



Klinikum rechts der Isar
Technische Universität München



Advanced ML for signal processing

AI in Medicine II

Özgün Turgut (oezguen.turgut@tum.de) | 21.06.2022

OVERVIEW

Motivation

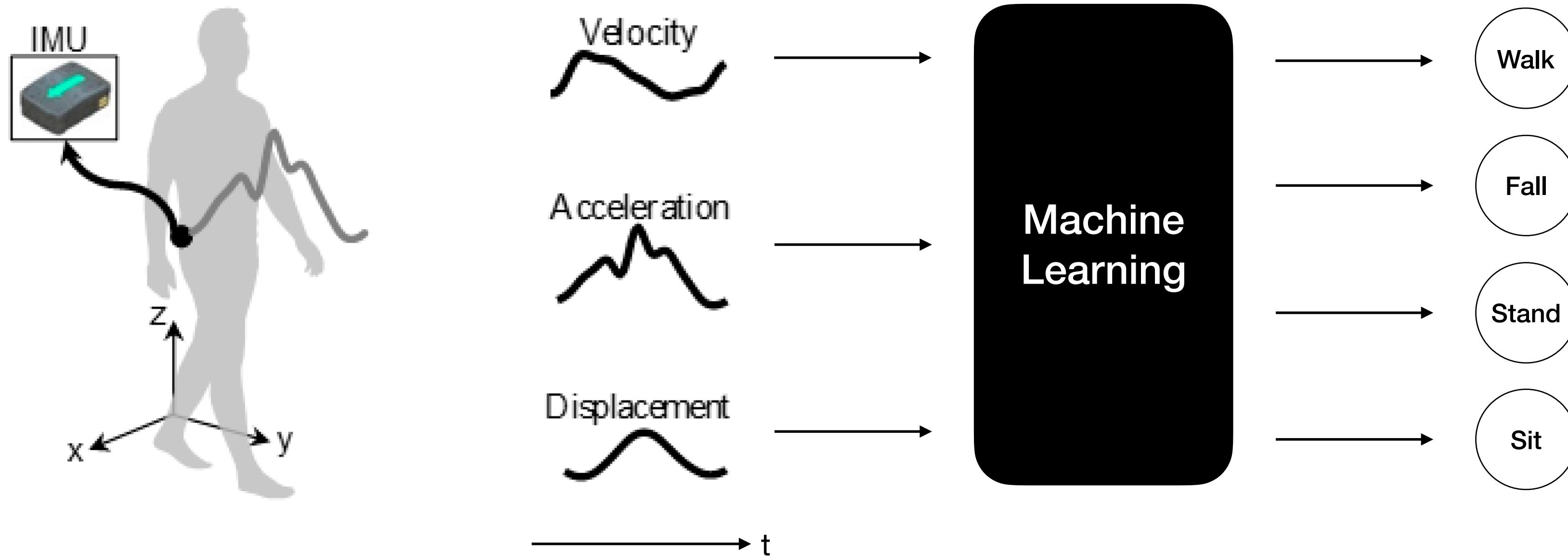
Time series data

Conventional EEG signal processing

EEG signal processing with AI

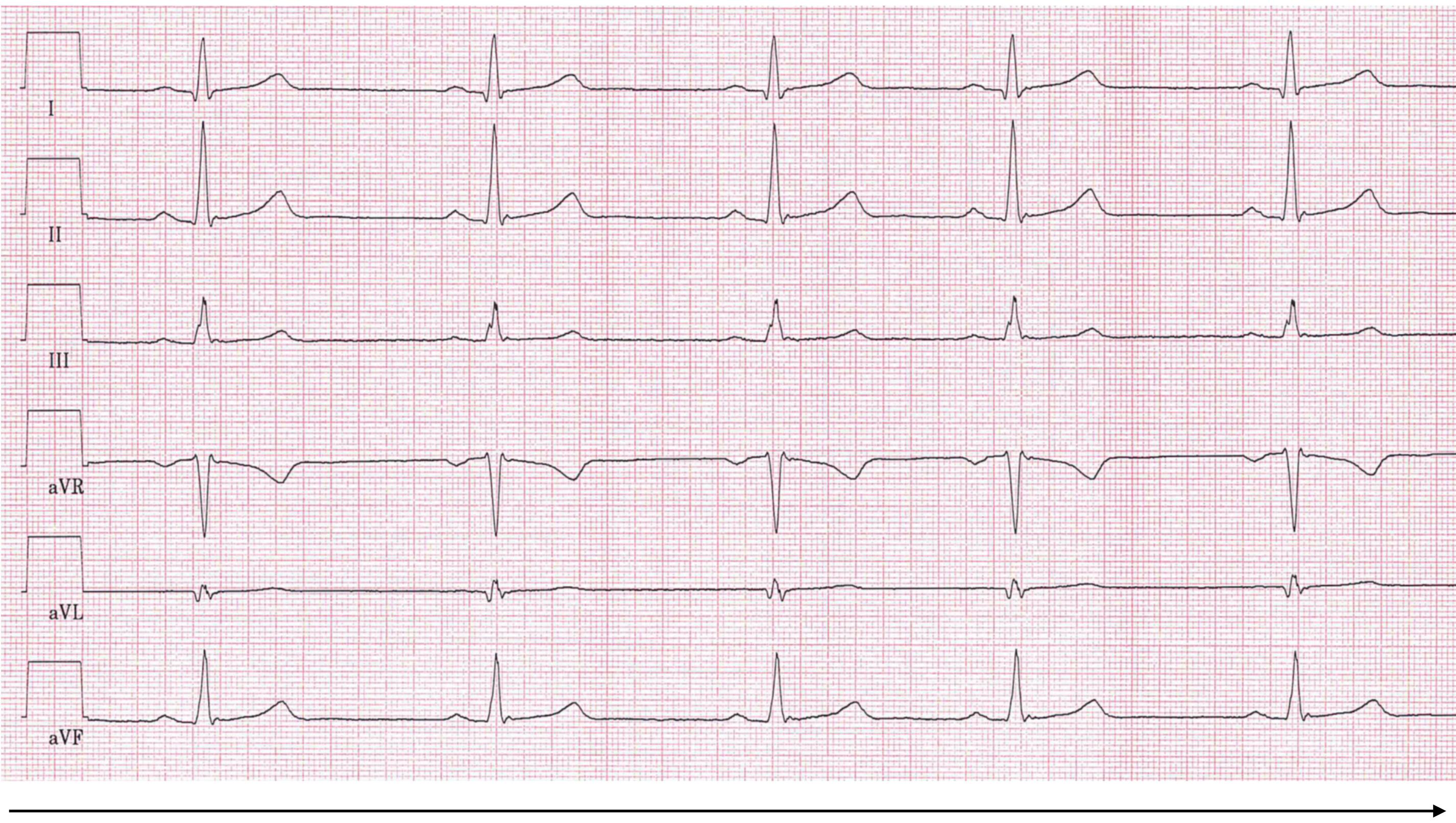
INERTIAL MEASUREMENT UNIT (IMU)

How often did the patient fall within a given time period?



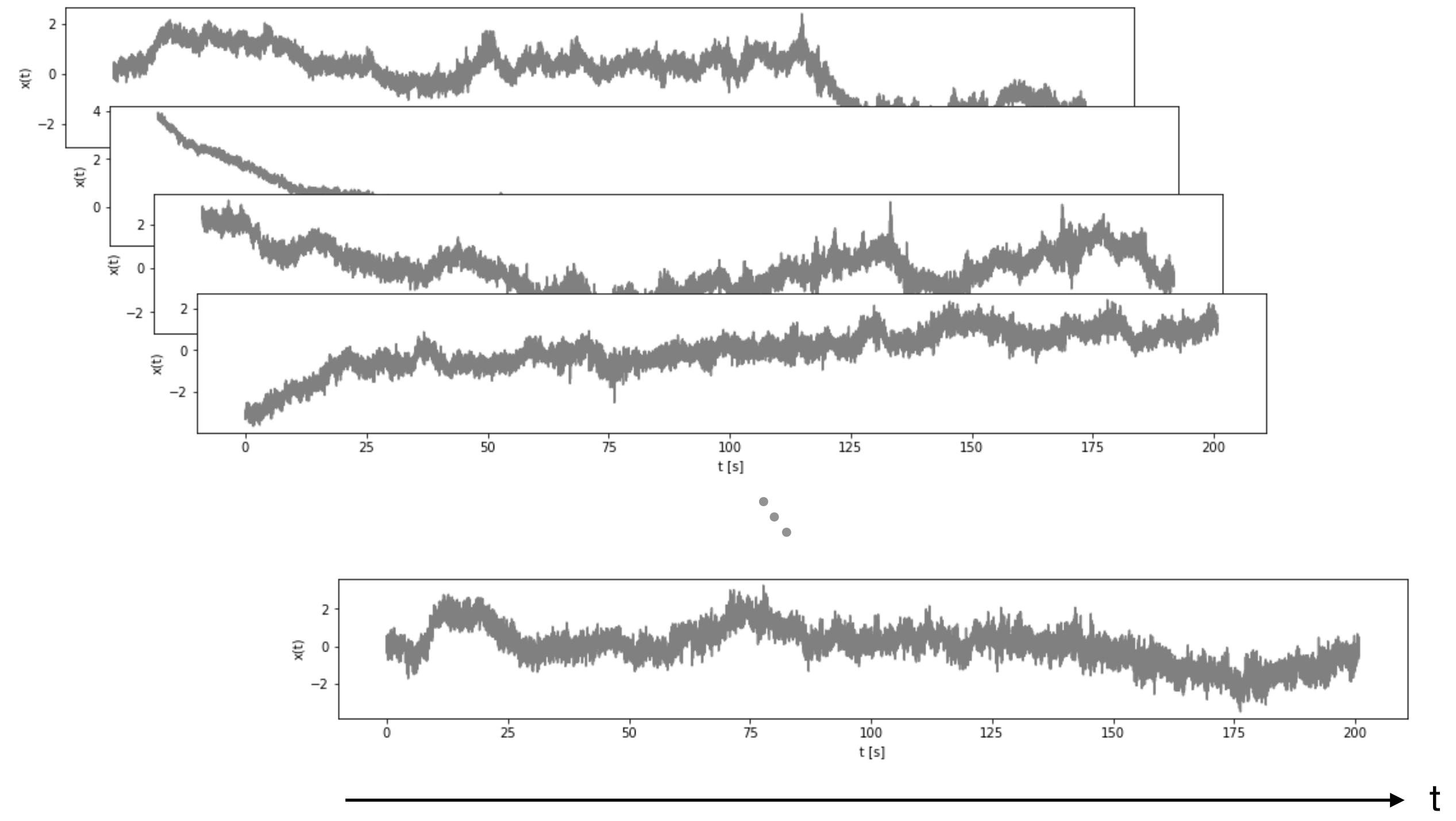
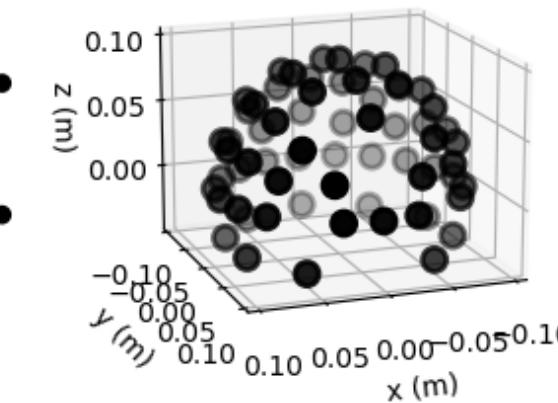
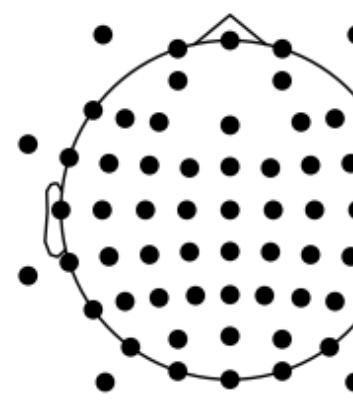
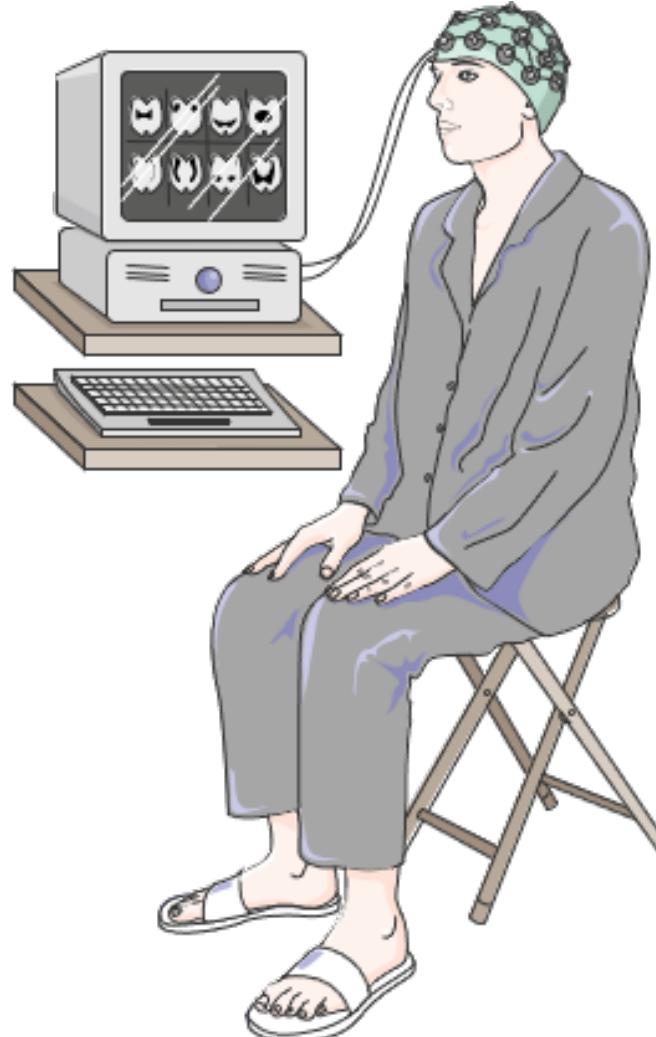
ELECTROCARDIOGRAM (ECG)

Did the patient have abnormal heart beats?



ELECTROENCEPHALOGRAPHY (EEG)

Does the patient have pain?



OVERVIEW

Motivation

Time series data

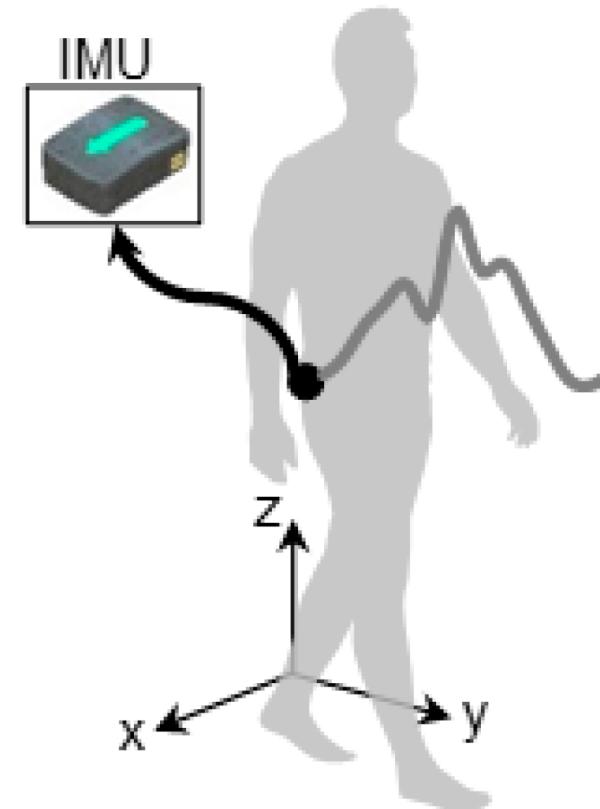
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MODELS

