Epileptic seizure prediction from EEG

Piotr Mirowski, Deepak Madhavan, Yann LeCun, Ruben Kuzniecky

New York University

Outline

- Seizure prediction **problem**, **approaches**
- **International Seizure Prediction Group**:
  - actors
  - dataset (clinical facts, preprocessing)
  - goals
- How to ensure seizure **predictability**?
  - ROC, sensitivity, specificity
  - Statistical: Seizure Time Surrogates
  - Algorithmic: training vs. testing dataset
- **Linear univariate** techniques
  - (Accumulated) energy [Esteller, Harrison]
- **Linear bivariate** techniques
  - Fitting autoregressive model [Jouny]
  - Cross-correlation [Mormann]
- **Non-linear bivariate** techniques
  - Non-linear systems
  - Dynamical entrainment [Iasemidis]
  - Nonlinear interdependence [Arhnold]
  - Phase locking
  - Phase synchronization [Le Van Quyen]
- Our research: **classification of bivariate dynamical patterns**

ElectroEncephaloGraphy (EEG)

Scalp EEG

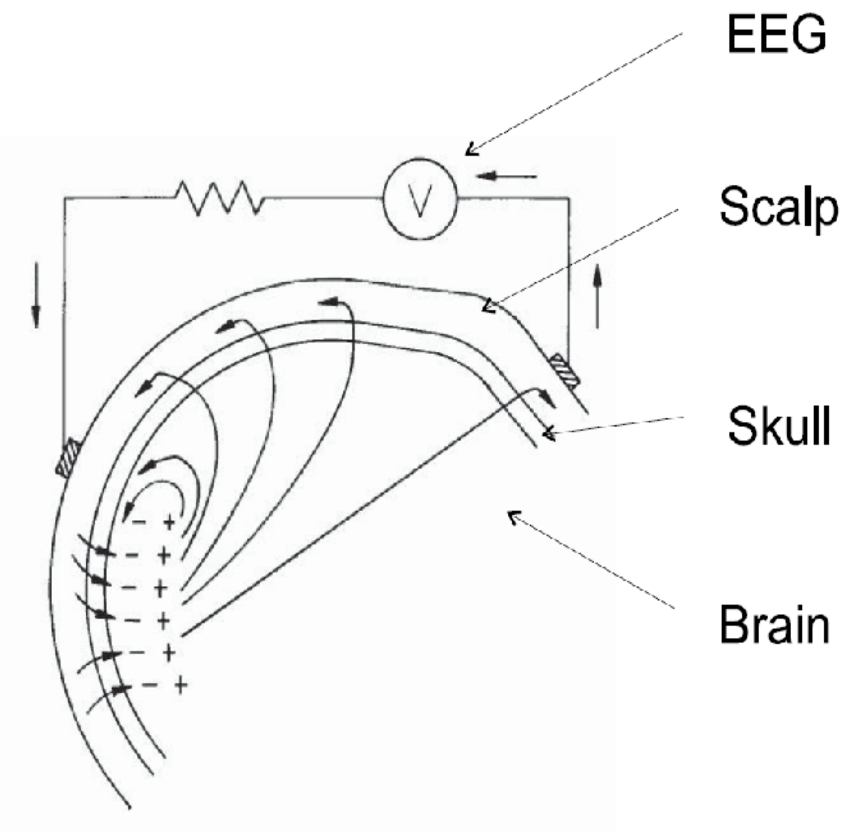
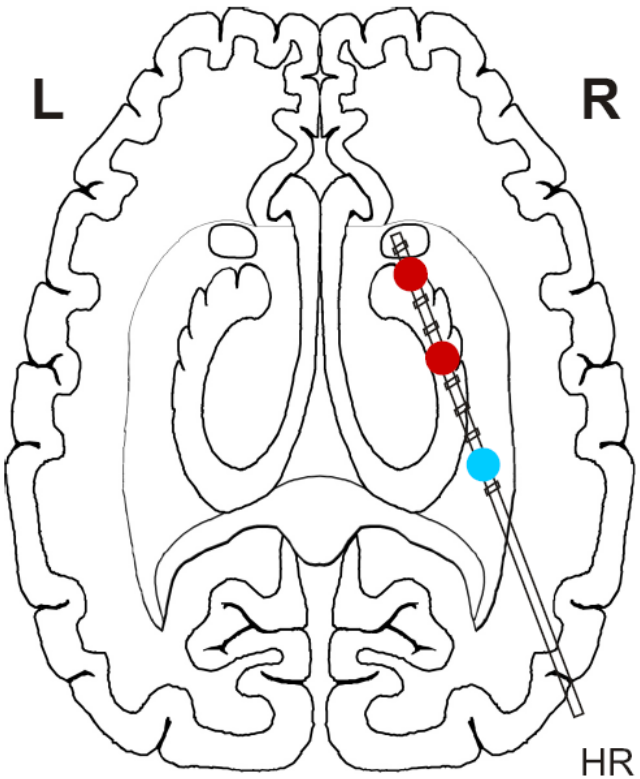


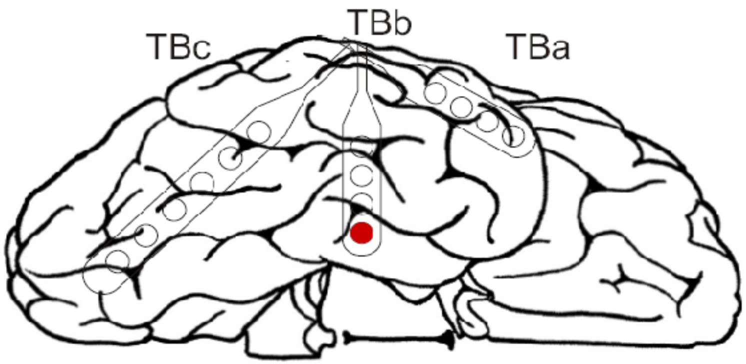
Figure 1.3: Origin of scalp potentials; Current in the EEG measuring circuit depends on the nature and location of the current sources, on the electrical properties of the brain, skull and scalp and on location of both electrodes. Modified from Nunez (1981)[69].

[Suffczynski, 2000, wikipedia.org]

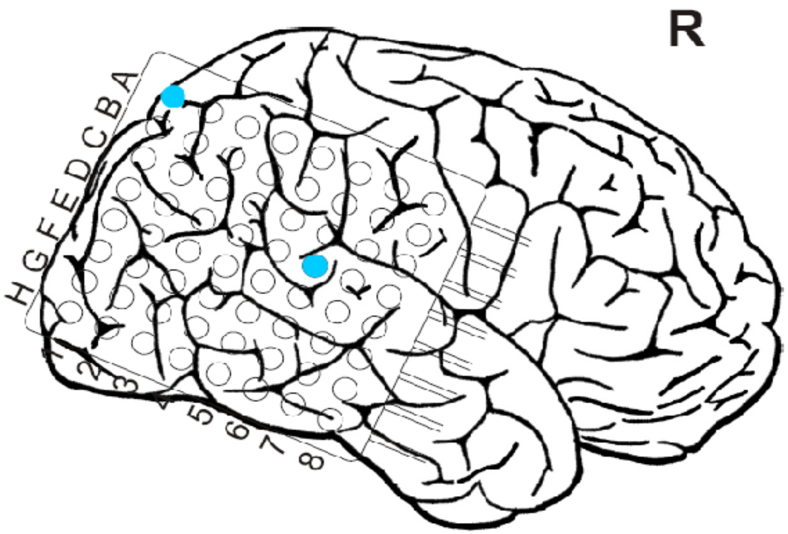
Intra(cranial/cerebral) EEG



Depth electrodes



Strip electrodes



Grid electrodes

[EEG database at Albert-Ludwigs-Universität in Freiburg, Germany]

Random facts about epilepsy

Epilepsy
Chronic illness
Affects **1% to 2% of world population**
40% of patients **refractory** to medication
Resective surgery as a treatment

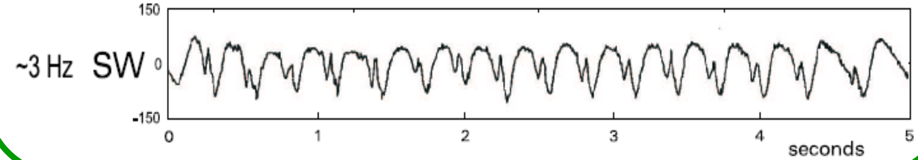
Partial ("focal")

