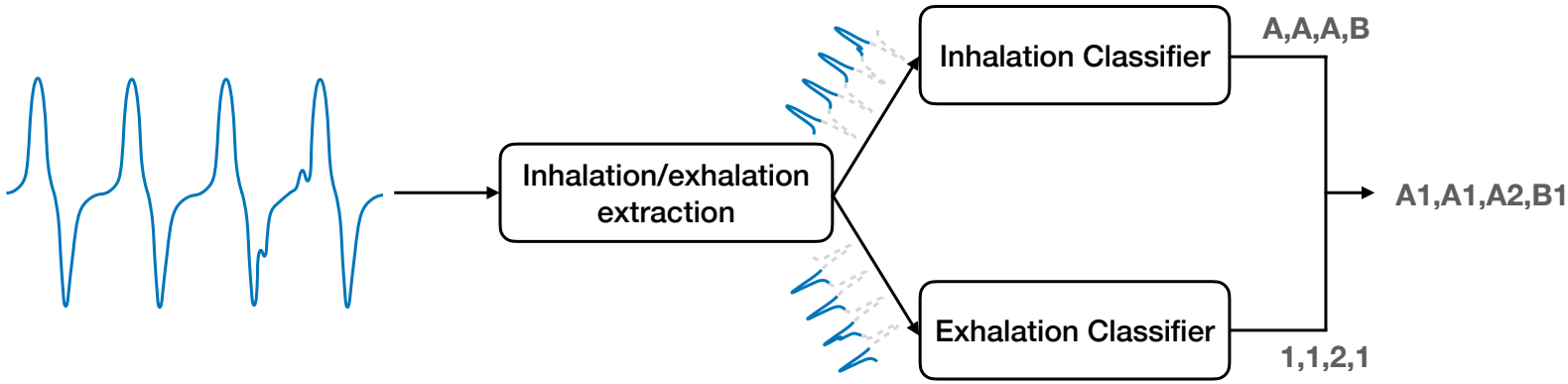


$$\underset{\mathbf{y}\in\mathbb{R}^L}{\operatorname{argmin}} \sum_{\mathbf{x}\in\mathcal{X}} \mathrm{DTW}^2(\mathbf{y}, \mathbf{x}') \tag{1}$$

- Approximate solution with subgradient descent method[4].
- For time efficiency, implementation of a stochastic batch version.

[4] David Schultz and Brijnesh Jain. "Nonsmooth analysis and subgradient methods for averaging in dynamic time warping spaces". In: *Pattern Recognition* 74 (2018), pp. 340–358.

Symbolic representation



Symbols correspond to the most typical inhalations/exhalations.

Inhalation/exhalation classifiers are **1-NN** with:

- **dataset:** Inhalation/exhalation reference sequences
- **label:** Unique letters/numbers paired with inhalation/exhalation reference sequences
- **measure of fit:** DTW

Remark: A breathing cycle symbol is a letter followed by a number (ex: A1).

Experiment

Data: Subset of recordings from an experiment on the impact of some neurotoxins on mice breathing[5][6].

Data characteristics:

- 12 mice: 6 Colq KO genotype, 6 WT genotype
- neurotoxin: physostigmine

Manipulation:

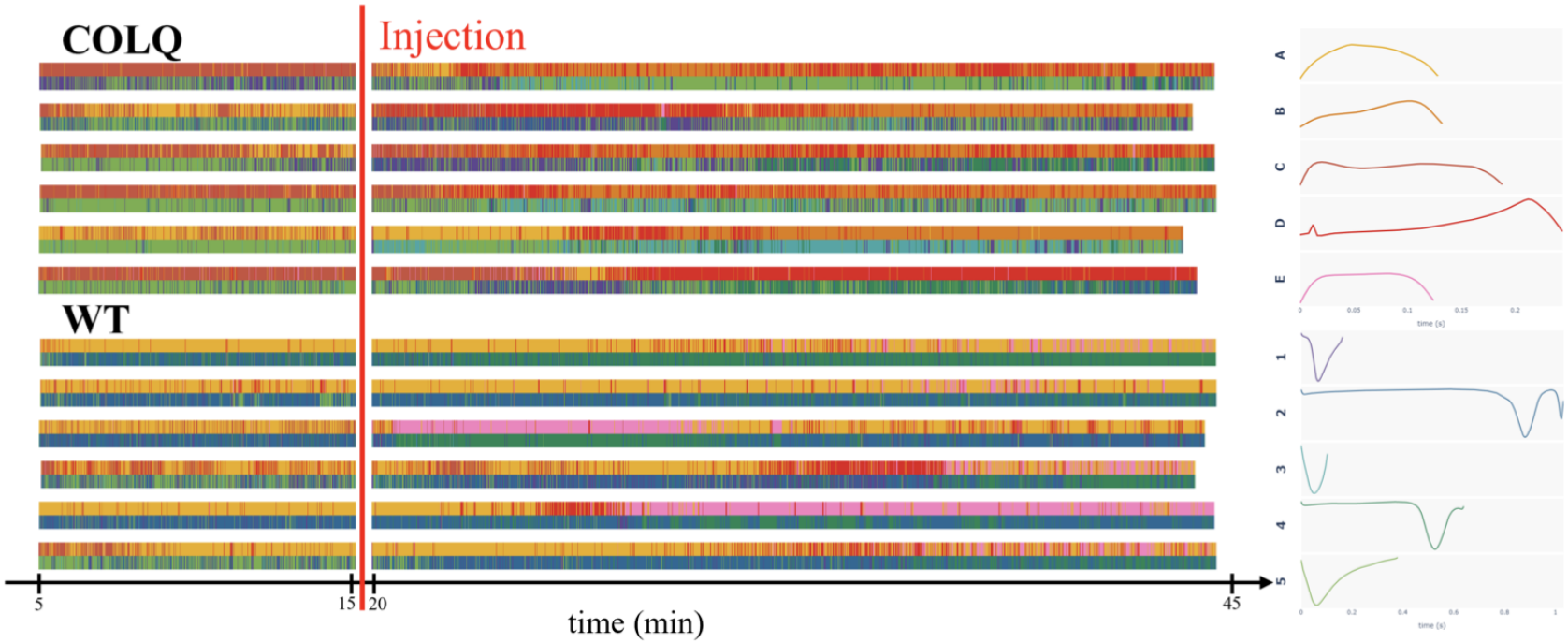
1. The mouse breathing is recorded for 15 minutes.
2. The mouse is exposed to the neurotoxin.
3. The mouse breathing is recorded for 25 minutes.

Main parameters: 5 inhalation, 5 exhalation reference sequences.

[5] Aurélie Nervo et al. "Respiratory failure triggered by cholinesterase inhibitors may involve activation of a reflex sensory pathway by acetylcholine spillover". In: *Toxicology* 424 (2019), p. 152232.

[6] All experiments were performed in accordance with the Council of European Committees Directive (86/609/EEC) and were approved by the Paris Descartes University Ethics Committee for Animal Experimentation (CEEA34.EK/AGC/LB.111.12).