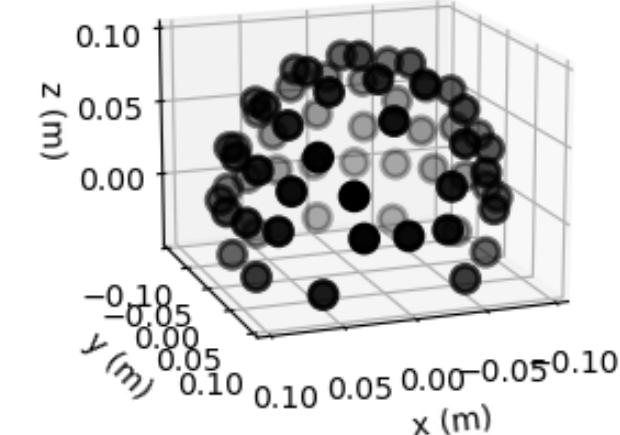
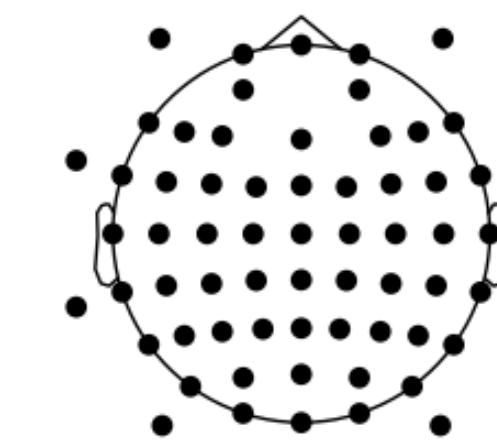
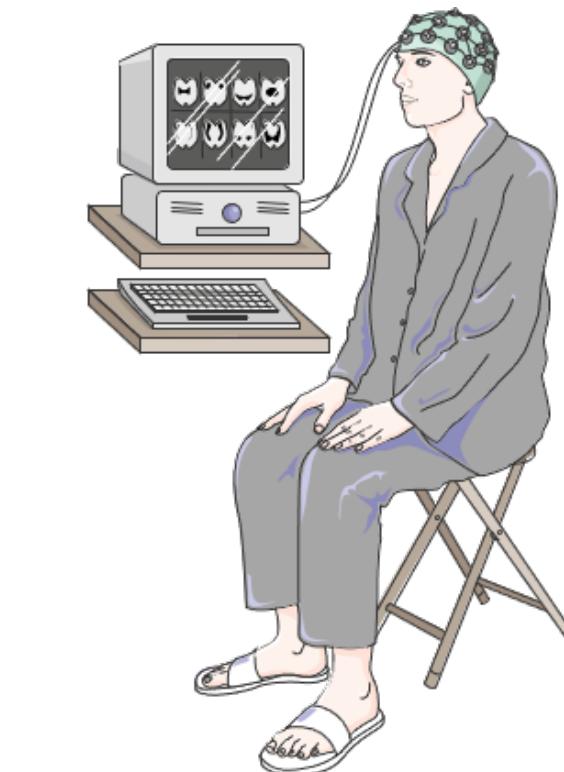
Temporal data

—> data collected across time



Spatio-temporal data

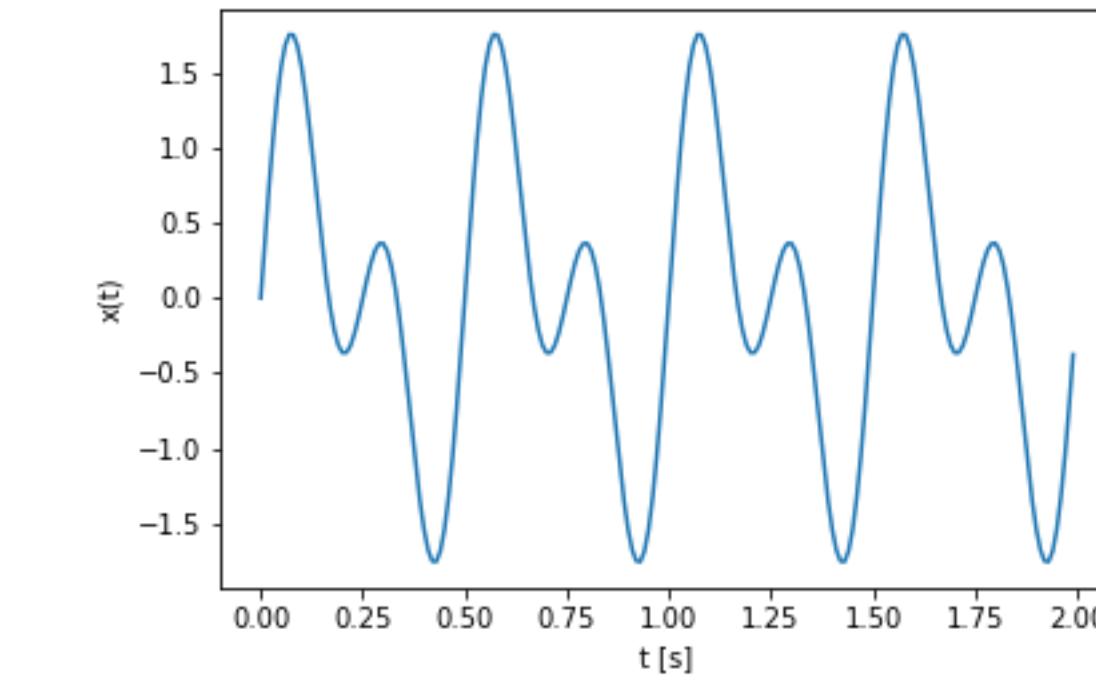
—> data collected across space and time



REPRESENTATION

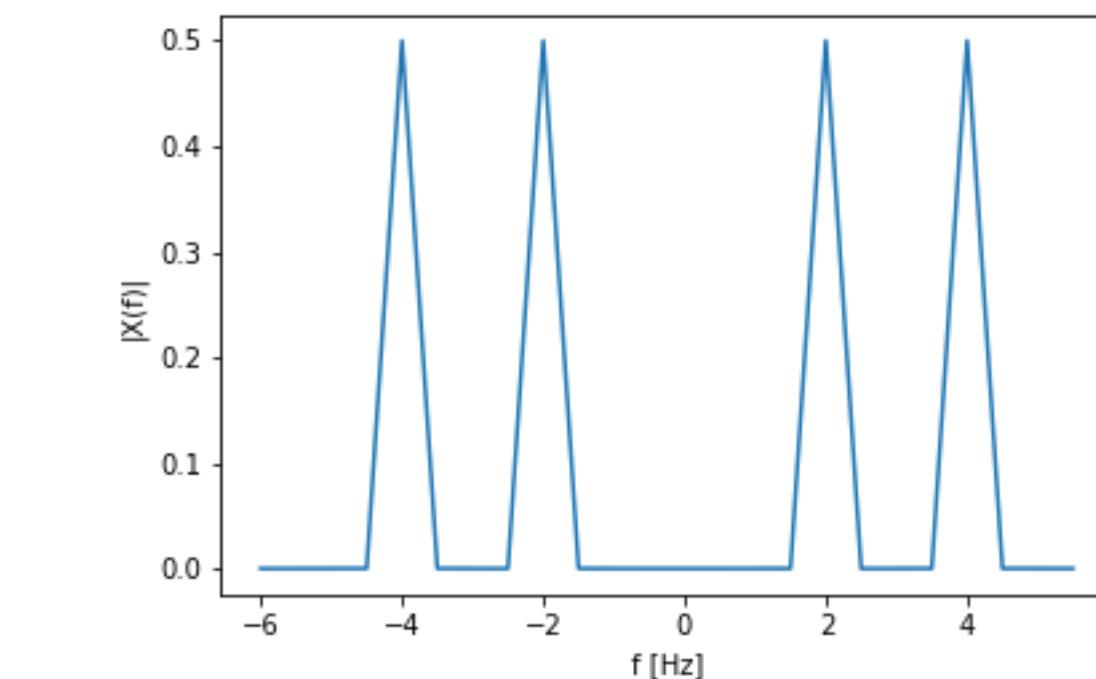
Time representation

→ time domain



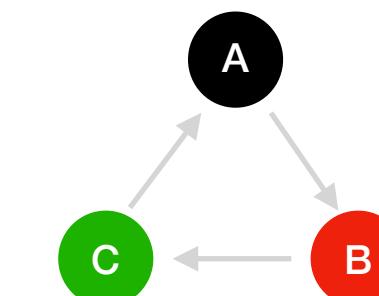
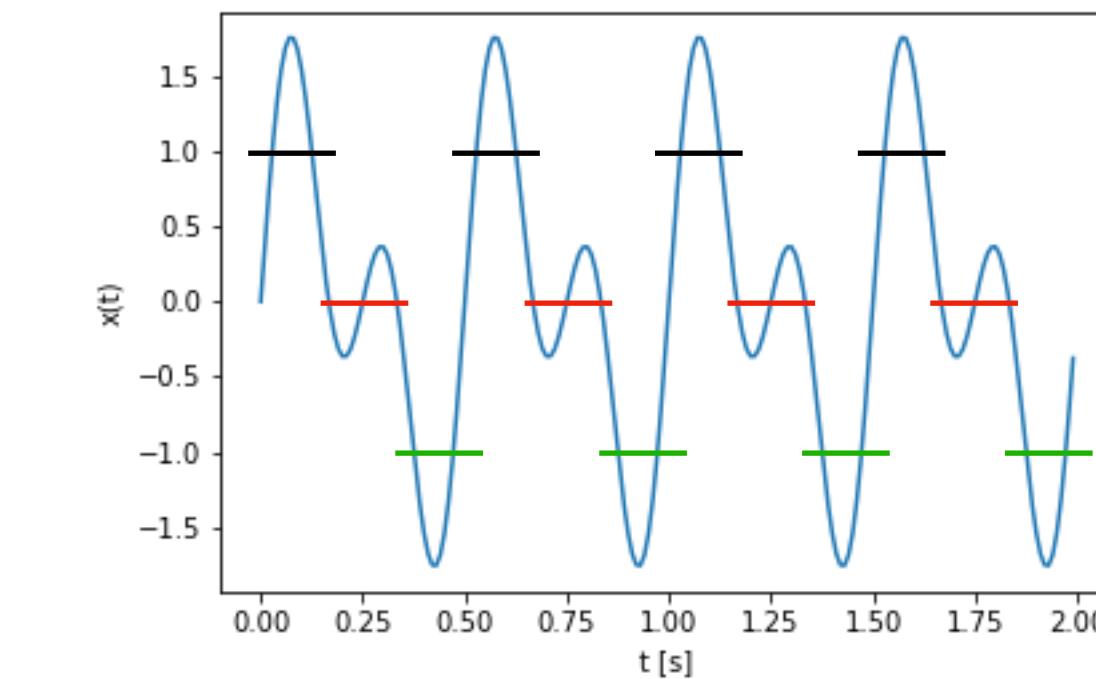
Spectral representation

→ frequency domain



State representation

→ graph domain



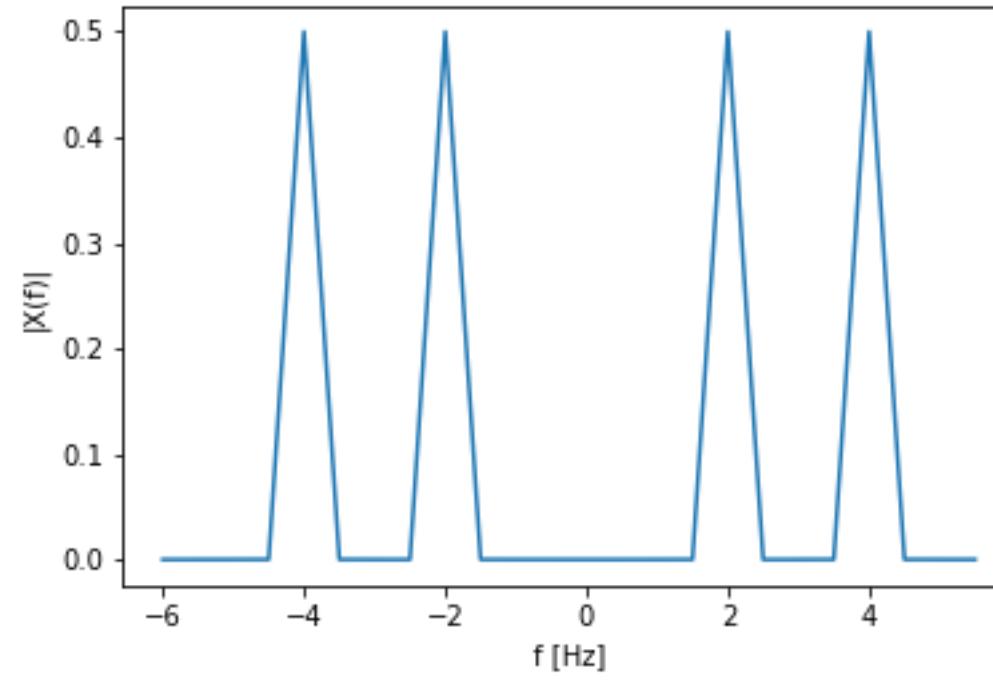
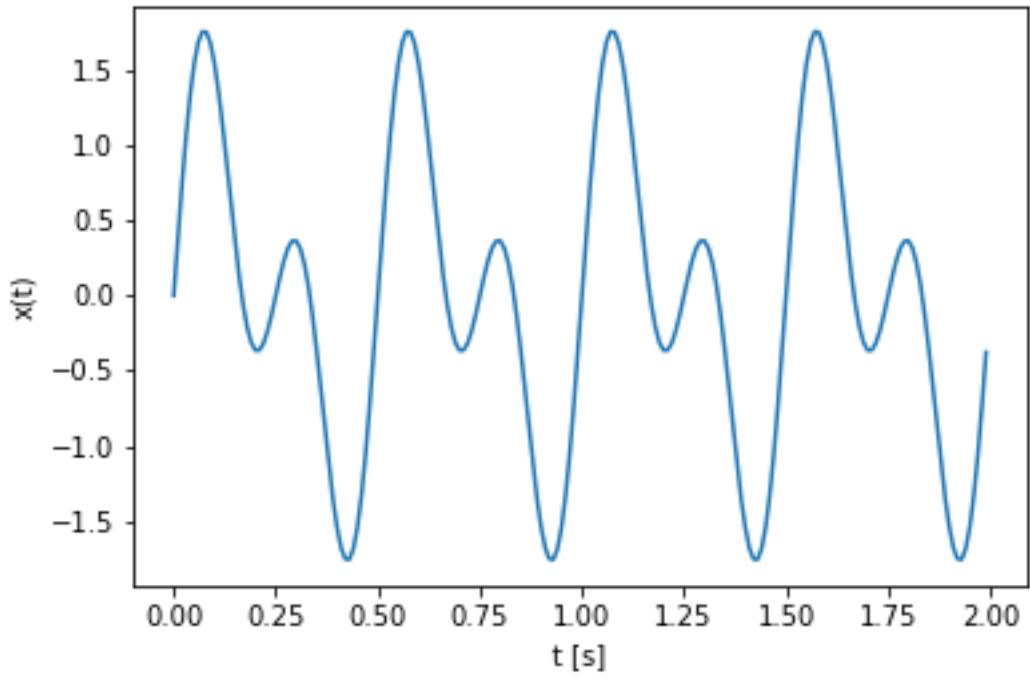
SPECTRAL REPRESENTATION

Fourier series

→ periodic signal $x(t) = x(t + T_0)$, $T_0 = \frac{1}{f_0} > 0$

$$x(t) = \sum_{k=-\infty}^{\infty} c_k \cdot e^{jk\omega_0 t}, \quad \omega_0 = \frac{2\pi}{T_0} = 2\pi \cdot f_0$$

$$c_k = \frac{1}{T_0} \cdot \int_{-T_0}^{T_0} x(t) \cdot e^{-jk\omega_0 t} dt$$

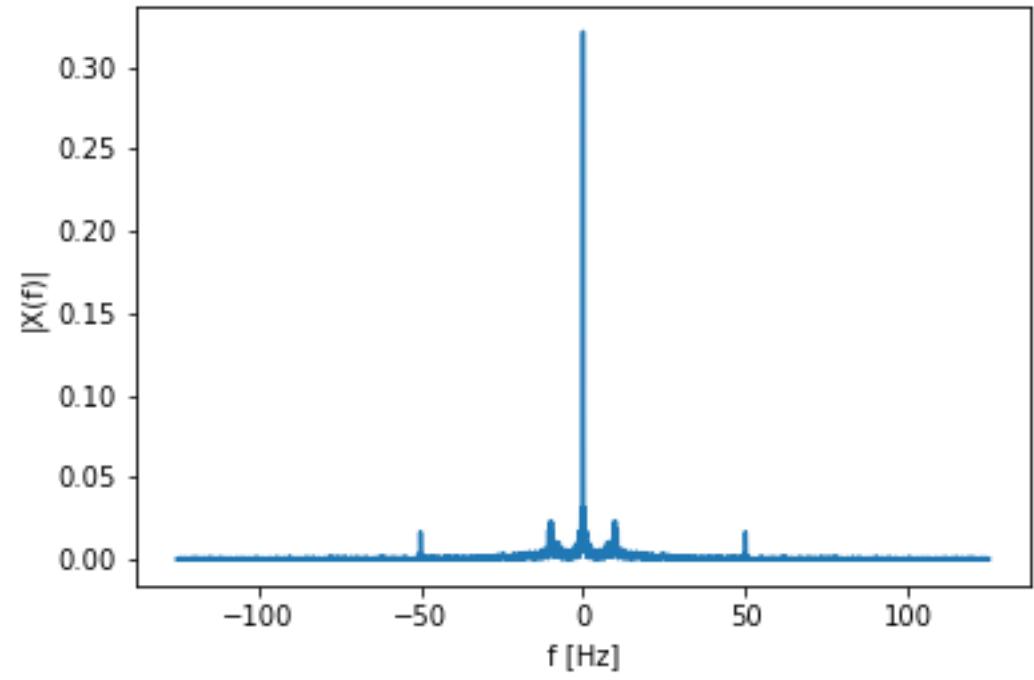
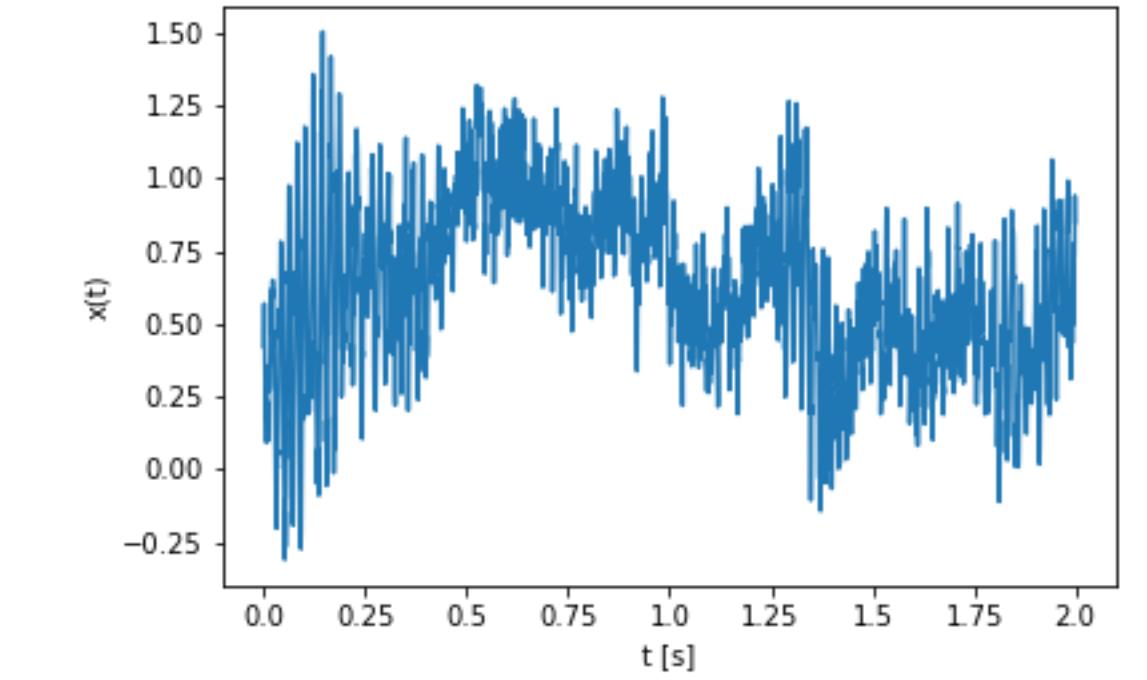