Impairment of consciousness or perception

Sometimes **aura** for other seizures

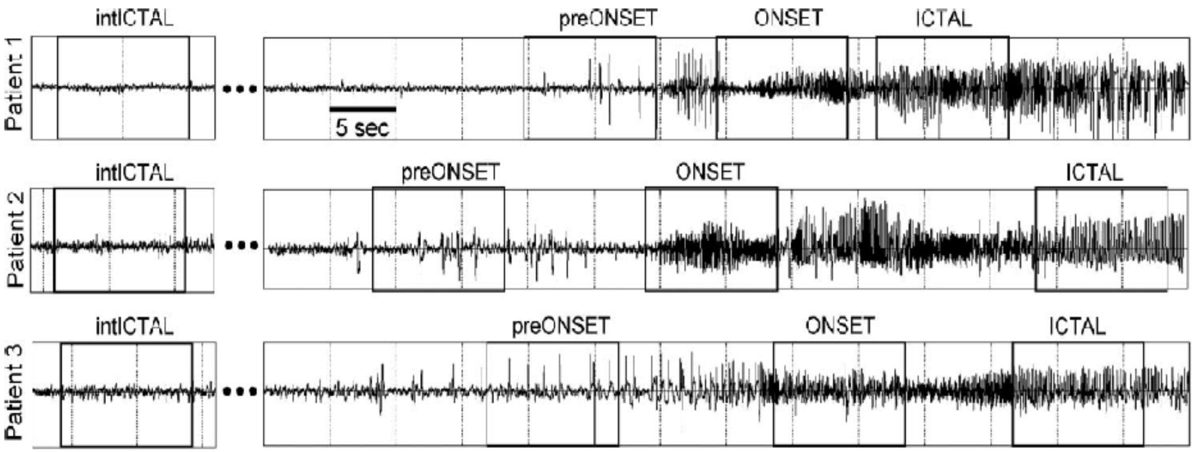
Generalized: Absence ("petit mal")

Impairment of consciousness
Abrupt start and termination, short duration
Unpredictable (?)



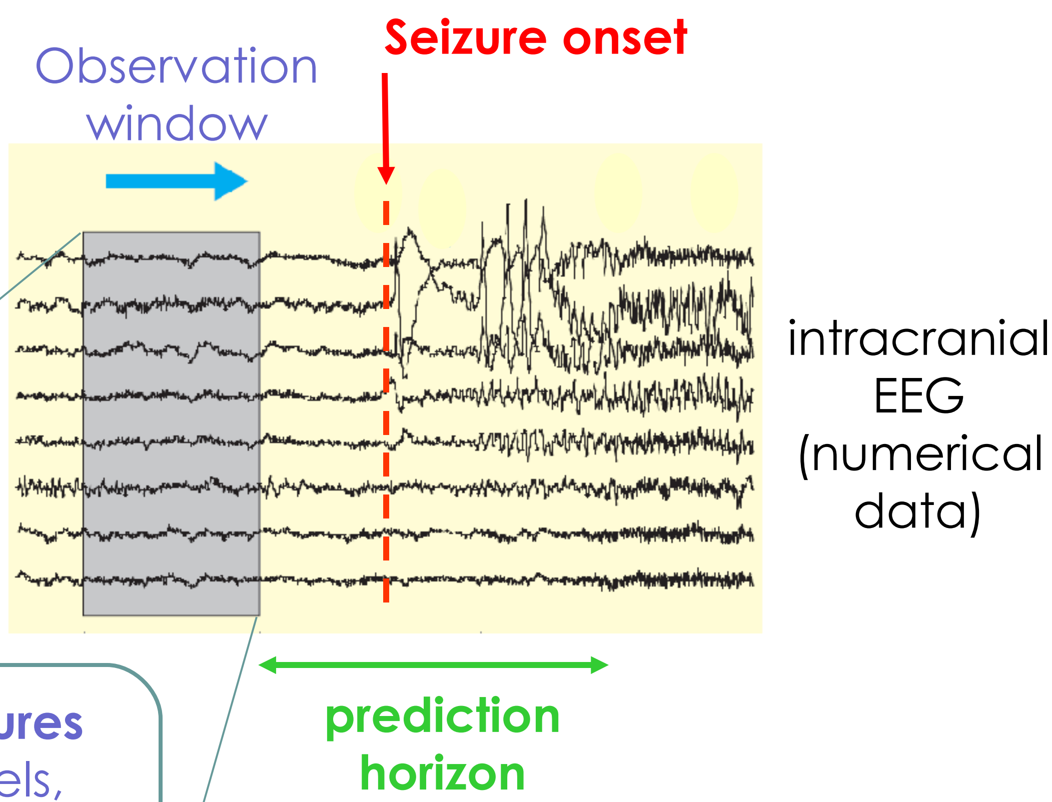
Generalized: Tonic-clonic ("grand mal")

Rhythmic muscle contractions
Loss of consciousness



[Kwan et al, 2000, Suffczynski, 2000, Suffczynski et al, 2006, Wendling et al, 2005]

Seizure prediction problem



Extraction of **features** from EEG channels, **pattern** recognition, …
+
classification

[Litt and Echauz, 2002]

Human NeuroProsthetics

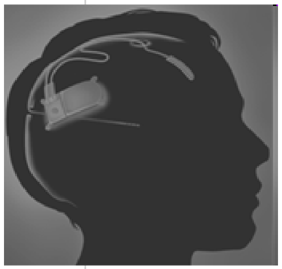
NEUROPACE

Responsive neurostimulation for the treatment of epilepsy

ABOUT US | PRODUCT | CLINICAL TRIALS | RESOURCES | PDMS | CONTACT US

Product

Tell a Friend



Overview

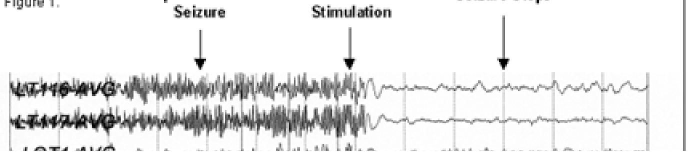
The RNS™ System, designed for the treatment of medically refractory partial epilepsy, includes implantable and external products.

Implantable components include the RNS neurostimulator as well as depth leads and cortical strip leads. The RNS neurostimulator is a programmable, battery powered, microprocessor-controlled device that delivers a short train of electrical pulses to the brain through implanted leads. In treating epilepsy, the RNS neurostimulator is designed to detect abnormal electrical activity in the brain and respond by delivering electrical stimulation to normalize brain activity before the patient experiences seizure symptoms. The neurostimulator is implanted in the cranium and connected to one or two leads that are implanted near the patient's seizure focus.

External products include the programmer, a laptop computer with proprietary software that has a wand and telemetry interface enabling communication with an implanted RNS neurostimulator. Physicians use the programmer to non-invasively program the detection and stimulation parameters of an implanted device. Additional features of the programmer include the ability to view the patient's electrocorticographic (ECoG) activity real-time and the ability to upload the patient's ECoGs that have been stored in the RNS neurostimulator.

Caution: The RNS™ System is an Investigational device. Limited by United States law to investigational use.

Figure 1.



[NeuroPace.com]

Approaches to the problem

Feature extraction from EEG:

Linear

System of noise-driven linear equations

$$\boldsymbol{y}(t) = a\boldsymbol{x}(t) + b + \eta(t)$$

Non-linear

Deterministic dynamical system of nonlinear equations

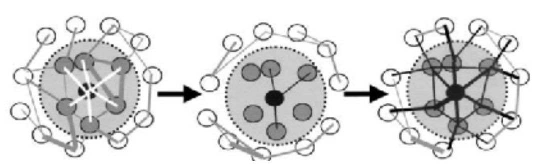
Relationship between EEG channels:

Univariate

1 channel at a time

Bivariate

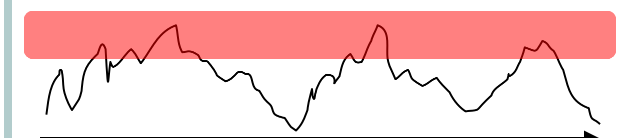
Varying synchronization of EEG channels



Classification based on:

Statistics

Discriminating measure



time

Algorithm

Machine Learning: neural networks, genetic optimization…

[Lehnertz et al, 2007], [Mormann et al, 2005], [Le Van Quyen et al, 2003]