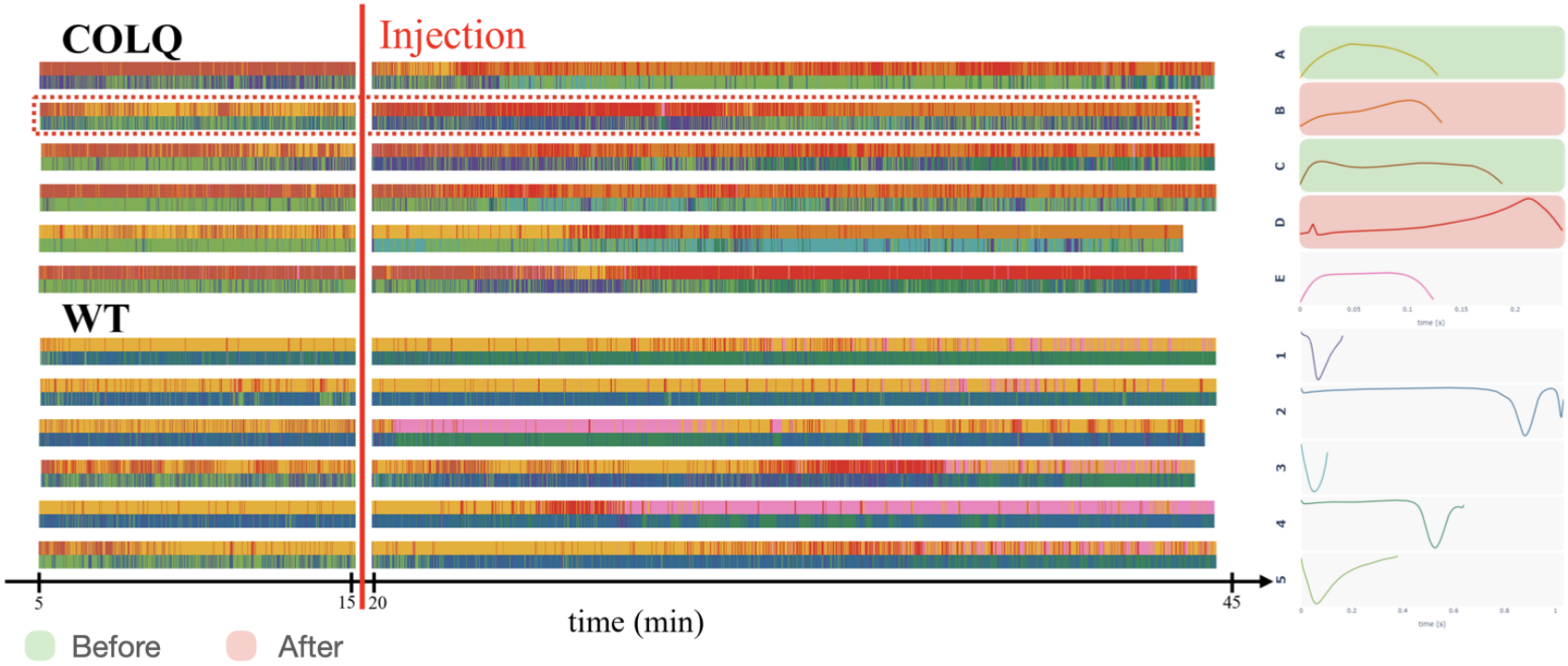
Results



Overall remark:

Frequent changes of inhalation/exhalation symbols.

Results



- Colq mice tend to have more difficulties to inhale after injection

Overall remark:

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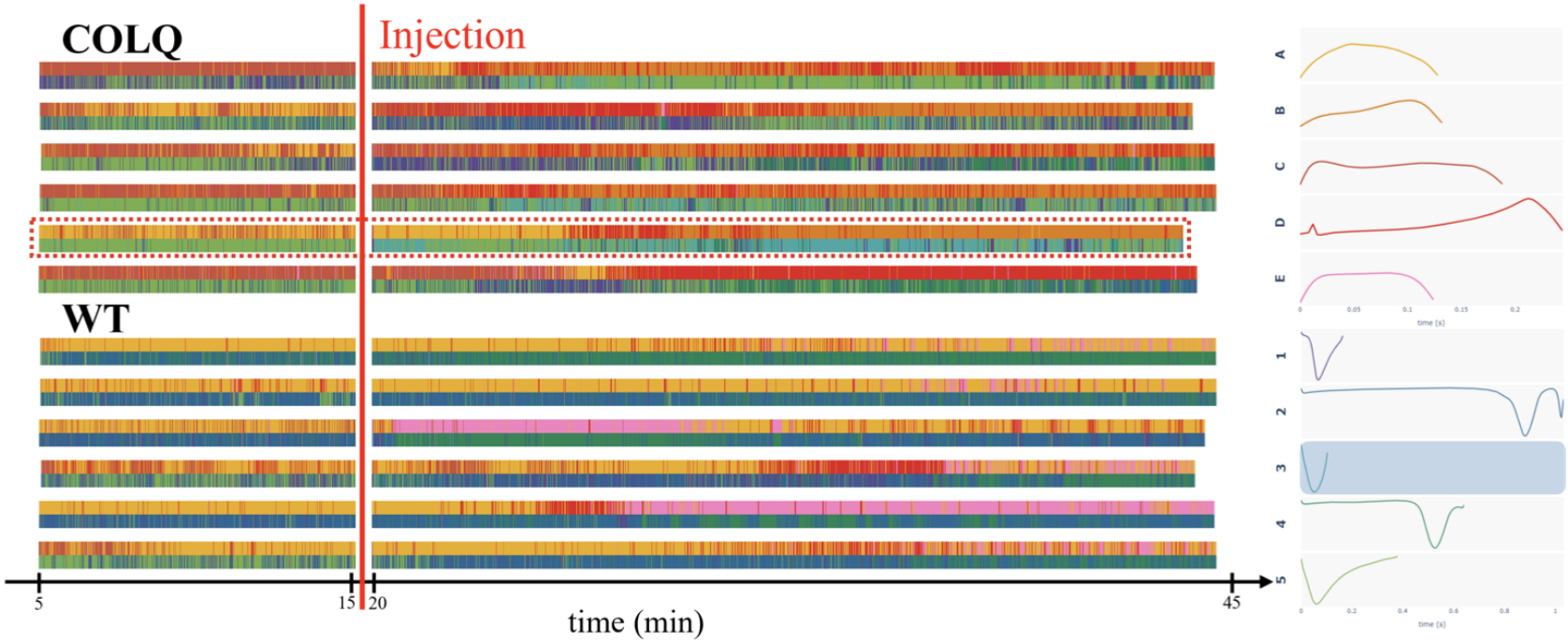
Results