Fourier transform

→ arbitrary signal $x(t)$

$$x(t) = \frac{1}{2\pi} \cdot \int_{-\infty}^{\infty} X(\omega) \cdot e^{j\omega t} d\omega, \quad \omega = 2\pi \cdot f$$

$$X(\omega) = \int_{-\infty}^{\infty} x(t) \cdot e^{-j\omega t} dt$$



SPECTRAL REPRESENTATION

Orthogonal functions

$$\langle \phi_n, \phi_m \rangle = \int_{T_0} \phi_n^*(t) \cdot \phi_m(t) dt = K \cdot \delta_{n,m}, \quad \delta_{n,m} = \begin{cases} 1 & \text{if } n = m \\ 0 & \text{else} \end{cases}$$

Example

$$\phi_k(t) = e^{jk\omega_0 t}, \quad \int_{T_0} e^{-jn\omega_0 t} \cdot e^{jm\omega_0 t} dt = \int_{T_0} e^{j(m-n)\omega_0 t} dt = T_0 \cdot \delta_{n,m}$$

$$n = m : \quad \int_{T_0} e^{-jn\omega_0 t} \cdot e^{jn\omega_0 t} dt = \int_{T_0} e^{j(n-n)\omega_0 t} dt = \int_{T_0} 1 dt = [t]_{t_0}^{t_0+T_0} = t_0 + T_0 - t_0 = T_0$$

$$\begin{aligned} n \neq m : \quad \int_{T_0} e^{-jn\omega_0 t} \cdot e^{jm\omega_0 t} dt &= \frac{1}{j(m-n)\omega_0} \cdot [e^{j(m-n)\omega_0 t}]_{t_0}^{t_0+T_0} = \frac{1}{j(m-n)\omega_0} \cdot [e^{j(m-n)\omega_0(t_0+T_0)} - e^{j(m-n)\omega_0 t_0}] = \\ &= \frac{1}{j(m-n)\omega_0} \cdot [e^{j(m-n)\omega_0 t_0} \cdot e^{j(m-n)\omega_0 T_0} - e^{j(m-n)\omega_0 t_0}] = \frac{1}{j(m-n)\omega_0} \cdot [e^{j(m-n)\omega_0 t_0} \cdot 1 - e^{j(m-n)\omega_0 t_0}] = 0 \end{aligned}$$

SPECTRAL REPRESENTATION

Idea of Fourier series

→ every periodic signal $x(t) = x(t + T_0)$, $T_0 = \frac{1}{f_0} > 0$, can be approximated by a series of orthogonal functions $\phi_k(t)$:

$$x(t) = \sum_{k=-\infty}^{\infty} c_k \cdot \phi_k(t)$$

$$\langle \phi_{k'}, x \rangle = \int_{T_0} \phi_{k'}^*(t) \cdot x(t) dt = \int_{T_0} \phi_{k'}^*(t) \cdot \left(\sum_{k=-\infty}^{\infty} c_k \cdot \phi_k(t) \right) dt = \sum_{k=-\infty}^{\infty} \left(c_k \cdot \int_{T_0} \phi_{k'}^*(t) \cdot \phi_k(t) dt \right) = \sum_{k=-\infty}^{\infty} (c_k \cdot K \cdot \delta_{k',k}) = c_{k'} \cdot K$$

$$\implies c_k = \frac{1}{K} \cdot \int_{T_0} \phi_k^*(t) \cdot x(t) dt$$

with $\phi_k(t) = e^{jk\omega_0 t}$:

$$x(t) = \sum_{k=-\infty}^{\infty} c_k \cdot e^{jk\omega_0 t}, \quad c_k = \frac{1}{T_0} \cdot \int_{T_0} x(t) \cdot e^{-jk\omega_0 t} dt$$

SPECTRAL REPRESENTATION

Energy (Parseval's theorem)

$$E_x = \int_{-\infty}^{\infty} |x(t)|^2 dt = \frac{1}{2\pi} \cdot \int_{-\infty}^{\infty} |X(\omega)|^2 d\omega = \int_{-\infty}^{\infty} |X(2\pi \cdot f)|^2 df, \quad \omega = 2\pi \cdot f$$

Power spectral density (Wiener-Khinchin theorem)

$$S_{XX}(\omega) = \int_{-\infty}^{\infty} R_{XX}(\tau) \cdot e^{-j\omega\tau} d\tau, \quad R_{XX}(\tau) = \lim_{T_F \rightarrow \infty} \frac{1}{T_F} \int_{-\frac{T_F}{2}}^{\frac{T_F}{2}} x(t) \cdot x(t + \tau) dt, \quad \omega = 2\pi \cdot f$$

OVERVIEW

Motivation

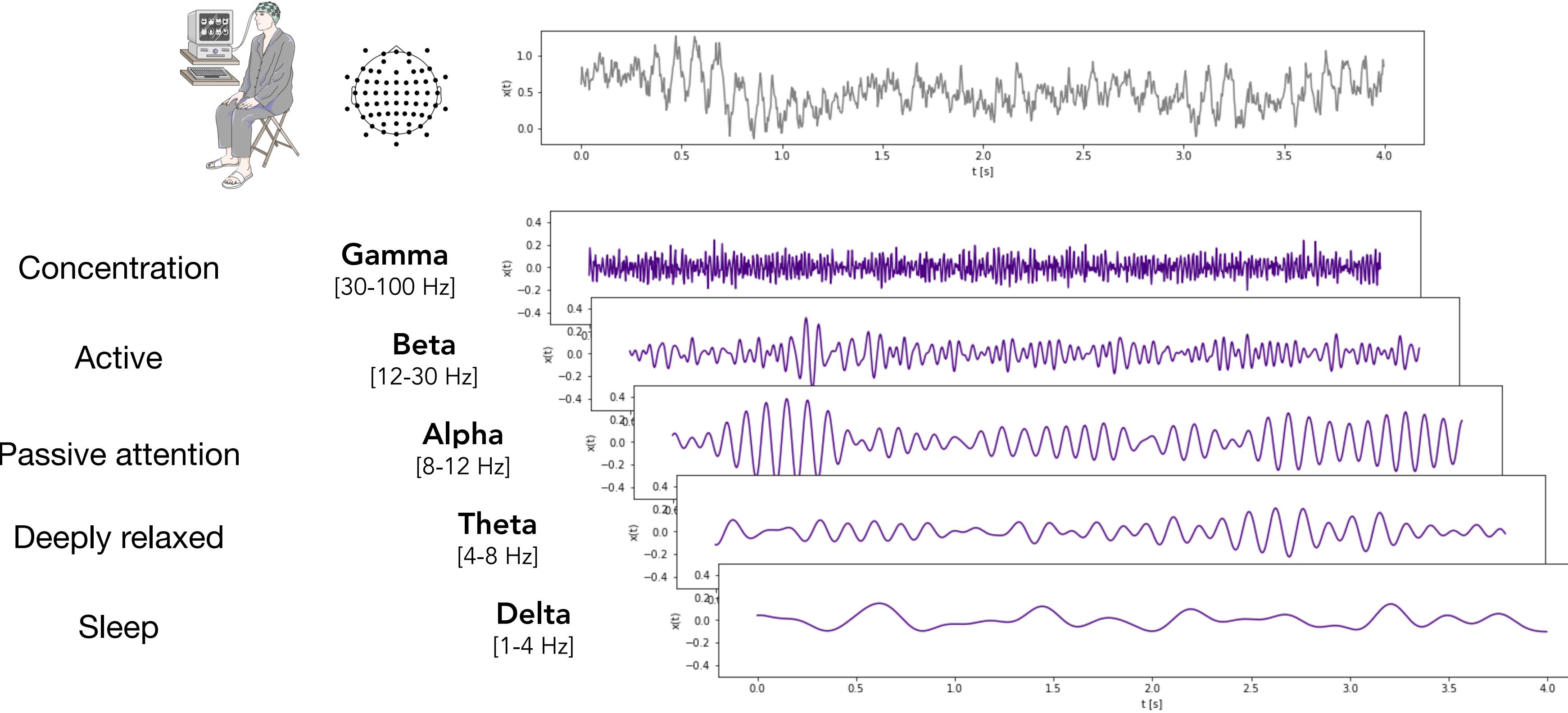
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BRAINWAVE FREQUENCIES

EEG signals are composed of signals from different frequency bands



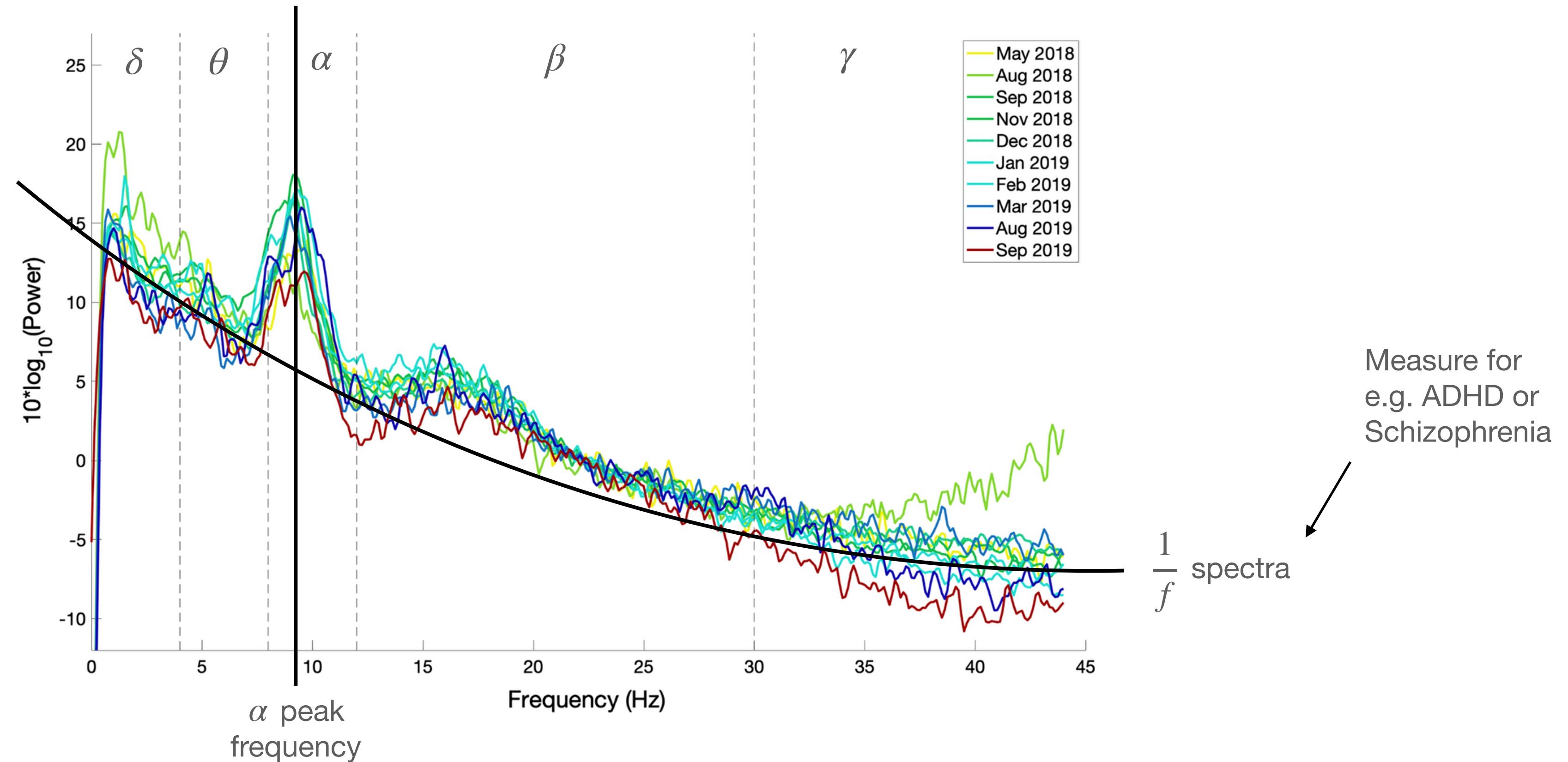
[4] Compute the average bandpower of an EEG signal. Accessed last: 04.06.2022. URL: <https://raphaelvallat.com/bandpower.html>

[5] Abhang, Priyanka A., Bharti W. Gawali, and Suresh C. Mehrotra. "Technological basics of EEG recording and operation of apparatus." *Introduction to EEG-and speech-based emotion recognition* (2016): 19-50.

EEG POWER SPECTRAL DENSITY (PSD)

PSD represents the power distribution of the EEG signal

→ How much do the signals from each frequency band contribute to the measured EEG signal?