Outline

- Seizure prediction **problem**, **approaches**
- **International Seizure Prediction Group**:
  - actors
  - dataset (clinical facts, preprocessing)
  - goals
- How to ensure seizure **predictability**?
  - ROC, sensitivity, specificity
  - Statistical: Seizure Time Surrogates
  - Algorithmic: training vs. testing dataset
- **Linear univariate** techniques
  - (Accumulated) energy [Esteller, Harrison]
- **Linear bivariate** techniques
  - Fitting autoregressive model [Jouny]
  - Cross-correlation [Mormann]
- **Non-linear bivariate** techniques
  - Non-linear systems
  - Dynamical entrainment [Iasemidis]
  - Nonlinear interdependence [Arhnold]
  - Phase locking
  - Phase synchronization [Le Van Quyen]
- Our research: **classification of bivariate dynamical patterns**

Main research groups (after 2002)

Harrison
Flint Hills Scientific (Kansas)
Energy
Statistical

Mormann, Andrzejak, Lehnertz
Bonn
Various features
Statistical

Lopes da Silva, Suffczynski
SEIN **Netherlands**, **Warsaw**
Models of epilepsy

Litt, Echauz, Esteller
UPenn, **GATech**, **Neuropace**
Energy
Statistical/Algorithmic

Chernihovskyi, Lehnertz
Bonn
Synchrony from Cellular NN
Algorithmic

Jerger, Sauer
George Mason (Virginia)
Covariance, synchrony
(Simple) algorithmic

International Seizure Prediction Group
Bonn, 2002

Iasemidis, Chaovalitwongse
Arizona State, **Florida**
Dynamical entrainment
Statistical

Jouny, Franaszczuk
John Hopkins
Univariate complexity, linear synchrony
Statistical

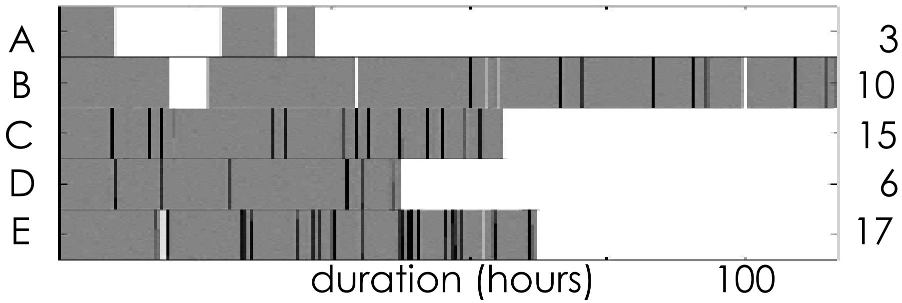
Le Van Quyen, Navarro, Varela
Pitié-Salpêtrière (Paris)
Wavelet synchrony, dynamic similarity
Statistical

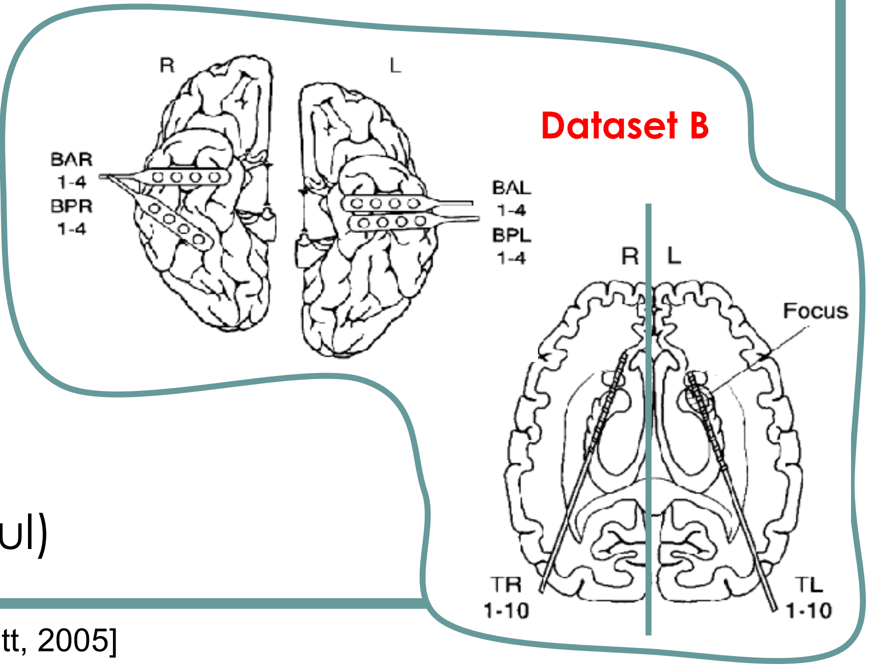
[Lehnerzt and Litt, 2005] [Lehnertz et al, 2007]

ISPG Bonn 2002 dataset

	Data set	Sampling rate (Hz)	A to D conversion	BandPass (Hz)	# Channels	#Seizures	ISI (h)
Netherlands	A	480	16 bits	0.16-70	32	3	13.9±13.7
Bonn	B	200	16 bits	0.30–70	48	10	5.9±4.8
Florida	C	200	10 bits	0.10–70	32	15	3.9±3.5
Kansas	D	239.75	10 bits	0.10–100	53	6	8.1±6.0
UPenn	E	200	12 bits	0.50–70	81	17	3.6±3.0

Continuous video+EEG recordings





Temporal lobe epilepsy, ages 18-65

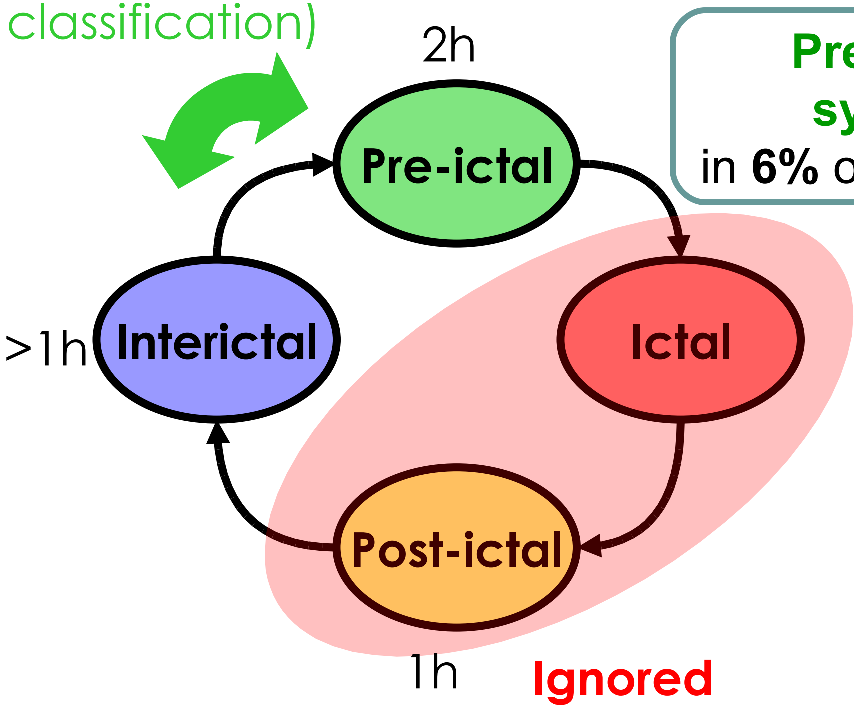
Seizure-free after surgery

Sleep-wake data **not provided** (yet useful)

[Lehnertz and Litt, 2005]

ISPG Bonn 2002 goals

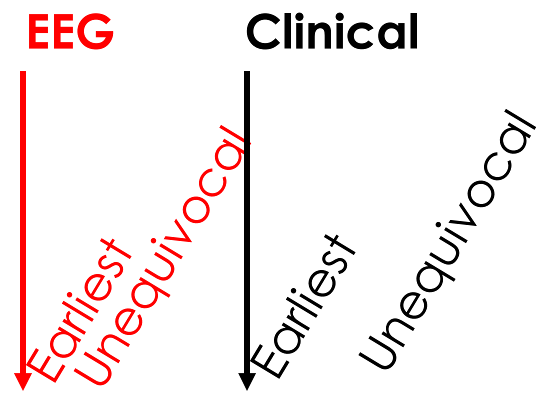
Discriminate
(binary classification)

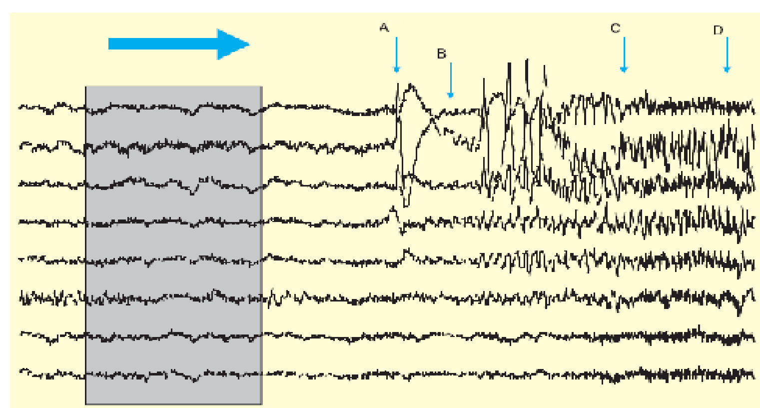


Focal epilepsies
(not generalized)