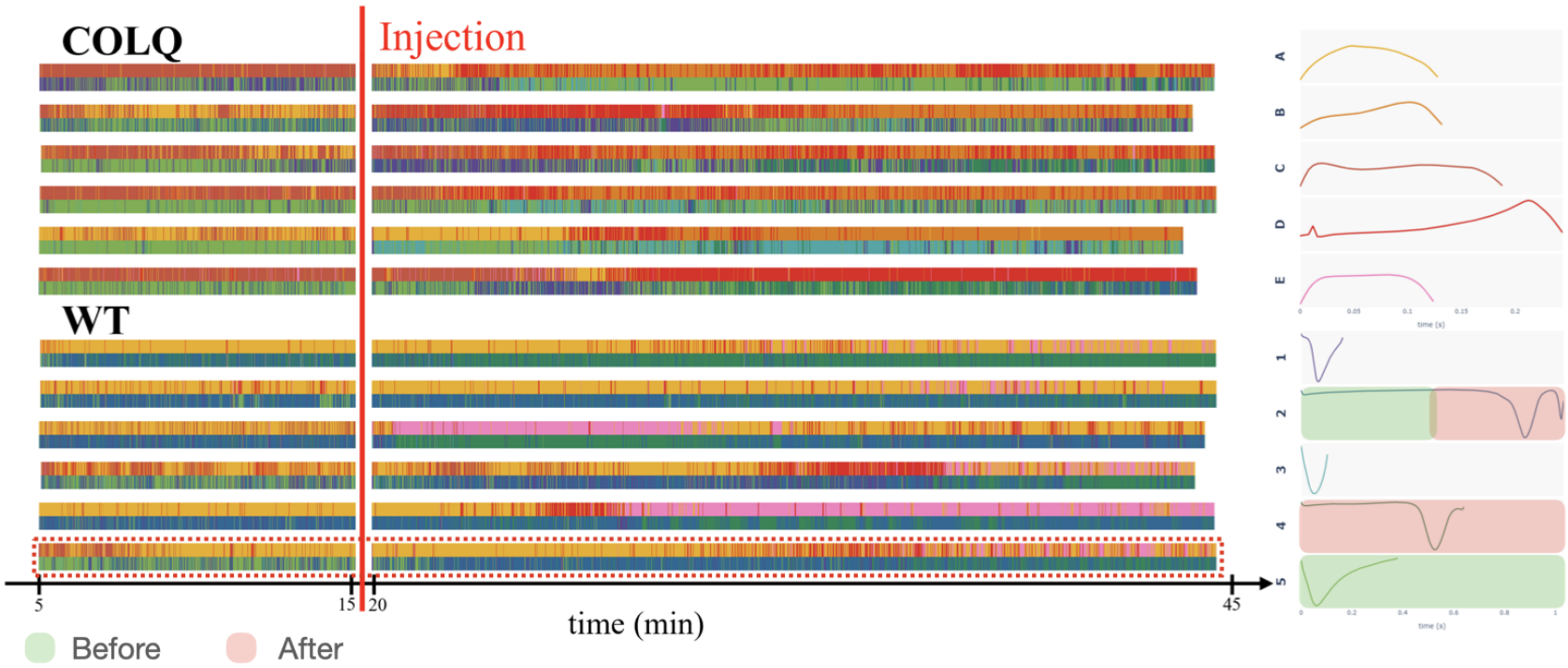


- A deviant behavior is detected by the algorithm

Overall remark:

Frequent changes of inhalation/exhalation symbols.

Results

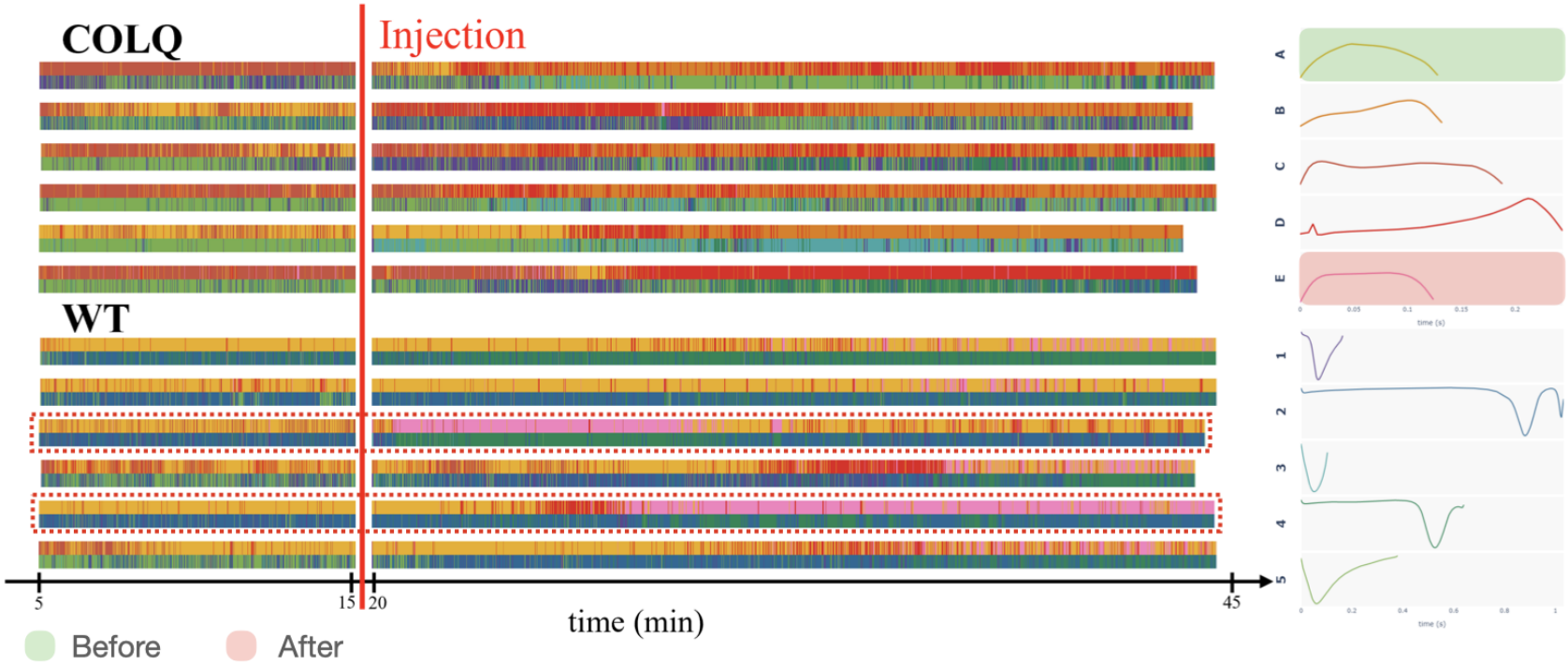


- WT mice tend to have more difficulty to exhale after injection

Overall remark:

Frequent changes of inhalation/exhalation symbols.