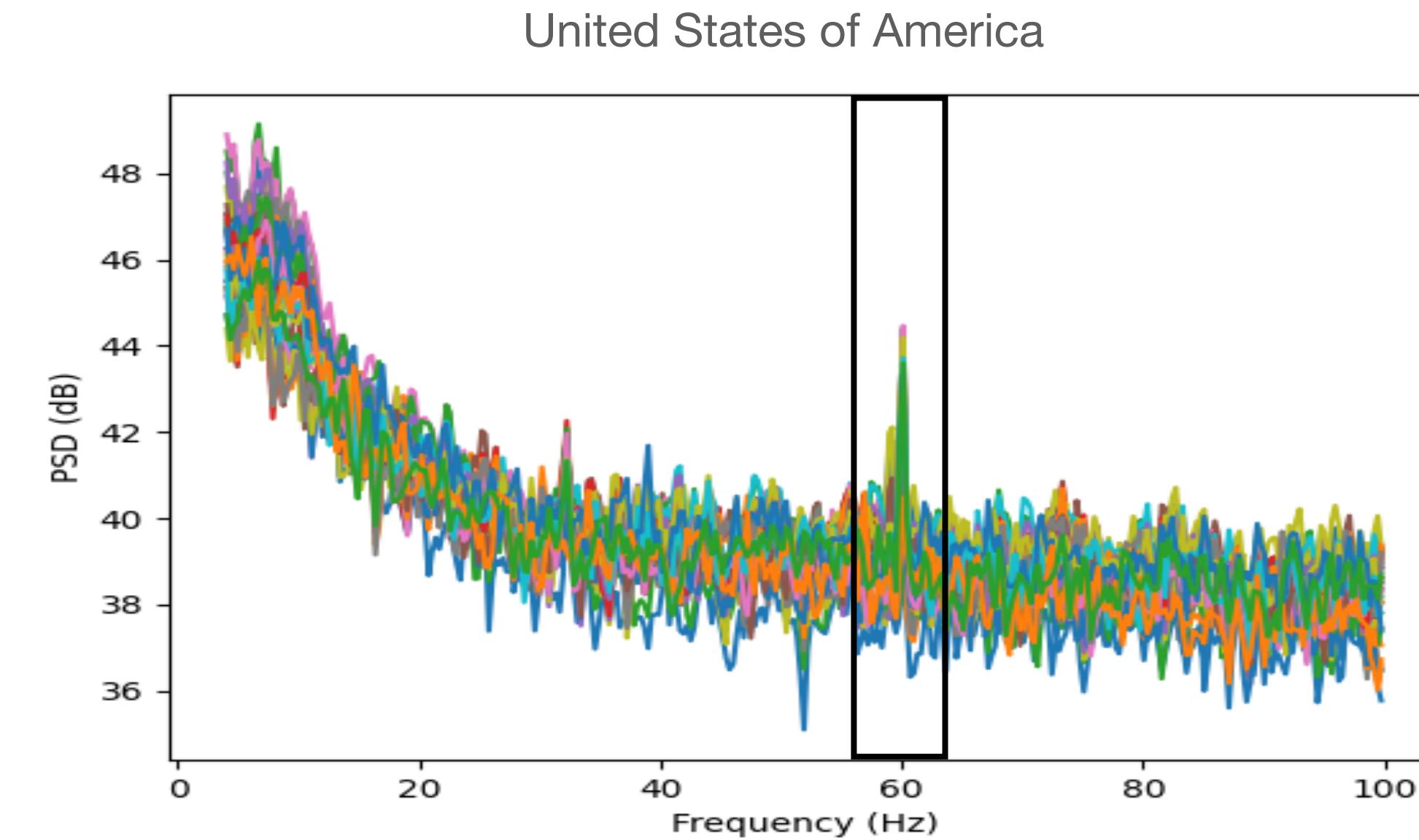
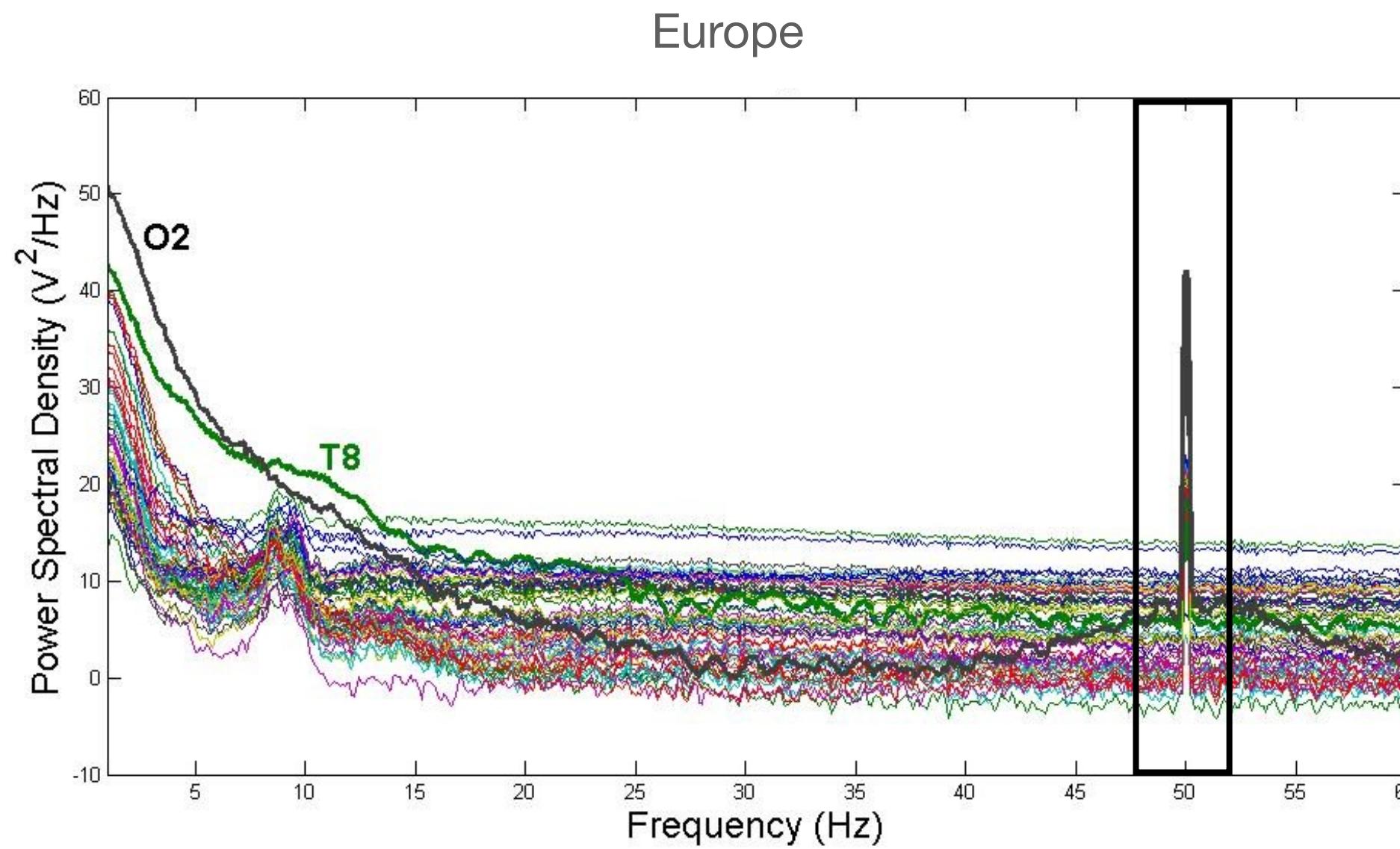
[6] Secco, Arianna, et al. "EEG power spectral density in locked-in and completely locked-in state patients: a longitudinal study." *Cognitive neurodynamics* 15.3 (2021): 473-480

[7] Donoghue, Thomas, et al. "Parameterizing neural power spectra into periodic and aperiodic components." *Nature neuroscience* 23.12 (2020): 1655-1665.

EEG POWER SPECTRAL DENSITY (PSD)

Noise from the outlet (i.e. electricity)

→ Has to be taken into account in the software



Raw EEG signals require pre-processing to remove artifacts

[8] Pre-processing for ERP analysis. Accessed last: 04.06.2022. URL: <https://blricrex.hypotheses.org/ressources/eeg/pre-processing-for-erps>

[9] Compute source power spectral density (PSD) in a label. Accessed last: 04.06.2022. URL: https://mne.tools/stable/auto_examples/time_frequency/source_power_spectrum.html

EEG PRE-PROCESSING

Artifacts

Some **unexpected or unwanted features in the data** that were acquired with the EEG system. Artifacts **can be physiological or non-physiological** in origin.

A physiological artifact: an eye-blink. The retina is electrically charged and the movement of the eye causes a deflection of the scalp potential. The contribution of this so-called electrooculogram is mainly visible on frontal electrodes, but when looking carefully enough, one can see it on all electrodes.

A non-physiological artifact: an EEG electrode that has poor contact with the scalp. The corresponding EEG channel will show a flat line, or potentially a lot of noise.

Besides considering the physiological or non-physiological aspect of the artifact, it can also be thought about whether the artifact is **caused by the behavior of the participant** (e.g., an eye movement), whether it is **caused by something in the environment** (e.g., 50Hz line noise) or whether it is **caused by a malfunction of the equipment** (e.g., a poorly attached electrode). Behavioral artifacts are typically short-lived, whereas environmental and instrumentation artifacts are typically more persistent.

There is no most optimal manner to detect artifacts: it depends on the data properties, the type of artifacts that is anticipated to be present (given the recording setup, the task, and the participants), and the own preferences.

EEG PRE-PROCESSING

Artifact detection

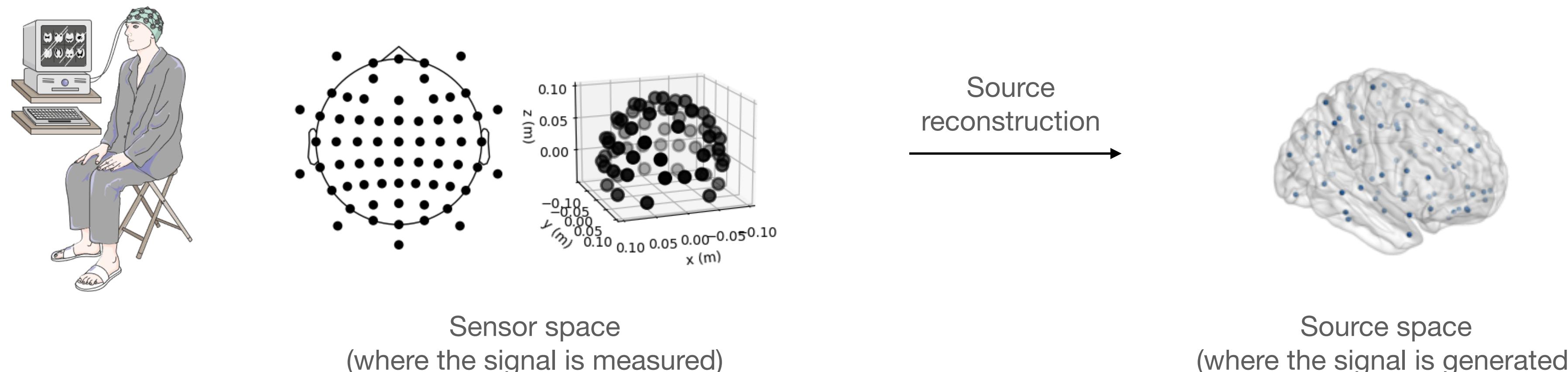
Can be done visually, or using automatic routines, or a combination of both.

Artifact removal

Can be done by rejecting the piece of data containing the artifact, e.g., for a short-lived artifact or poorly attached EEG electrode, or by subtracting the spatio-temporal contribution of the artifact from the data, e.g., using a filter (e.g. to eliminate 50Hz line noise) or Independent Component Analysis (ICA) (e.g. to eliminate eye-blanks).

SOURCE RECONSTRUCTION

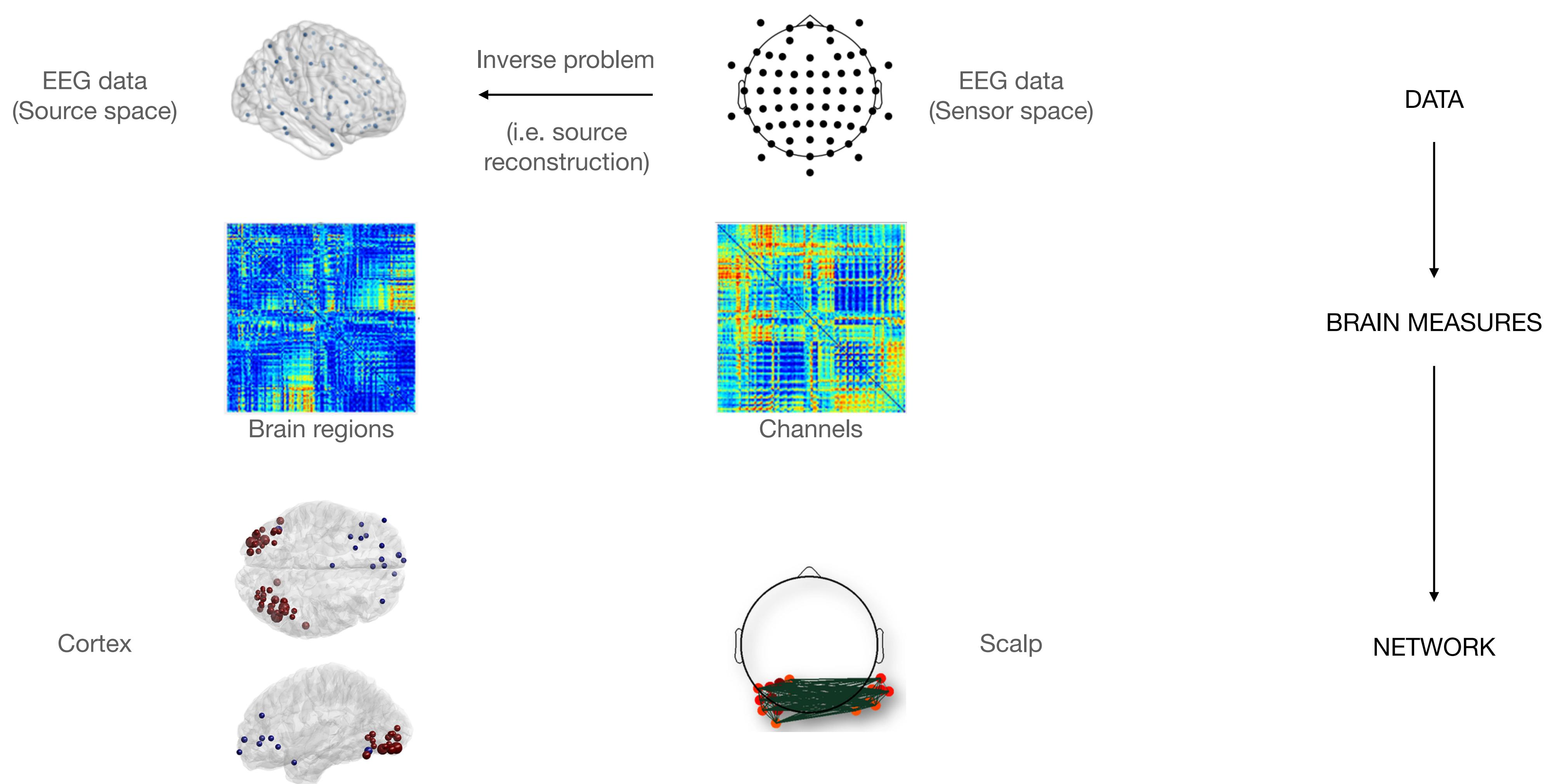
The EEG signals measured on the scalp do not directly reflect the location of the activated neurons. To reconstruct the location and the time-course or spectral content of a source in the brain, various source-localization methods are available.



[11] Creating a BEM volume conduction model of the head for source-reconstruction of EEG data. Accessed last: 06.06.2022. URL: https://www.fieldtriptoolbox.org/tutorial/headmodel_eeg_bem/

[12] Chang, Qi, et al. "Classification of First-Episode Schizophrenia, Chronic Schizophrenia and Healthy Control Based on Brain Network of Mismatch Negativity by Graph Neural Network." *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 29 (2021): 1784-1794.

SOURCE RECONSTRUCTION



[12] Chang, Qi, et al. "Classification of First-Episode Schizophrenia, Chronic Schizophrenia and Healthy Control Based on Brain Network of Mismatch Negativity by Graph Neural Network." *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 29 (2021): 1784-1794.

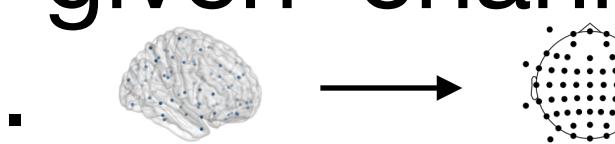
[13] Hassan, Mahmoud, et al. "EEGNET: An open source tool for analyzing and visualizing M/EEG connectome." *PloS one* 10.9 (2015): e0138297.

SOURCE RECONSTRUCTION

The level of activity at a source location is estimated from four ingredients:

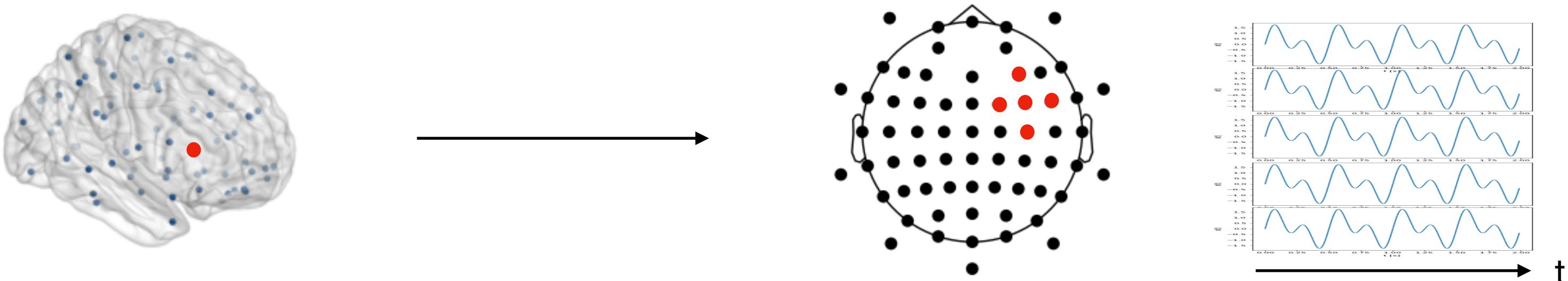
1. **EEG signal** measured on the scalp
2. Spatial arrangements of the electrodes (i.e. sensors) (**channel positions**)
3. Location of the source (**source model**)
4. Geometrical and electrical/magnetic properties of the head (**head model**)

Using this information, source estimation comprises two major steps:

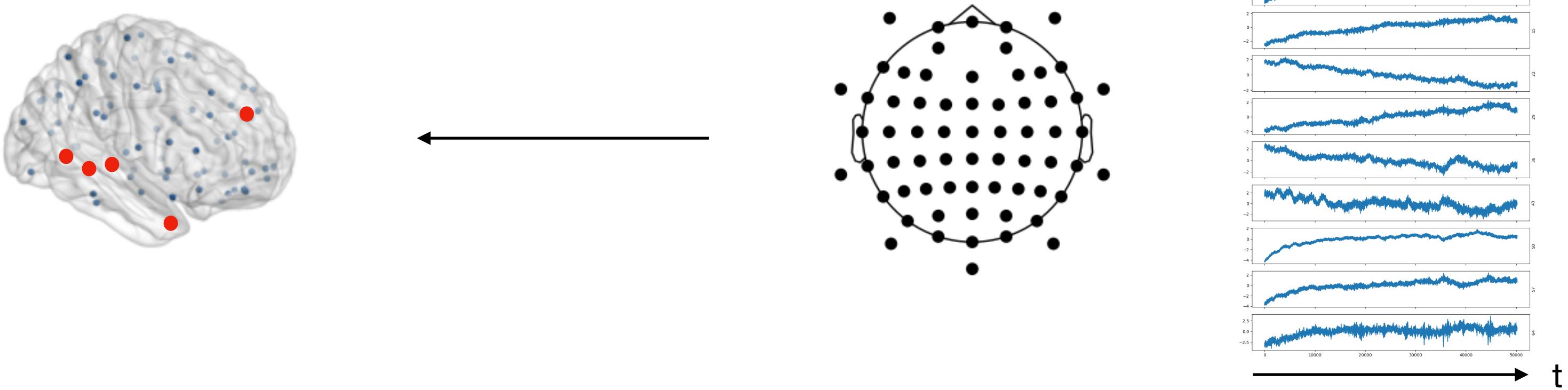
1. Estimation of the potential or field distribution with the given channel positions, source model, and head model is referred to as **forward modeling**.  Prerequisite of forward modeling is that the geometrical description of all elements (channel positions, head model and source model) is registered in the same coordination system with the same units.
2. Estimation of the unknown sources corresponding to the measured EEG or MEG is referred to as **inverse modeling**. 