Premonitory symptoms
in **6%** of 500 **patients**

Seizure onset





Observation window

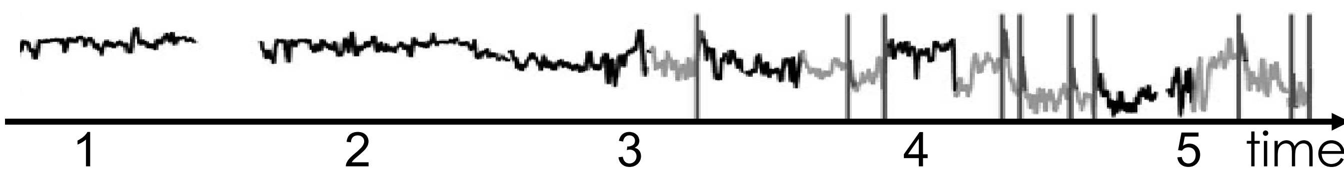
Data requirement:
4h between seizures

[Lehnertz and Litt, 2005], [Litt and Echaz, 2002]

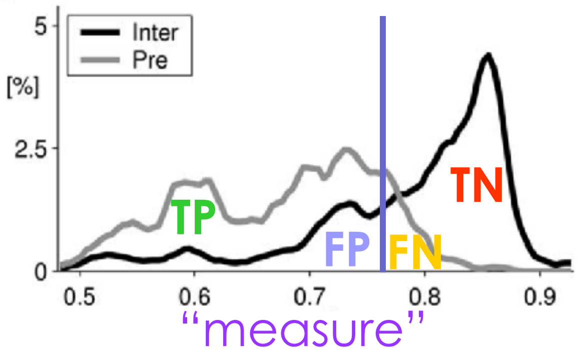
Outline

- Seizure prediction **problem**, **approaches**
- **International Seizure Prediction Group**:
  - actors
  - dataset (clinical facts, preprocessing)
  - goals
- **How to ensure seizure predictability**?
  - ROC, sensitivity, specificity
  - Statistical: Seizure Time Surrogates
  - Algorithmic: training vs. testing dataset
- **Linear univariate** techniques
  - (Accumulated) energy [Esteller, Harrison]
- **Linear bivariate** techniques
  - Fitting autoregressive model [Jouny]
  - Cross-correlation [Mormann]
- **Non-linear bivariate** techniques
  - Non-linear systems
  - Dynamical entrainment [Iasemidis]
  - Nonlinear interdependence [Arhnold]
  - Phase locking
  - Phase synchronization [Le Van Quyen]
- Our research: **classification of bivariate dynamical patterns**

Receiver-Operator Characteristic



Hypothesis: ↓
pre-ictal decrease



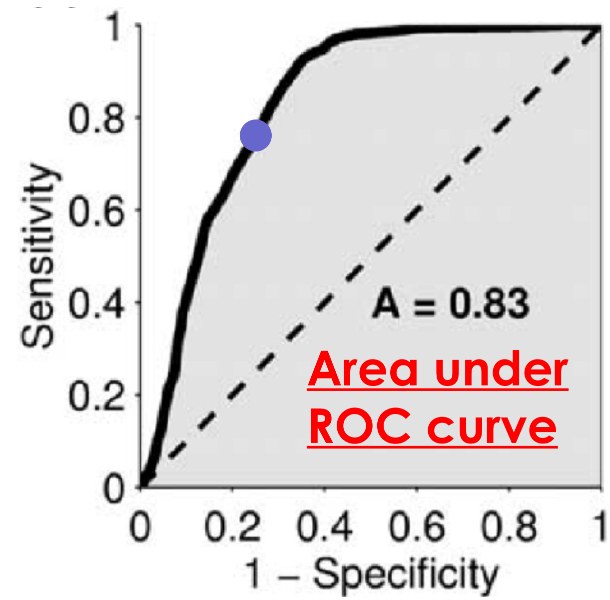
TP **true positive**
seizure,
>1 alarm(s)

FP **false positive**
alarm,
no seizure

during prediction horizon

$$\textbf{sensitivity} = \frac{TP}{TP+FN}$$

$$\textbf{specificity} = \frac{TN}{TN+FP}$$

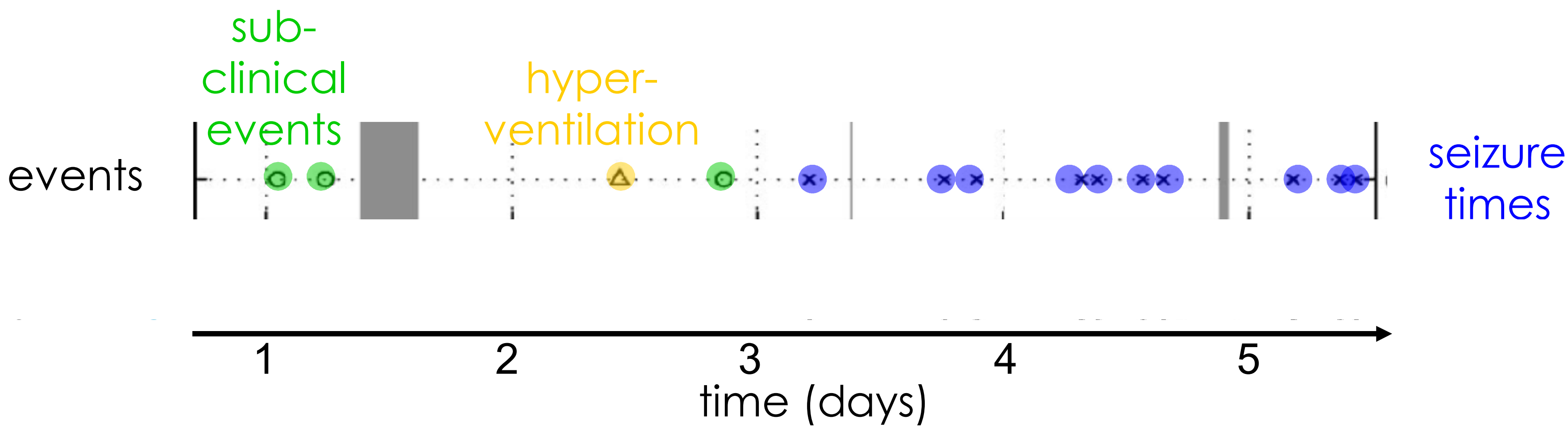


False prediction rate = FP/interictal time

Shorter prediction horizons
= less waiting (wasted) time

[Lehnertz et al, 2007], [Mormann et al, 2006]

Statistical validation



<u>Null hypothesis</u>: "**no** **pre-ictal state** [can be found]"

given a particular tested set of discriminating measures…

<u>How to disprove it?</u> Same EEG Same measures **Ignore seizure times**

Random generation of **Seizure Time Surrogates**

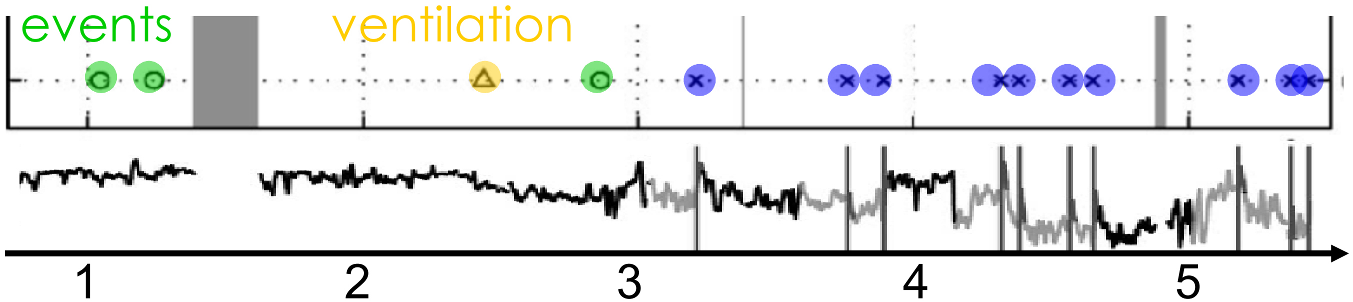
→ Same number as real seizure times

→ Same distribution of intervals between seizures

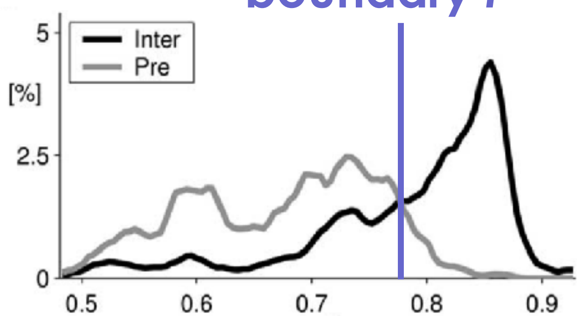
→ Occurring in the same time-frame as real seizures