Results



- Bronchoconstriction detected on WT mice

Overall remark:

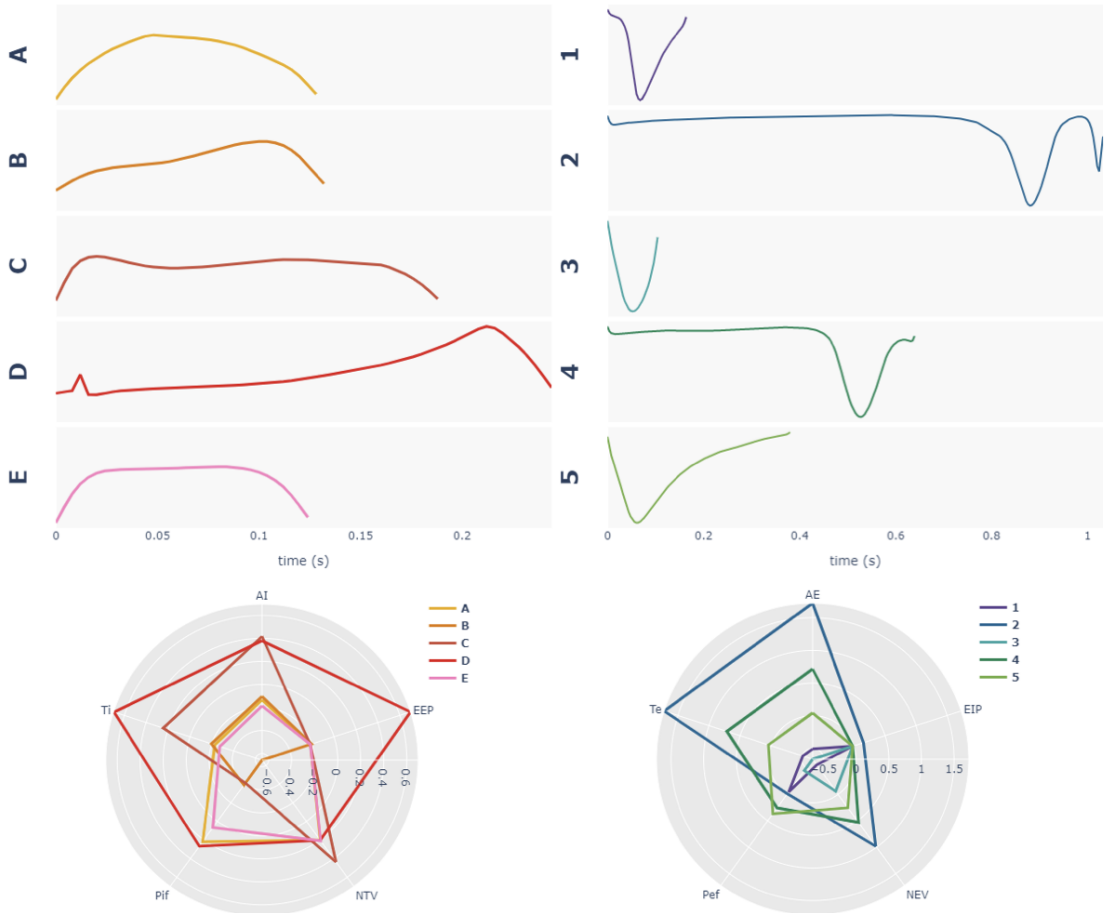
Frequent changes of inhalation/exhalation symbols.

Conclusion

- Robust algorithm to extract inhalation/exhalation sequences.
- Learned interpretable symbols representing most typical inhalations and exhalations.
- Create a symbolic representation which opens up the analysis of the fast changing dynamic of breathing behavior.

Thank you!

Appendix



Descriptors:

Ti/Te, (s): inhalation/exhalation duration.

Pif/Pef (ml/s): maximum/minimum flow during the inhalation/exhalation.

NTV/NEV, (ml): nasal volume of air inhaled/exhaled during inhalation/exhalation.

AI/AE, (s): duration of the period which starts when the flow reaches 5% of the Pif/Pef and ends at the beginning of the next exhalation/inhalation.

EIP/EEP, (s): duration of the period between the inhalation/exhalation start and active inhalation/exhalation start.