SOURCE RECONSTRUCTION

Forward modeling:



Inverse modeling:



SOURCE RECONSTRUCTION METHOD

Beamformer

A **spatial filter** that reconstructs source activity by scanning through a grid of pre-defined source points and estimating activity at each of those source points independently.

A set of weights is constructed for each defined source location which **defines** the **contribution of each sensor to this source**. (Lead field matrix w/ dimensions: channels \times source points)

The spatial filter is **computed from** two ingredients: the **forward model solution** and the **covariance matrix of the data**. The data covariance matrix should be estimated from a time window that includes the brain signal of interest, and incorporate enough samples for a stable estimate. A rule of thumb is to use more samples than there are channels in the data set.

Beamforming method that operates on time series data is the linearly constrained minimum variance (LCMV) beamformer. Frequency-resolved data can be reconstructed with the dynamic imaging of coherent sources (DICS) beamforming method.

BRAIN MEASURES

Connectivity

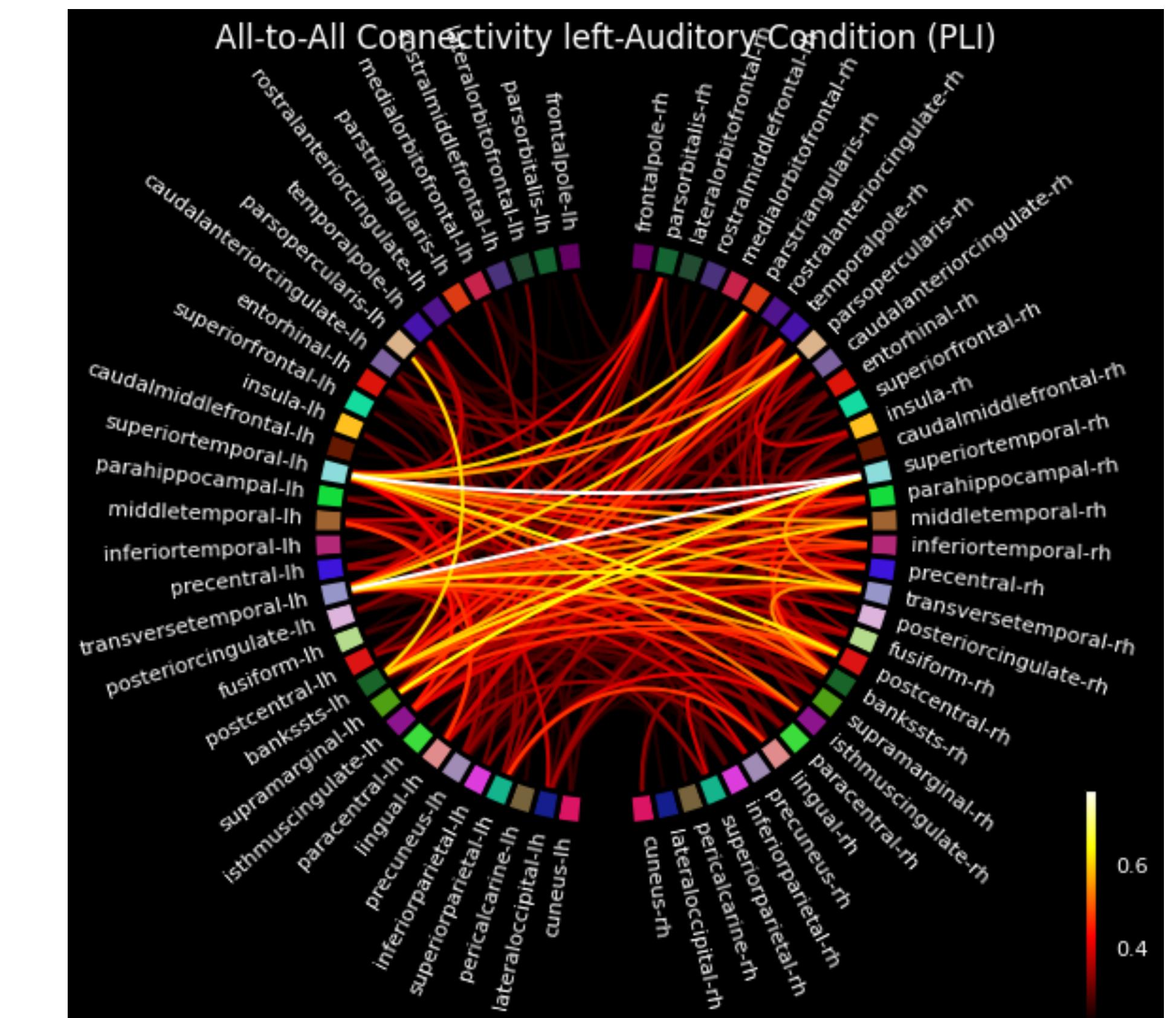
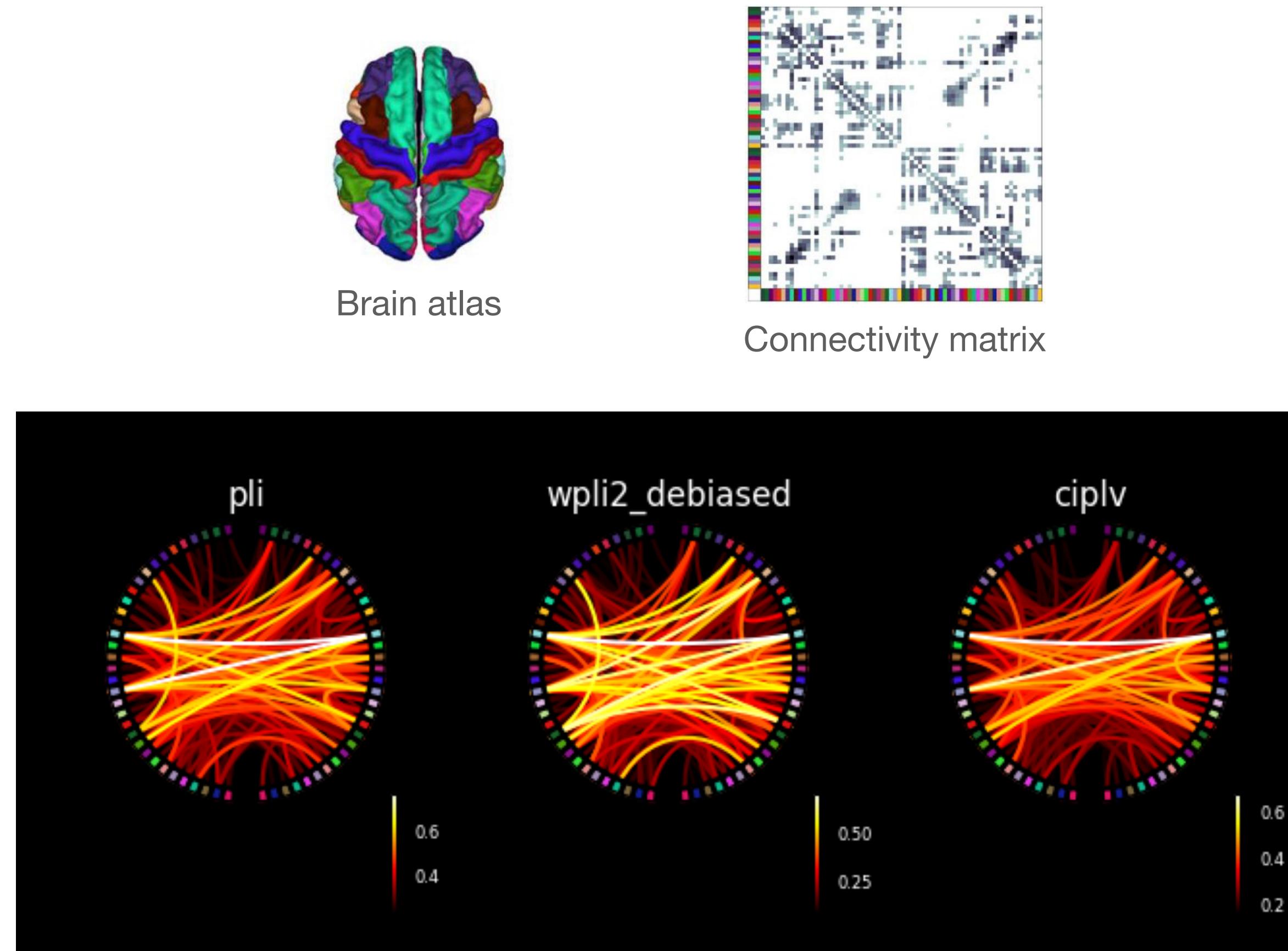
The **brain** is organized in functional units, which at the smallest level consists of neurons, and at higher levels consists of larger neuronal populations. The brain is considered to be **organized in specialized neuronal modules corresponding to specific areas in the brain**. These functionally specialized **brain areas** have to **pass information back and forth along anatomical connections**. Identifying these functional connections and determining their functional relevance is the goal of connectivity analysis.

The nomenclature for connectivity analysis can be adopted from graph theory, in which brain areas correspond to nodes or vertices and the connections between the nodes is given by edges. One of the fundamental challenges in the analysis of brain networks from EEG data lies not only in identifying the “edges”, i.e. the functional connections, but also the “nodes”.

Many measures of connectivity exist, and they can be broadly divided into measures of **functional connectivity** (denoting statistical dependencies between measured signals, without information about causality/directionality), and measures of **effective connectivity**, which describe directional interactions.

BRAIN MEASURES

Connectivity



[16] Jang, Sooboom, Seong-Eun Moon, and Jong-Seok Lee. "EEG-based video identification using graph signal modeling and graph convolutional neural network." *2018 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP)*. IEEE, 2018.

[17] Compute source space connectivity and visualize it using a circular graph. Accessed last: 07.06.2022. URL: https://mne.tools/mne-connectivity/stable/auto_examples/mne_inverse_label_connectivity.html

OVERVIEW

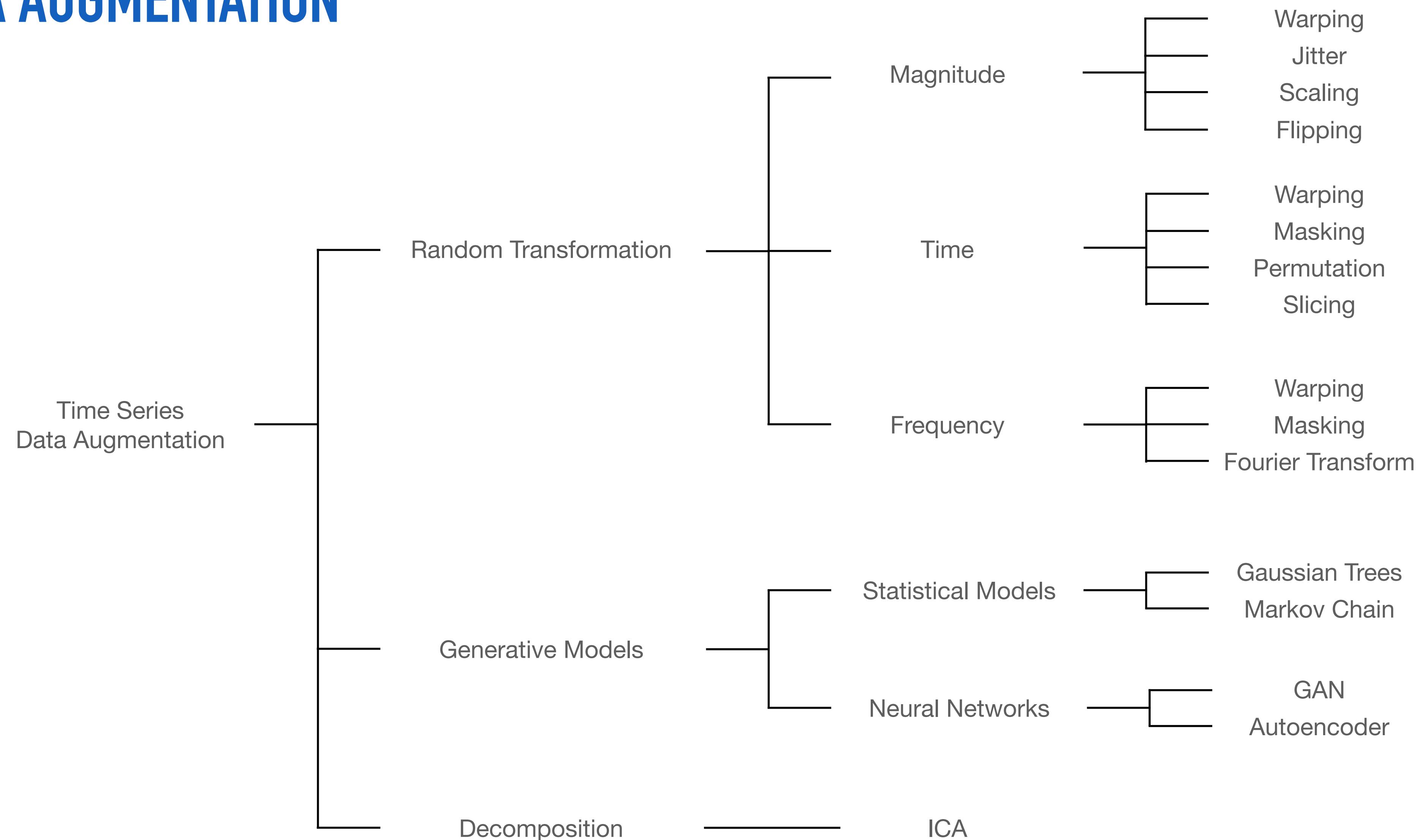
Motivation

Time series data

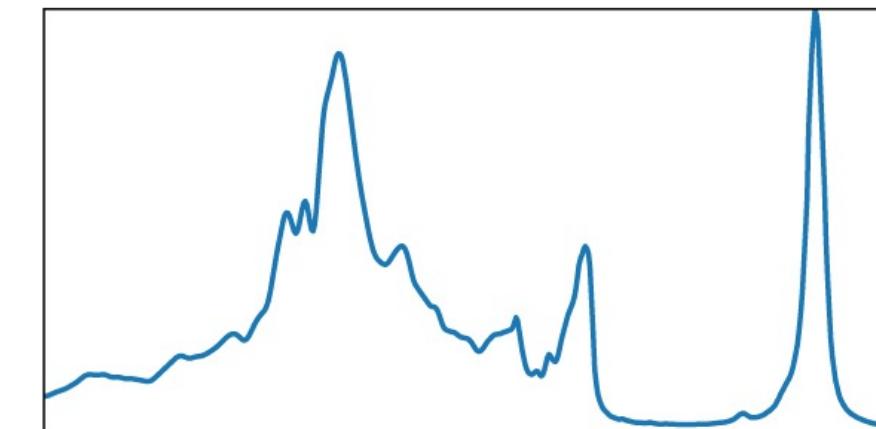
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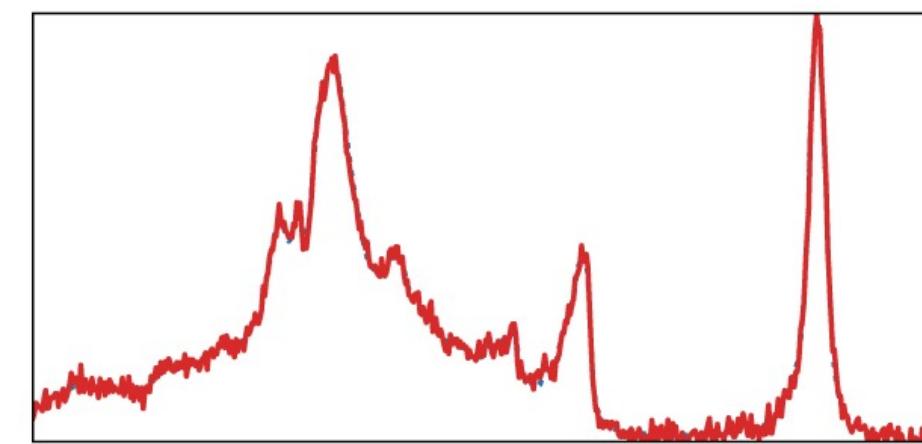
DATA AUGMENTATION