[Andrzejak et al, 2003]

Statistical validation



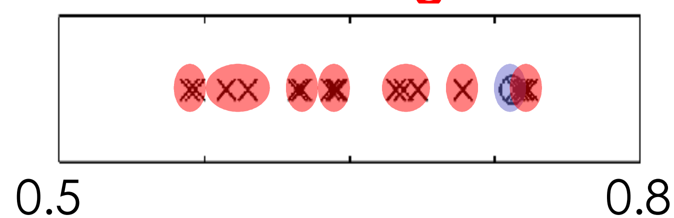
decision boundary *F*



"measure"

e.g. *F*=average over all channels

Compare 1 **original** vs. 19 **surrogates**



F (original) falls into same distribution as F (surrogates)

measure = **Failure**

[Andrzejak et al., ...]

Machine Learning

Training dataset
"**in-sample**"

X = EEG **data**, measures
Y = label (pre-ictal, interictal)
W = neural network **parameters**

$$\min_{\mathbf{W}}\{L(\mathbf{X},\mathbf{Y},\mathbf{W})\} = \min_{\mathbf{W}}\left\{\sum_i E_{\mathbf{W}}(X_i,Y_i) + \|\mathbf{W}\|\right\}$$

loss/risk on training data

per-sample error

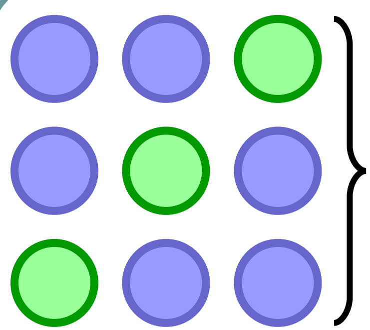
regularization (keep it simple)

Testing dataset
"**out-of-sample**"

=

new, unseen data

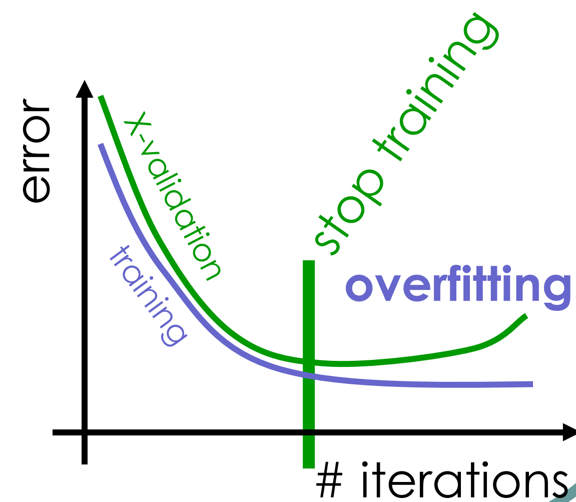
e.g. same patient, new seizures



N –fold
cross-validation

1 2 3
N seizures

Training
(adjusting parameters W)
=
iterative process



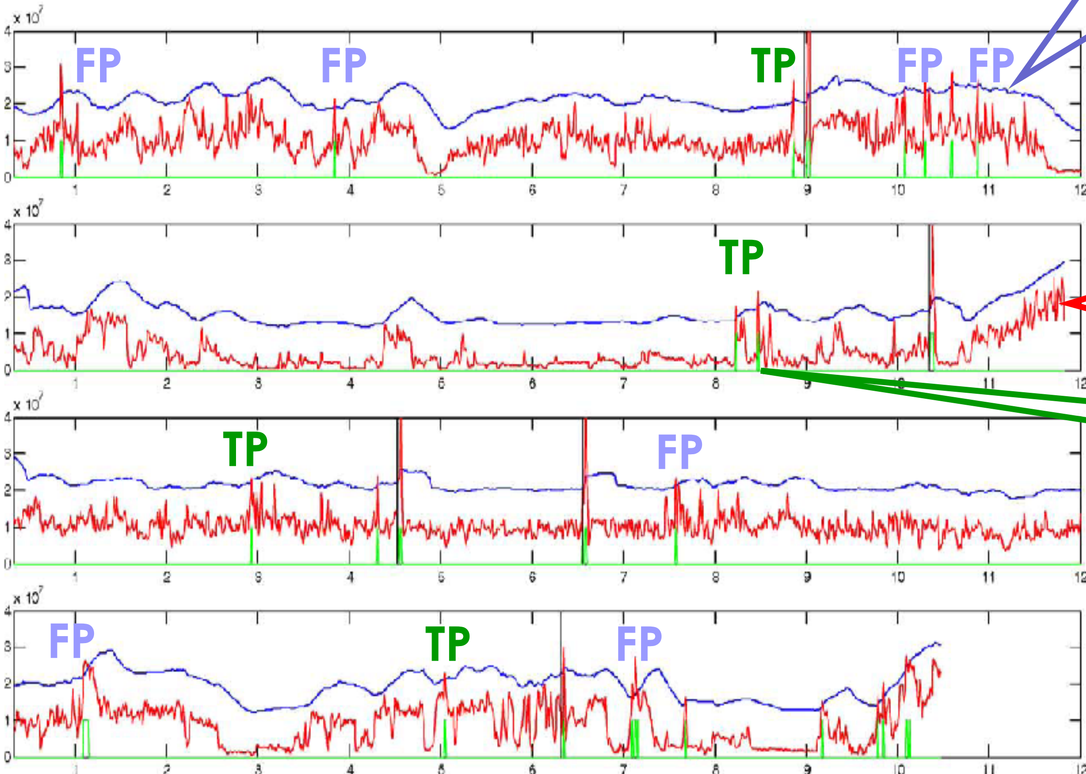
Outline

- Seizure prediction **problem**, **approaches**
- **International Seizure Prediction Group**:
  - actors
  - dataset (clinical facts, preprocessing)
  - goals
- How to ensure seizure **predictability**?
  - ROC, sensitivity, specificity
  - Statistical: Seizure Time Surrogates
  - Algorithmic: training vs. testing dataset
- **Linear univariate** techniques
  - (Accumulated) energy [Esteller, Harrison]
- **Linear bivariate** techniques
  - Fitting autoregressive model [Jouny]
  - Cross-correlation [Mormann]
- **Non-linear bivariate** techniques
  - Non-linear systems
  - Dynamical entrainment [Iasemidis]
  - Nonlinear interdependence [Arhnold]
  - Phase locking
  - Phase synchronization [Le Van Quyen]
- Our research: **classification of bivariate dynamical patterns**

Continuous energy variation [Linear, univariate, statistical]

Energy ≈ spikes, bursts in EEG activity

Patient B (4 segments of 12h)



Time (h)

Decision threshold
20-min energy + offset

$$E_{20\,\mathrm{min}}(t) = \sum_{t'=t\pm 10\,\mathrm{min}} x(t')^2 + E_{\mathrm{offset}}$$

Moving Average
1-min energy

$$E_{1\,\mathrm{min}}(t) = \sum_{t'=t\pm 0.5\,\mathrm{min}} x(t')^2$$

Seizure prediction

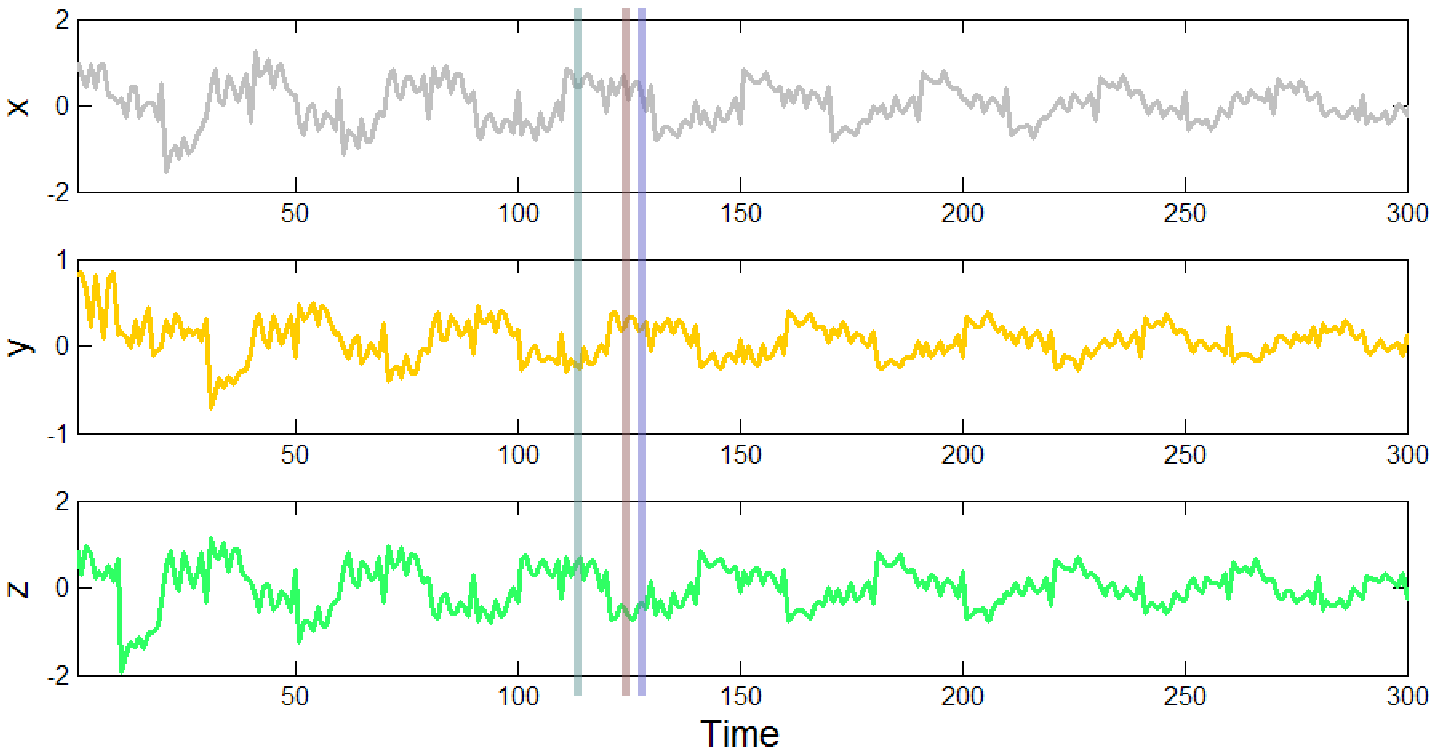
Prediction **horizon 3h**
Sensitivity 71%
1 FP every 10h
No statistical validation

[Esteller et al, 2005]

Outline

- Seizure prediction **problem**, **approaches**
- **International Seizure Prediction Group**:
  - actors
  - dataset (clinical facts, preprocessing)
  - goals
- How to ensure seizure **predictability**?
  - ROC, sensitivity, specificity
  - Statistical: Seizure Time Surrogates
  - Algorithmic: training vs. testing dataset
- **Linear univariate** techniques
  - (Accumulated) energy [Esteller, Harrison]
- **Linear bivariate** techniques
  - Fitting autoregressive model [Jouny]
  - Cross-correlation [Mormann]
- **Non-linear bivariate** techniques
  - Non-linear systems
  - Dynamical entrainment [Iasemidis]
  - Nonlinear interdependence [Arhnold]
  - Phase locking
  - Phase synchronization [Le Van Quyen]
- Our research: **classification of bivariate dynamical patterns**

(Multivariate) linear systems



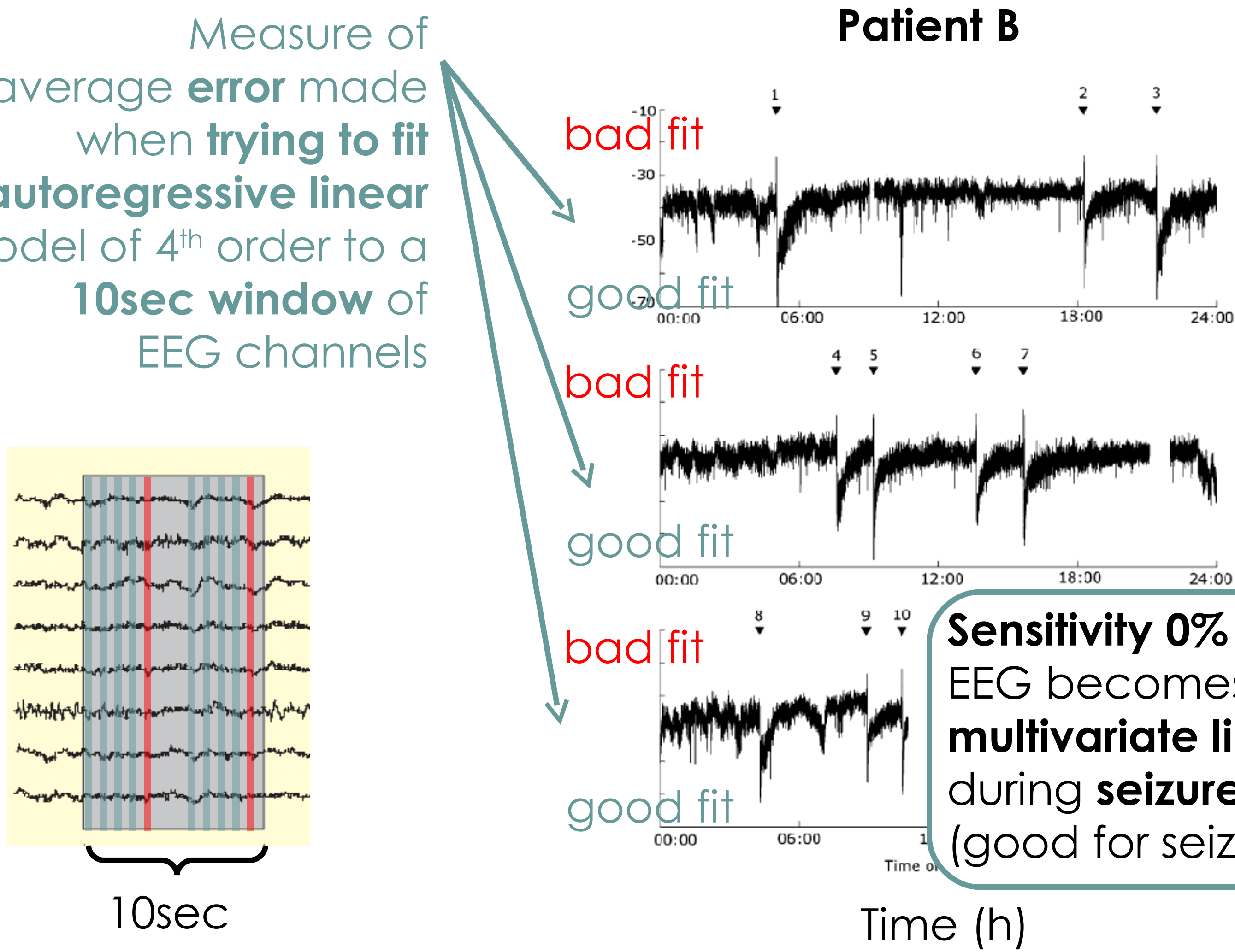
$$\begin{bmatrix} x(t) \\ y(t) \\ z(t) \end{bmatrix} = \begin{bmatrix} 0.01x(t-1) + 0.13y(t-1) - 0.1z(t-1) \\ -0.06x(t-1) + 0.52y(t-1) + 0.03z(t-1) \\ -0.5x(t-1) - 0.31y(t-1) - 0.68z(t-1) \end{bmatrix}$$

time t time t-1

Autoregressive linear system of 10^{th} order

Fitting an autoregressive model [Linear, multivariate, statistical]