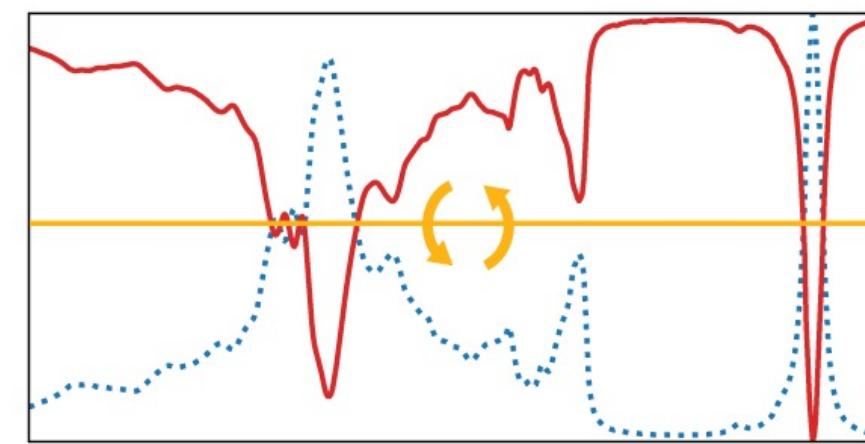
DATA AUGMENTATION (RANDOM TRANSFORMATION)



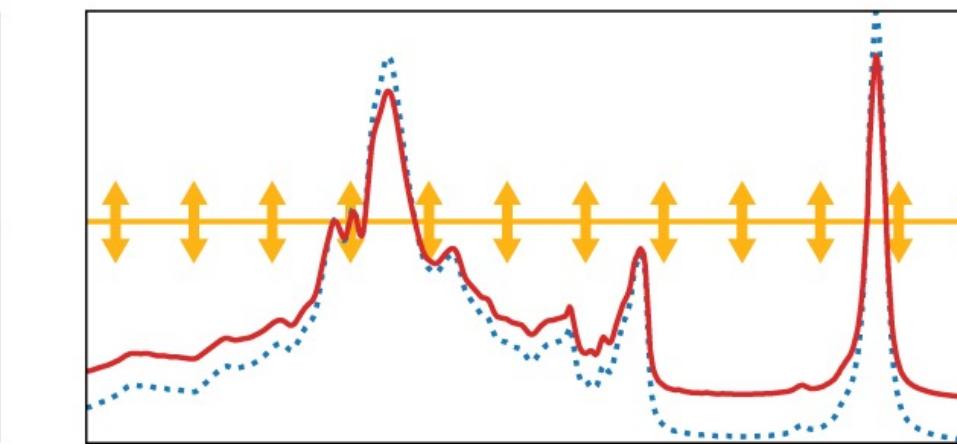
(a) Original



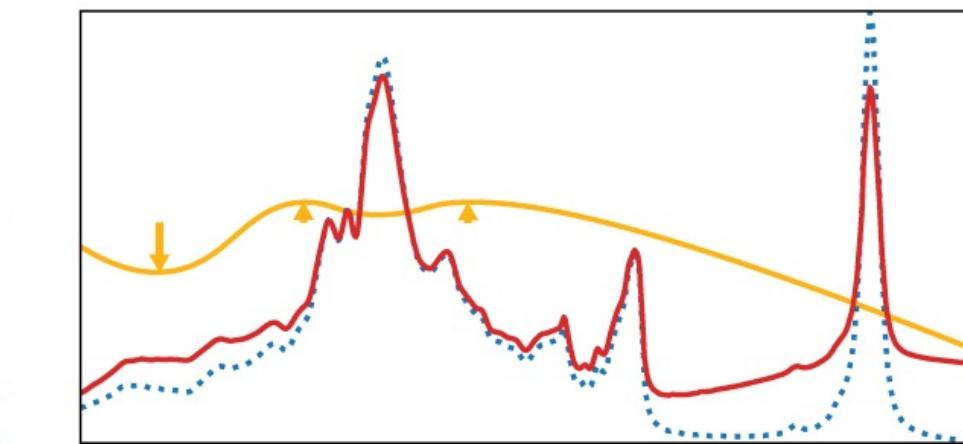
(b) Jittering



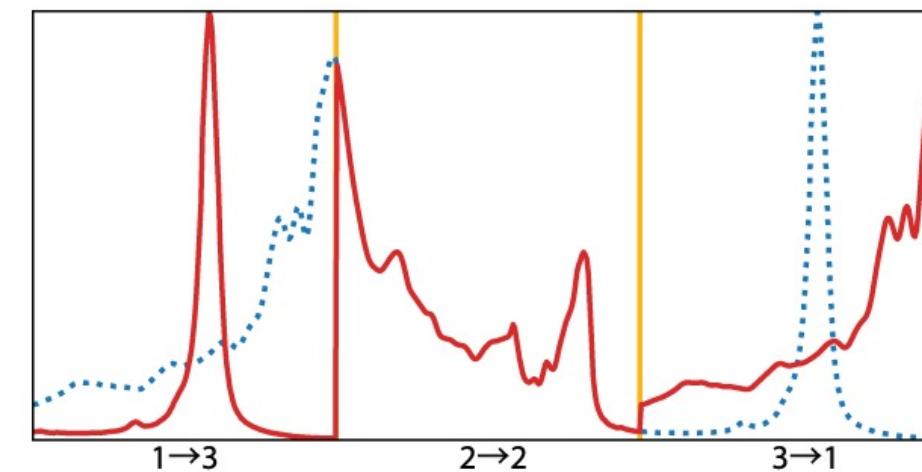
(c) Flipping



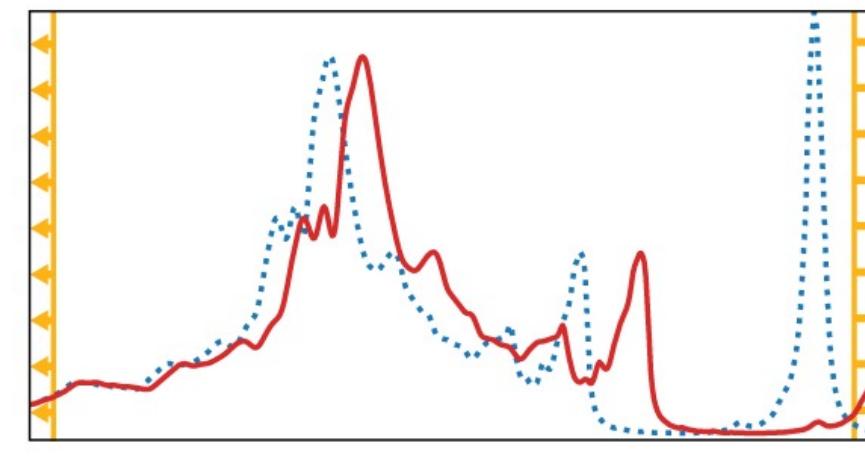
(d) Scaling



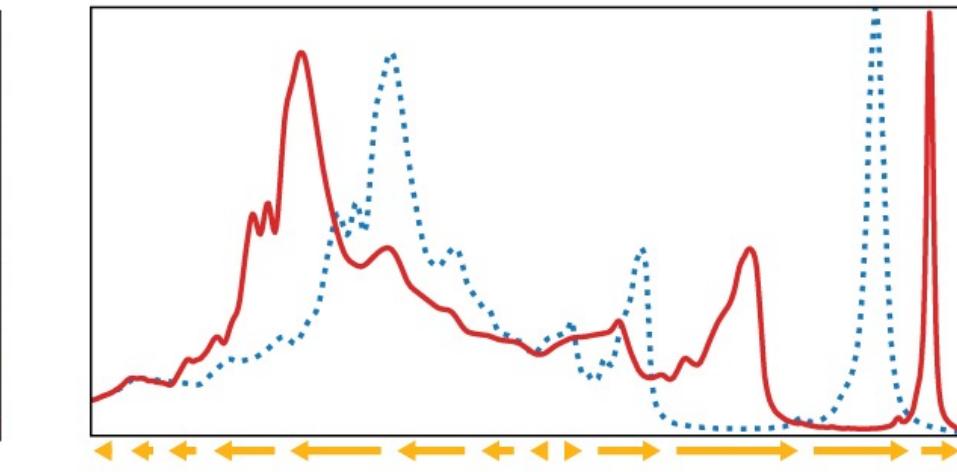
(e) Magnitude Warping



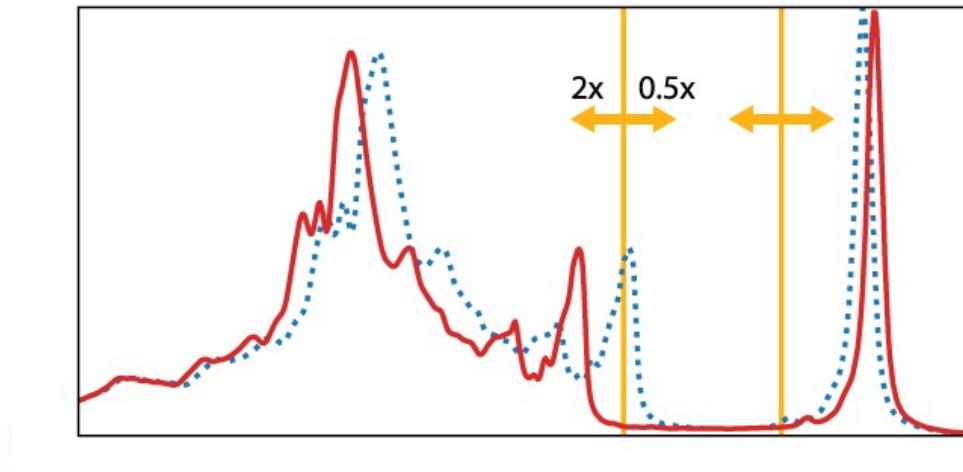
(f) Permutation



(g) Window Slicing



(h) Time Warping

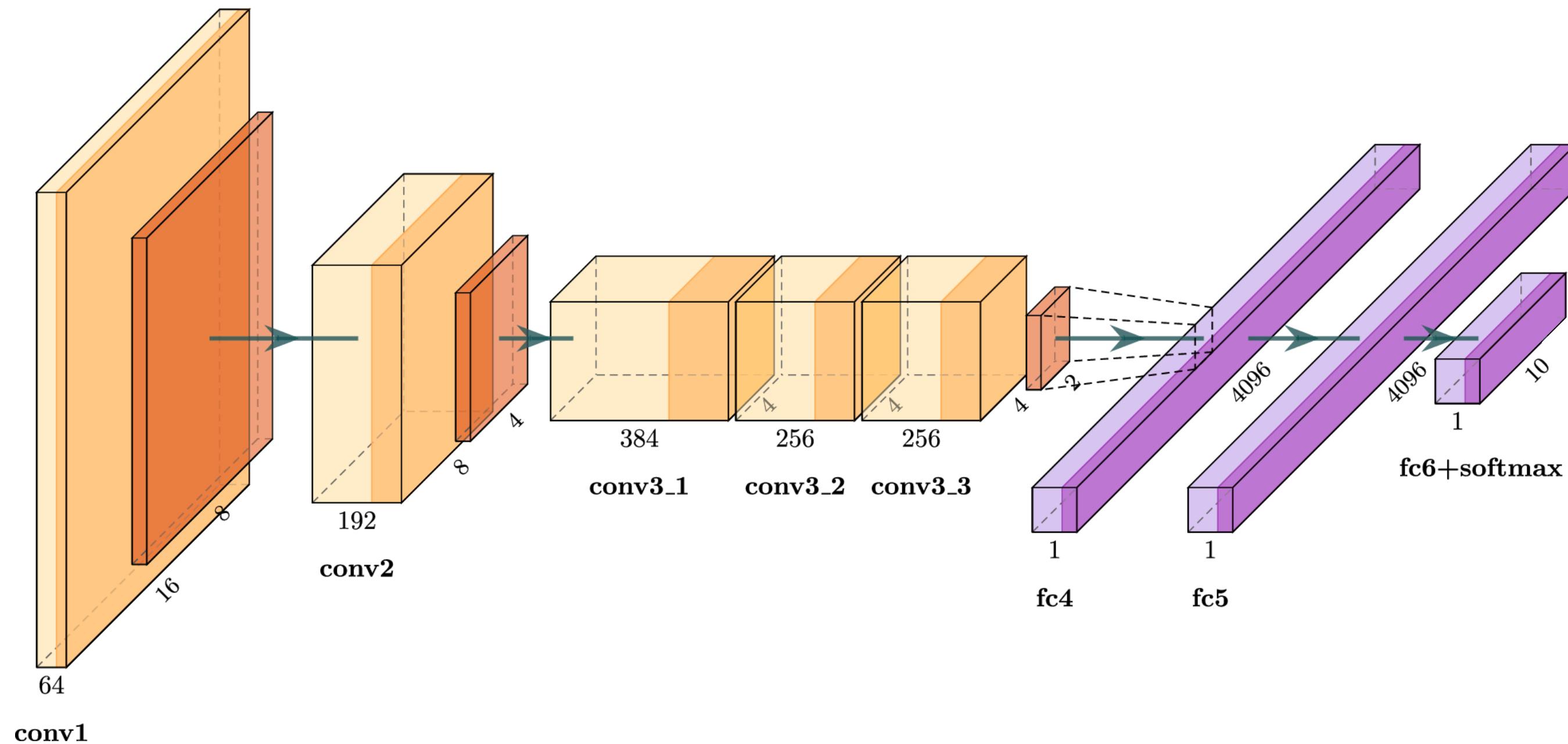


(i) Window Warping

CONVOLUTIONAL NEURAL NETWORK (CNN)

CNN

→ to iteratively aggregate local information



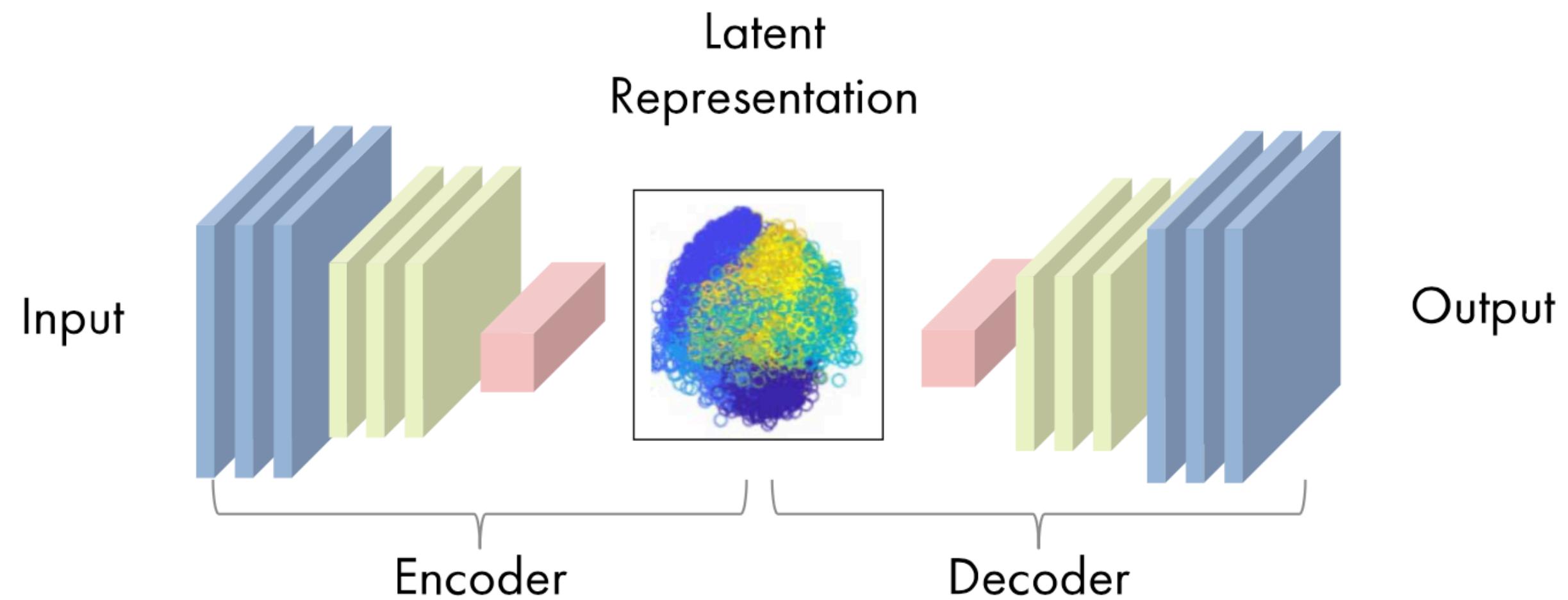
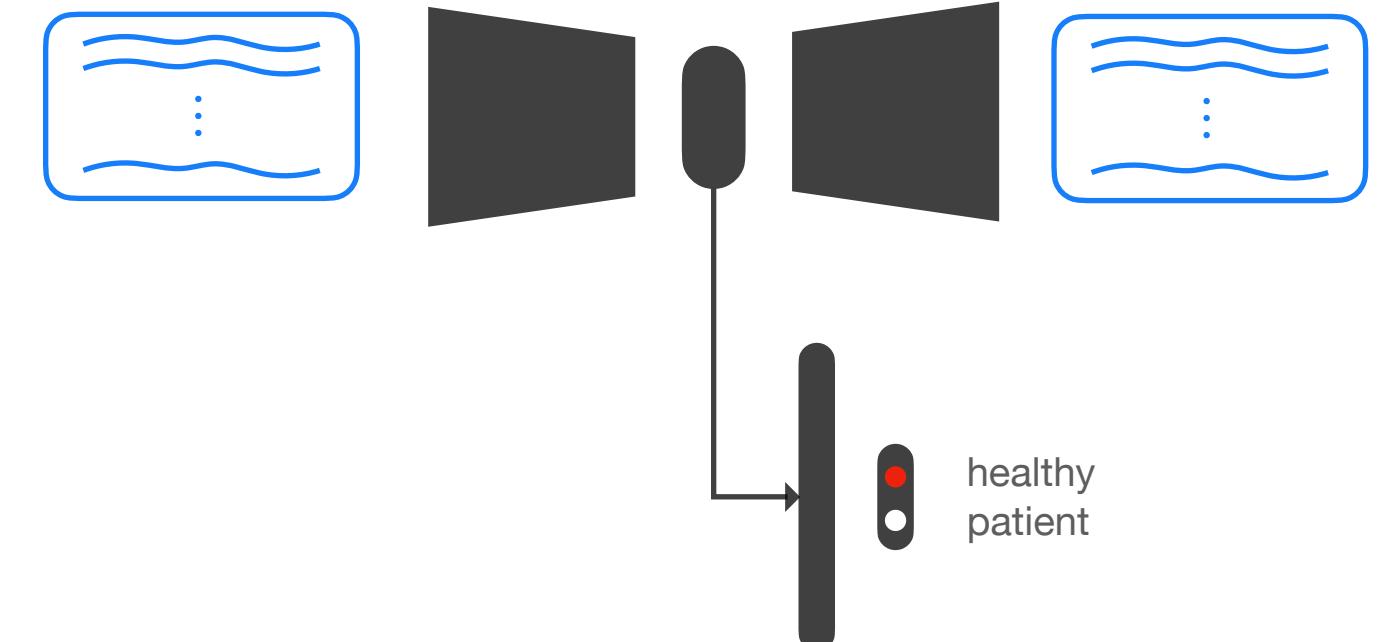
[19] Krizhevsky, Alex, Ilya Sutskever, and Geoffrey E. Hinton. "Imagenet classification with deep convolutional neural networks." *Advances in neural information processing systems* 25 (2012).