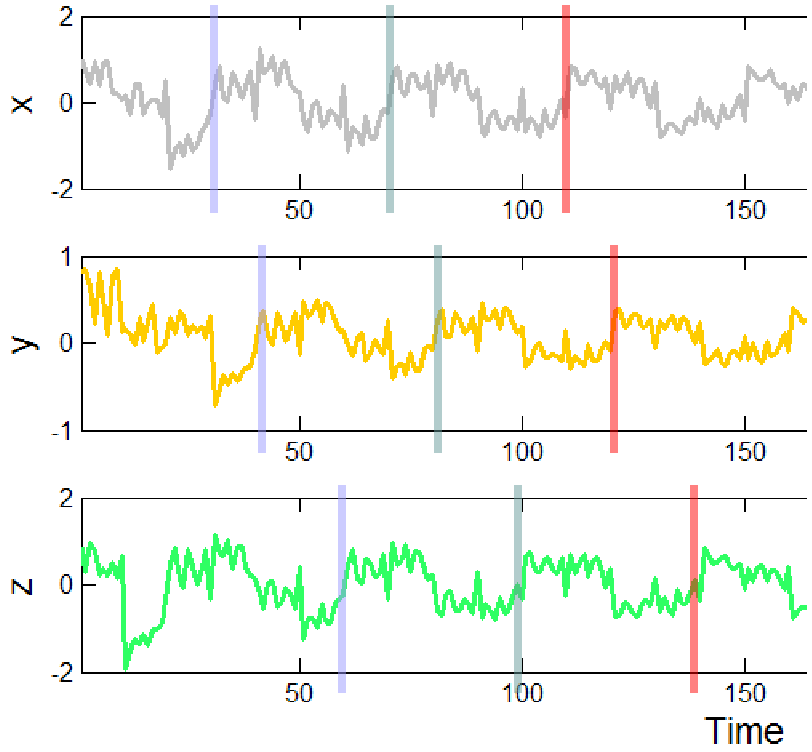
Measure of average **error** made when **trying to fit an autoregressive linear** model of 4^{th} order to a **10sec window** of EEG channels



Sensitivity 0%
EEG becomes more like a **multivariate linear system** during **seizures** (good for seizure **detection**)

[Jouny et al, 2005]

Maximum cross-correlation [Linear, bivariate, statistical]



Cross-correlation between channels
For **each channel, choice of delay** giving **best** cross-correlation

Prediction **horizon 3h**

Different hypothesis of ↑ or ↓ of cross-correlation,
depending on pairs of channels

All seizures together
Area under ROC = 0.75 (good)

Each seizure separately
Area under ROC = 0.86 (good)

Statistical significance (surrogates) at **0.05**

As good as nonlinear multivariate

[Mormann et al, 2005]

Outline

- Seizure prediction **problem**, **approaches**
- **International Seizure Prediction Group**:
  - actors
  - dataset (clinical facts, preprocessing)
  - goals
- How to ensure seizure **predictability**?
  - ROC, sensitivity, specificity
  - Statistical: Seizure Time Surrogates
  - Algorithmic: training vs. testing dataset
- **Linear univariate** techniques
  - (Accumulated) energy [Esteller, Harrison]
- **Linear bivariate** techniques
  - Fitting autoregressive model [Jouny]
  - Cross-correlation [Mormann]
- **Non-linear bivariate** techniques
  - Non-linear systems
  - Dynamical entrainment [Iasemidis]
  - Nonlinear interdependence [Arhnold]
  - Phase locking
  - Phase synchronization [Le Van Quyen]
- Our research: **classification and regression of bivariate dynamical patterns**

Nonlinear dynamical systems (example: chaotic Lorenz system)

Lorenz = (very) simple model of atmosphere

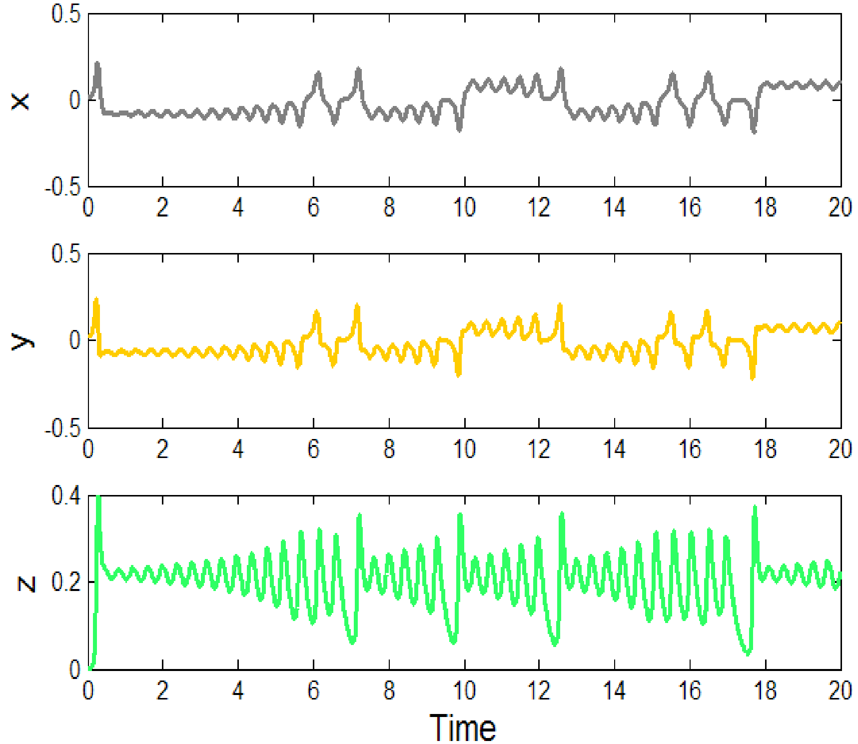
State S = variables **x**, **y**, **z** at time t

$$\frac{\partial x}{\partial t} = -16x + 16y$$

$$\frac{\partial y}{\partial t} = 45.92x - y - x \times z$$

$$\frac{\partial z}{\partial t} = x \times y - 2z$$

nonlinearity



Nonlinear function f

(**x**,**y**,**z**) at time t → (**x**,**y**,**z**) at time $t+\Delta t$

$S_{t+\Delta t} = f(S_t)$

[Stam, 2005]

Nonlinear dynamical systems (example: chaotic Lorenz system)

Lorenz = (very) simple model of atmosphere

State S = variables **x**, **y**, **z** at time t

$$\frac{\partial x}{\partial t} = -16x + 16y$$

$$\frac{\partial y}{\partial t} = 45.92x - y - x \times z$$

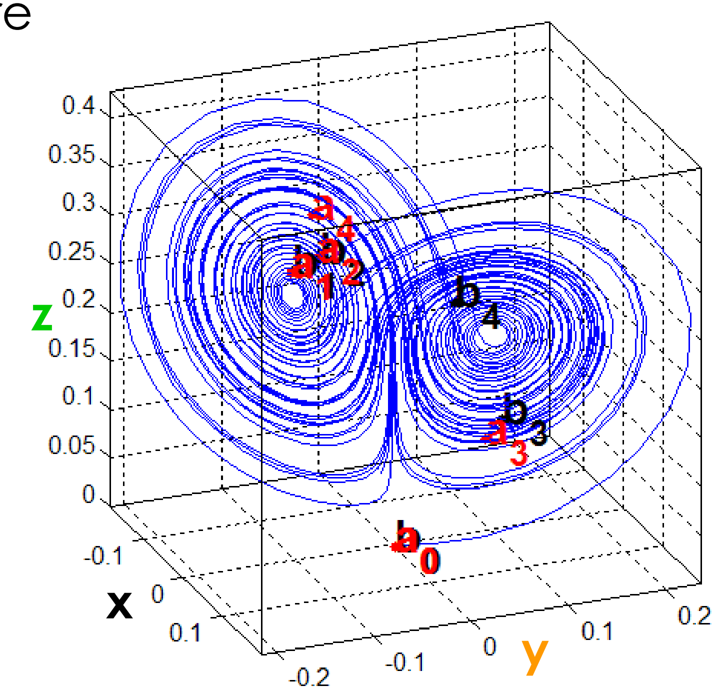
$$\frac{\partial z}{\partial t} = x \times y - 2z$$

nonlinearity

Nonlinear function f

(**x**,**y**,**z**) at time t → (**x**,**y**,**z**) at time $t+\Delta t$

$S_{t+\Delta t} = f(S_t)$

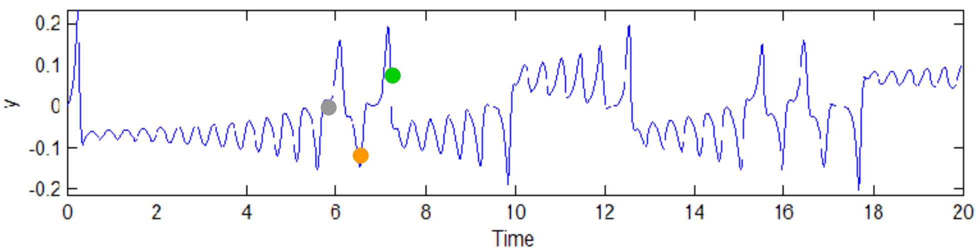


Phase plot
in
state-space

[Stam, 2005]