[20] Strisciuglio, Nicola, Manuel Lopez-Antequera, and Nicolai Petkov. "Enhanced robustness of convolutional networks with a push–pull inhibition layer." *Neural Computing and Applications* 32.24 (2020): 17957-17971.

AUTOENCODER

Autoencoder

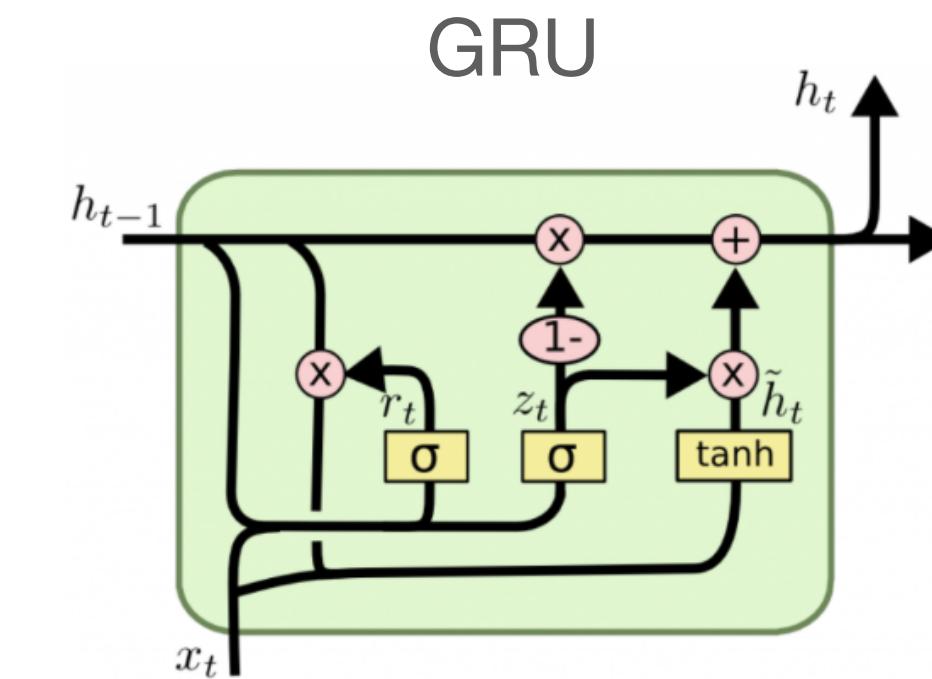
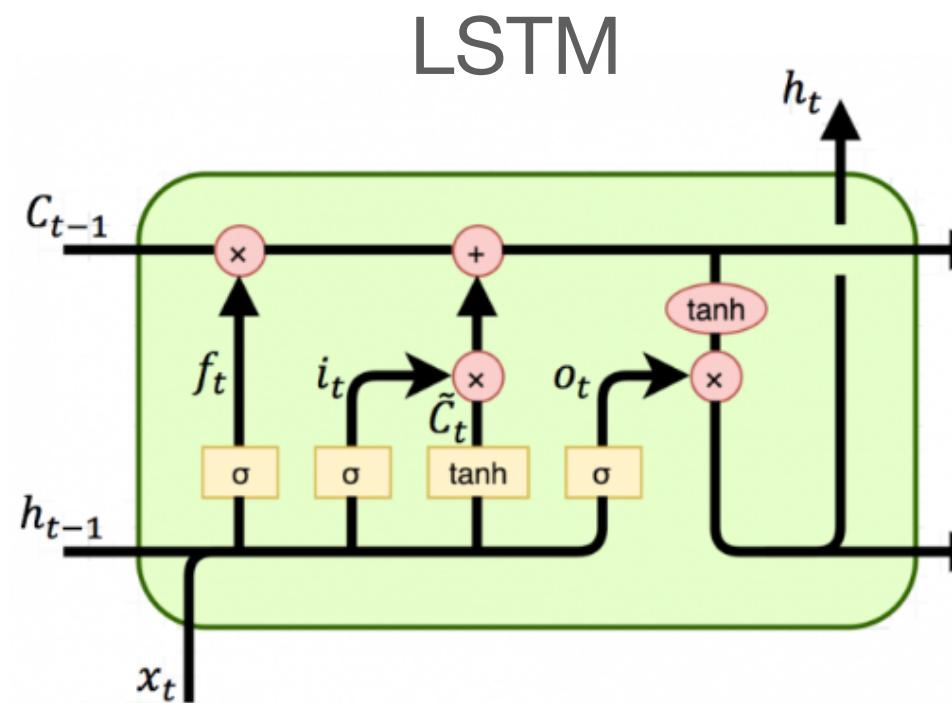
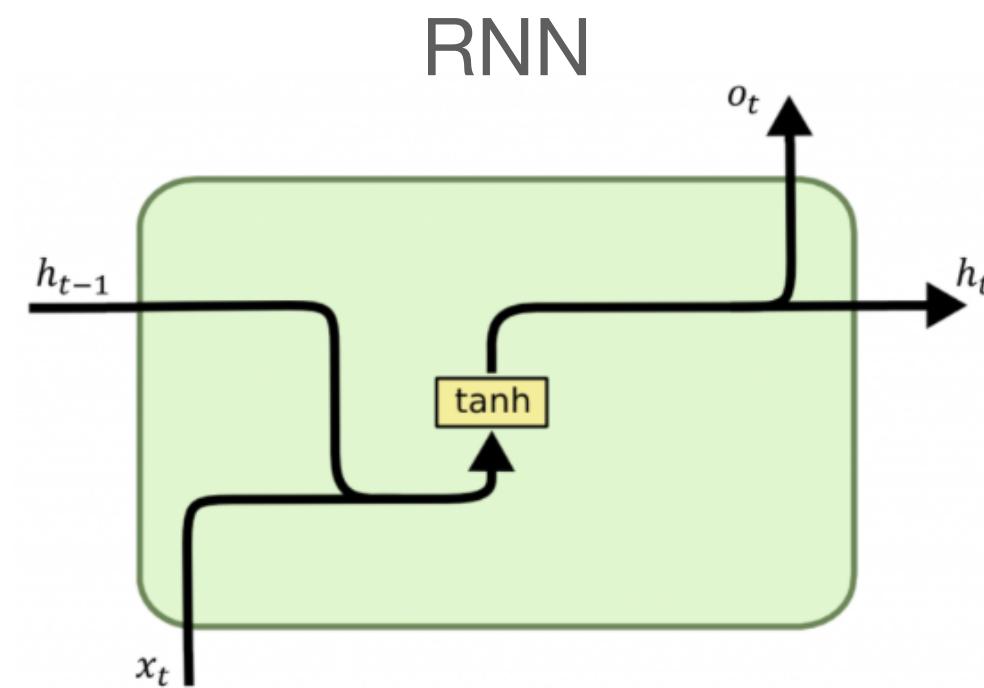
→ to learn a meaningful latent representation



RECURRENT NEURAL NETWORKS

RNN, LSTM & GRU

→ to process dynamic behavior and to carry relevant information throughout a sequence



+ Processing of sequence w/ dynamic lengths

- Cannot handle long sequences:
 - Hidden state is overwritten
 - Vanishing gradients

+ Cell state modified (not overwritten)
→ capture longer dependencies
+ Explicit control over cell state and output via forget, input, and output gate
+ Gating based on previous hidden state

- Requires high computational effort

+ Less gates and thus less parameter
→ computationally more efficient

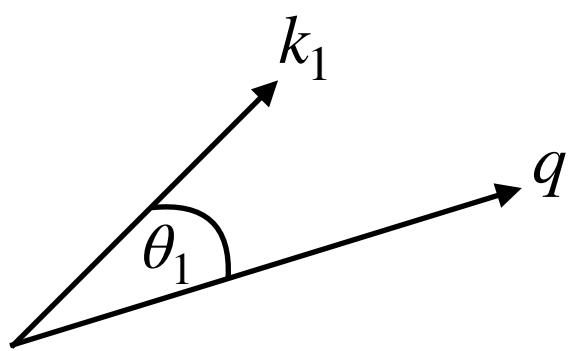
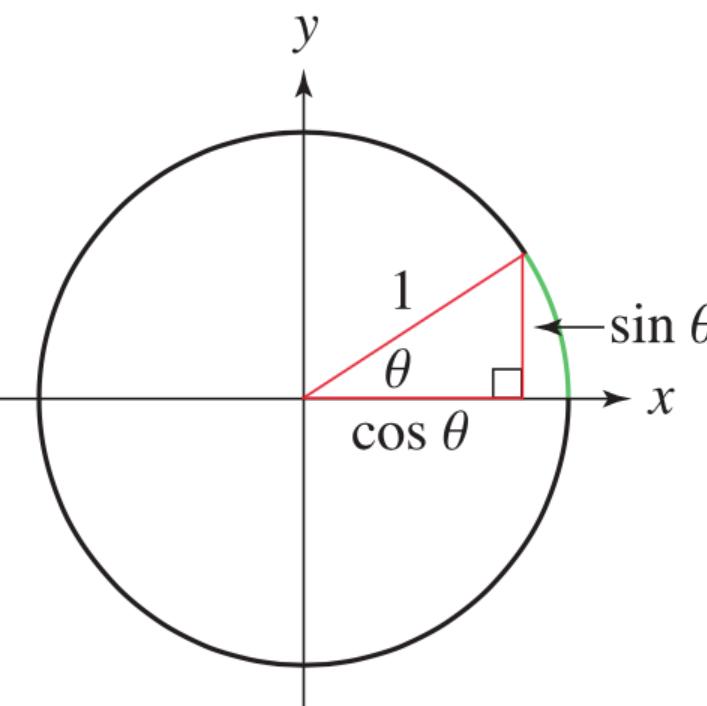
- Inferior on large datasets compared to LSTMs

TRANSFORMER

Vector Dot Product

$$a, b \in \mathbb{R}^{d_k}$$

$$a \cdot b = |a| |b| \cos(\theta)$$



$$\theta_1 = 27^\circ, \quad \cos(\theta_1) = c_1 = 0.891$$

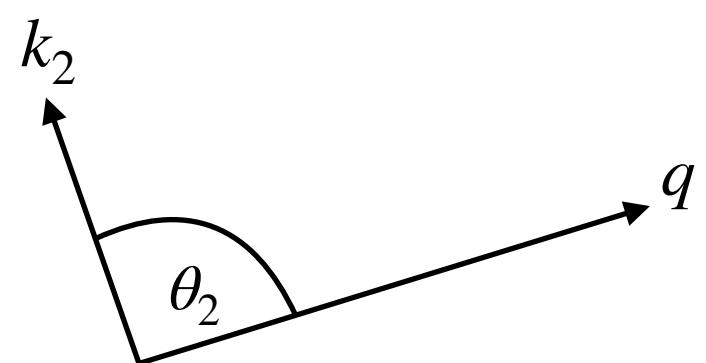
Softmax

$$\sigma(c_i) = \frac{e^{c_i}}{\sum_{j=1}^K e^{c_j}} \quad \forall i = 1, 2, \dots, K$$

$$\sum_{i=1}^K \sigma(c_i) = 1$$

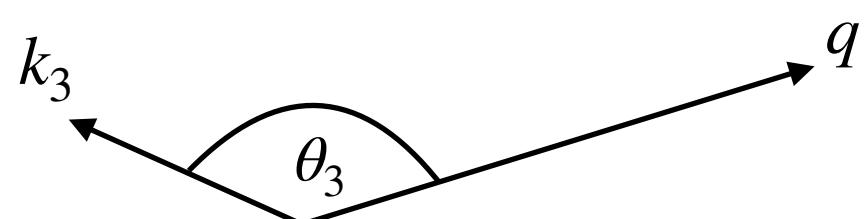
$$\sigma(c_1) = 0.6201$$

q is most similar to k_1



$$\theta_2 = 90^\circ, \quad \cos(\theta_2) = c_2 = 0$$

$$\sigma(c_2) = 0.2544$$



$$\theta_3 = 135^\circ, \quad \cos(\theta_3) = c_3 = -0.707$$

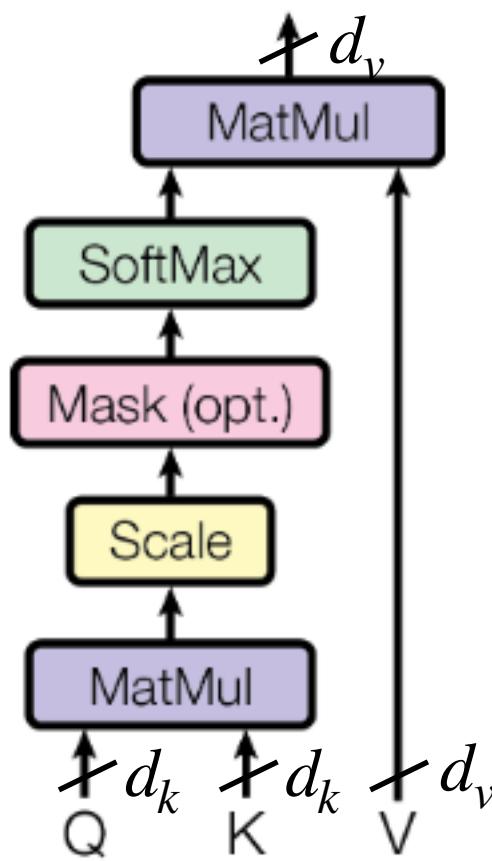
$$\sigma(c_3) = 0.1255$$

TRANSFORMER

Attention

→ to allow modeling of dependencies without regard to their distance in the input or output sequences

Scaled Dot-Product Attention



$$\text{Attention}(Q, K, V) = \text{softmax}\left(\frac{QK^T}{\sqrt{d_k}}\right)V$$

$$Q = \begin{bmatrix} q_1 \in \mathbb{R}^{1 \times d_k} \\ \vdots \\ q_{N_Q} \in \mathbb{R}^{1 \times d_k} \end{bmatrix} \in \mathbb{R}^{N_Q \times d_k}$$

$$QK^T \in \mathbb{R}^{N_Q \times N_K}$$

$$K = \begin{bmatrix} k_1 \in \mathbb{R}^{1 \times d_k} \\ \vdots \\ k_{N_K} \in \mathbb{R}^{1 \times d_k} \end{bmatrix} \in \mathbb{R}^{N_K \times d_k}$$

$$\text{softmax}\left(\frac{QK^T}{\sqrt{d_k}}\right) \in \mathbb{R}^{N_Q \times N_K}$$

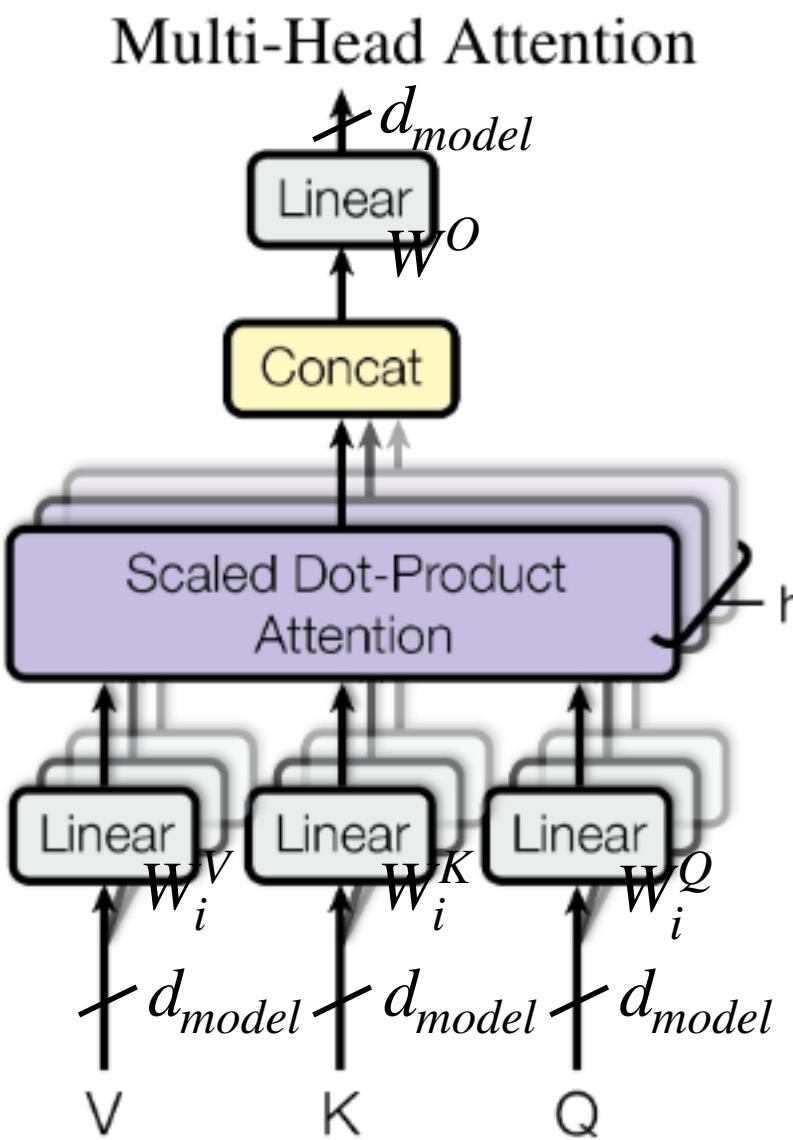
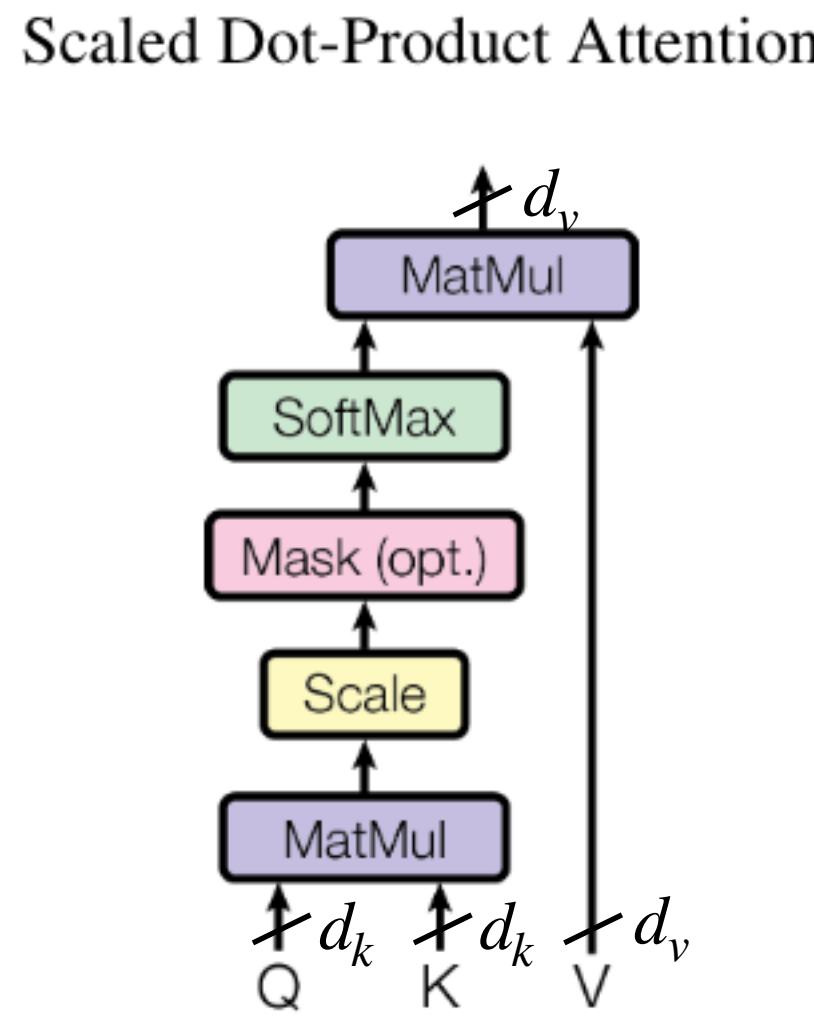
$$V = \begin{bmatrix} v_1 \in \mathbb{R}^{1 \times d_v} \\ \vdots \\ v_{N_K} \in \mathbb{R}^{1 \times d_v} \end{bmatrix} \in \mathbb{R}^{N_K \times d_v}$$

$$\text{softmax}\left(\frac{QK^T}{\sqrt{d_k}}\right)V \in \mathbb{R}^{N_Q \times d_v}$$

TRANSFORMER

Multi-Head Attention

→ to allow attention on information from different representation subspaces at different positions



$$\text{Attention}(Q, K, V) = \text{softmax} \left(\frac{QK^T}{\sqrt{d_k}} \right) V$$

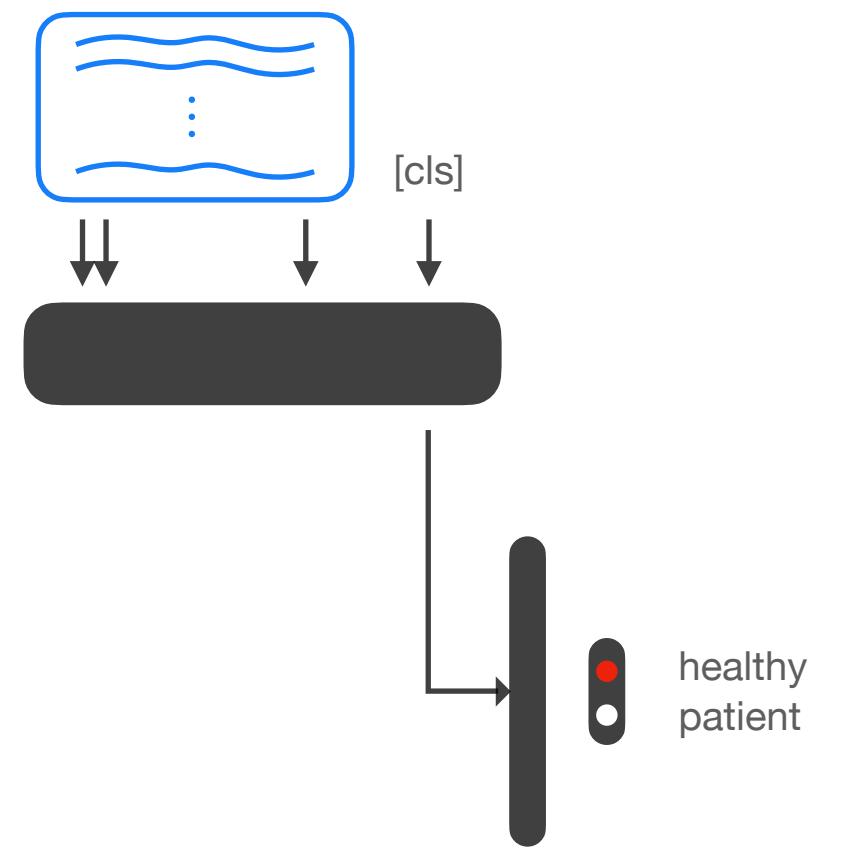
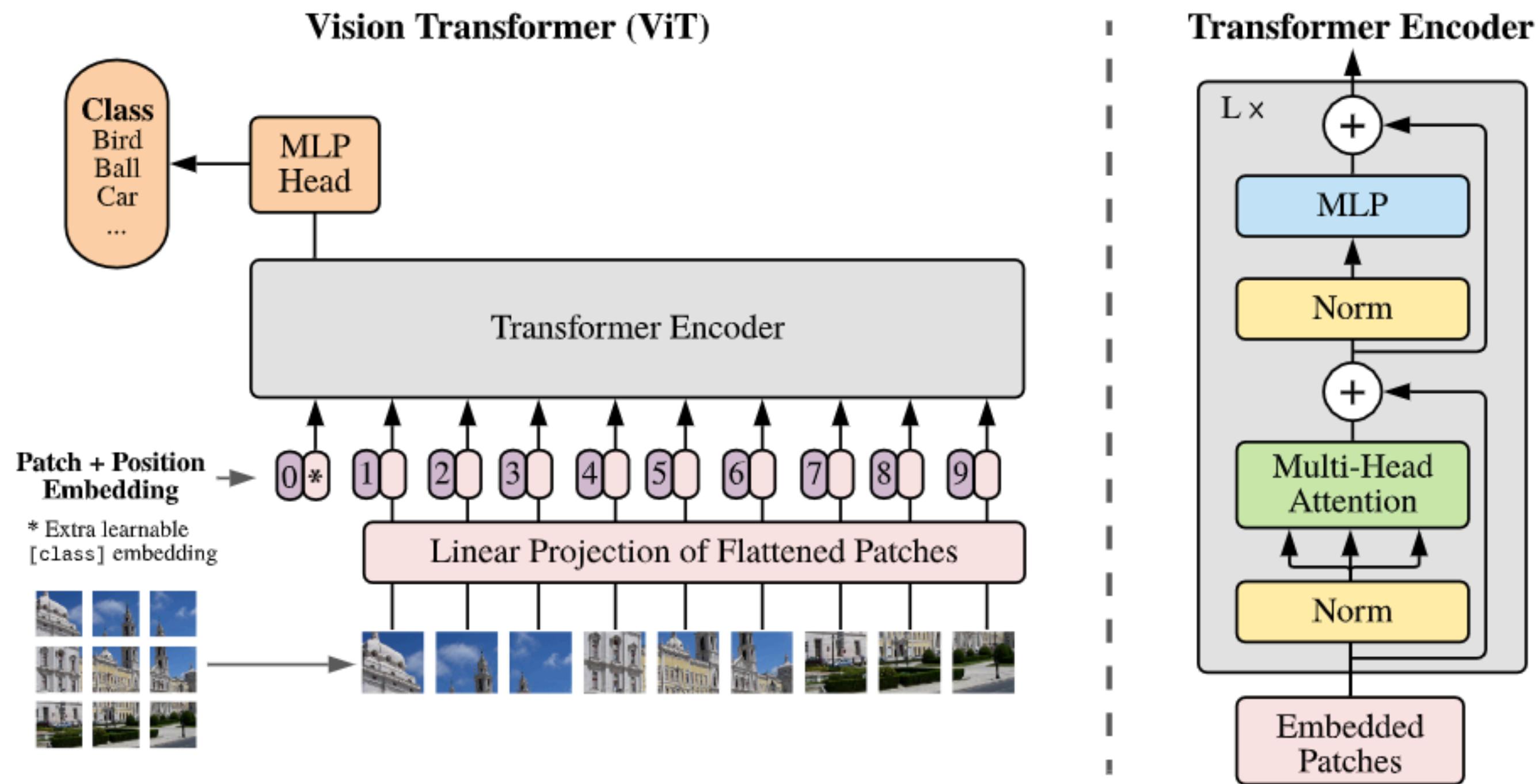
$$\begin{aligned} \text{MultiHead}(Q, K, V) &= \text{concat}(\text{head}_1, \dots, \text{head}_h) W^O \\ \text{head}_i &= \text{Attention}(QW_i^Q, KW_i^K, VW_i^V) \end{aligned}$$

$$W_i^Q, W_i^K \in \mathbb{R}^{d_{\text{model}} \times d_k}, \quad W_i^V \in \mathbb{R}^{d_{\text{model}} \times d_v}, \quad W^O \in \mathbb{R}^{hd_v \times d_{\text{model}}}$$

TRANSFORMER

Transformer

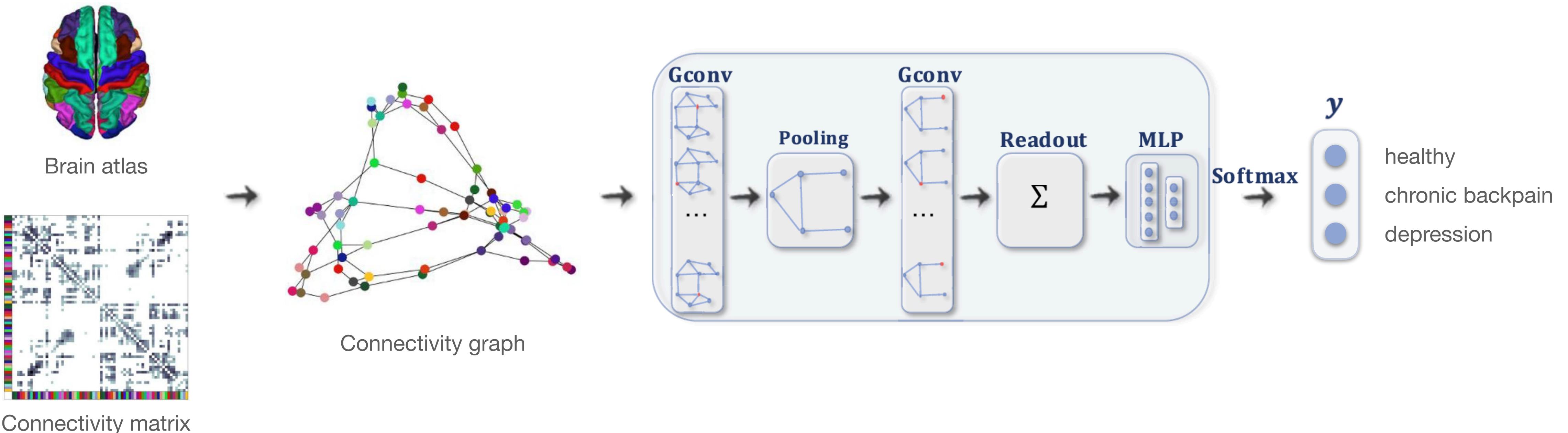
→ to learn bidirectional relations



GEOMETRIC DEEP LEARNING

Graph neural networks

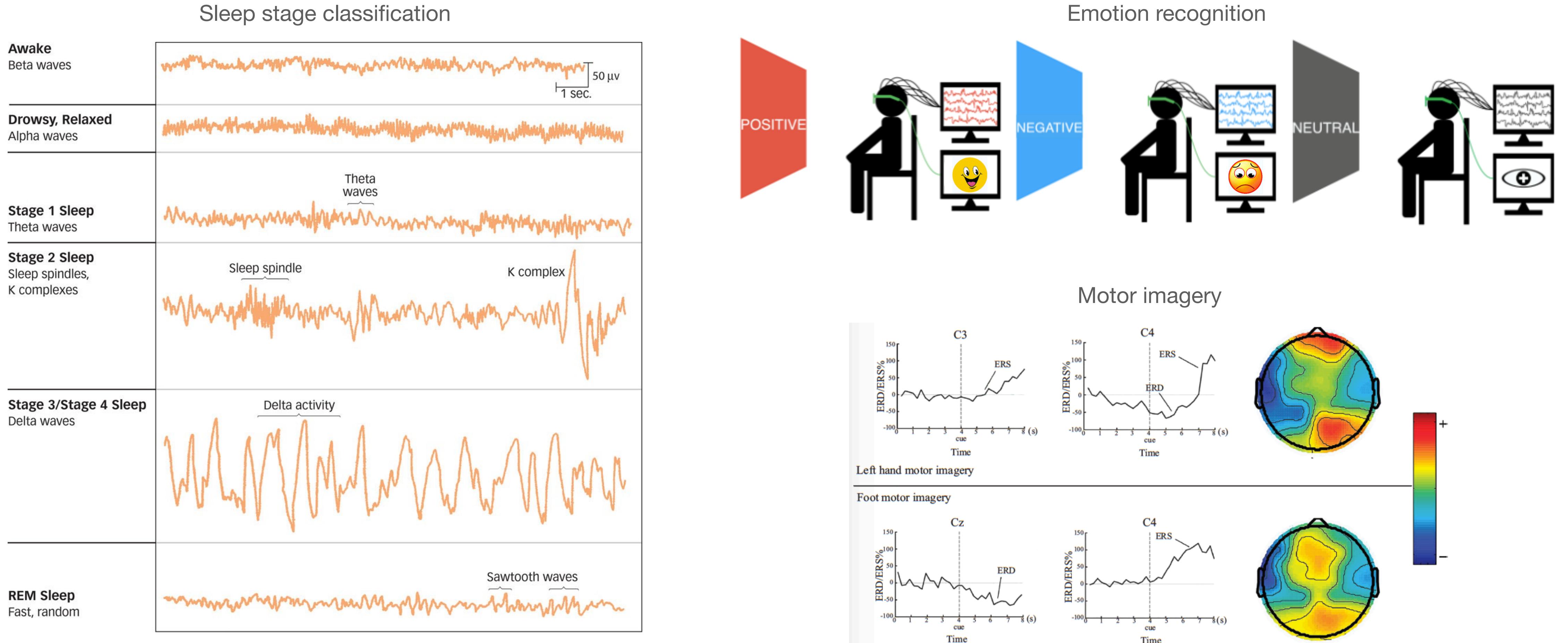
→ to learn from graph structured data



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TRANSFER LEARNING



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