Nonlinear dynamical systems (example: chaotic Lorenz system)

Observation (state unknown)



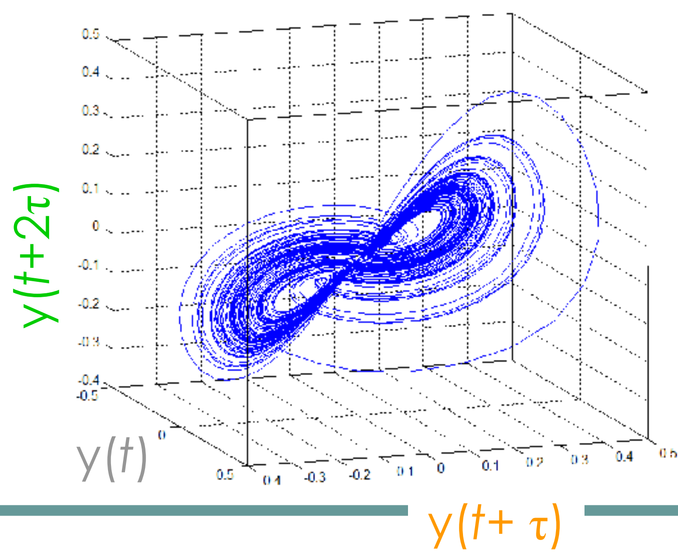
Dynamical reconstruction:
Time-delay embedding

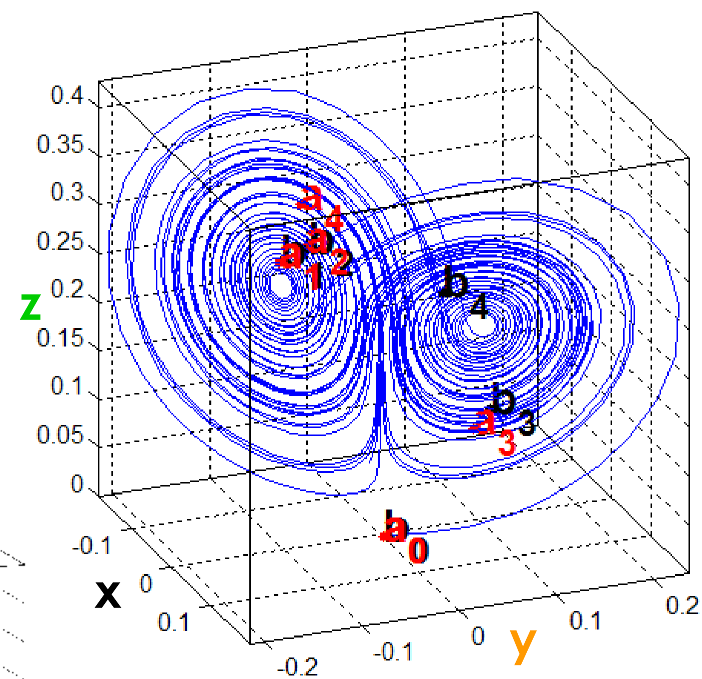
$$S_t = y(t-\tau), y(t-2\tau), \ldots, y(t-d\tau)$$

Time delay τ

Embedding dimension d

EEG:
***d*=7**
τ=5Δ*t*

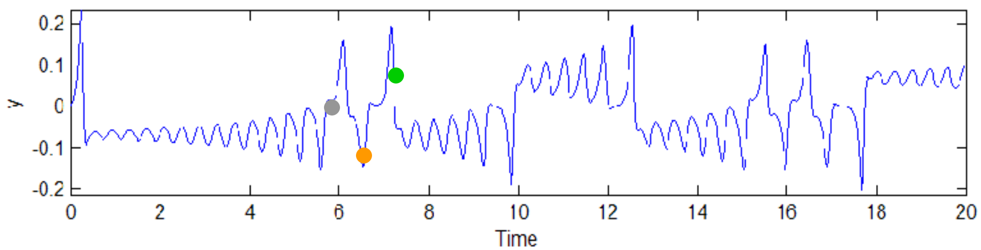




Phase plot in state-space

Nonlinear dynamical systems (example: chaotic Lorenz system)

Observation (state unknown)



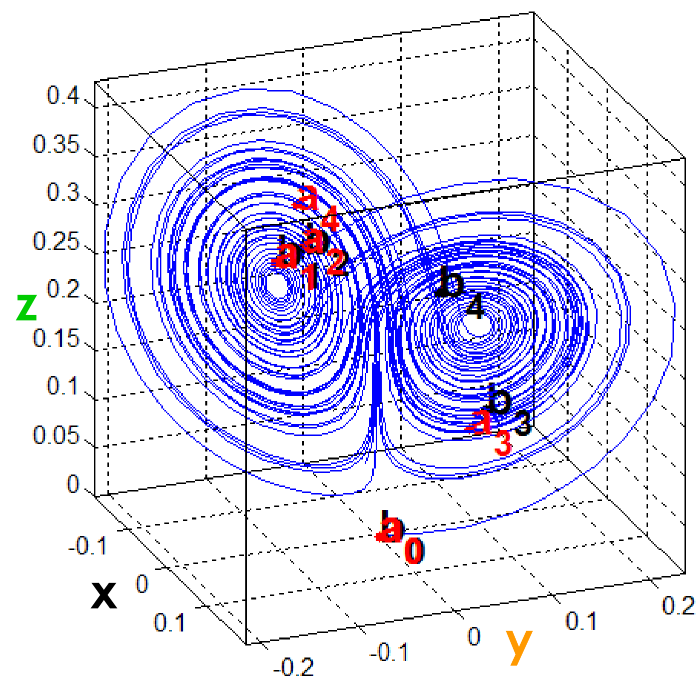
Butterfly effect:
Exponential rate of growth of
a small perturbation

$$|\Delta S_{t+n\Delta t}| = |\Delta S_t| e^{n\lambda}$$ **Lyapunov exponent**

Local flow =
Average on directions of trajectory

Correlation dimension =
Estimation of dimension of chaotic orbit

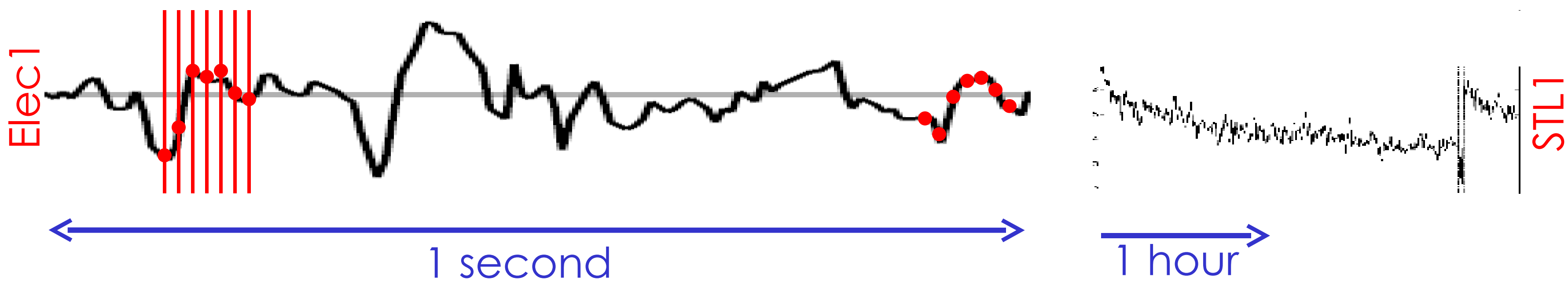
EEG: dynamics change with time?
(pre-ictal, ictal, post-ictal, interictal…)



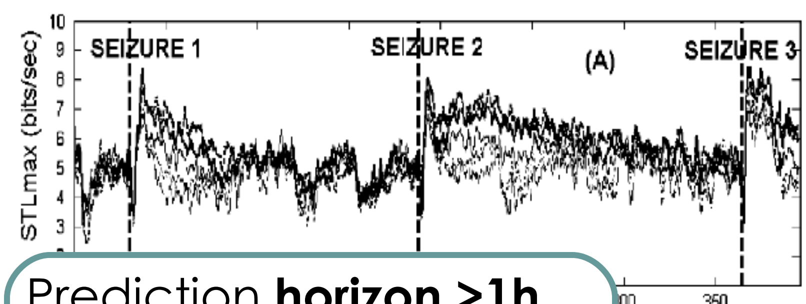
Phase plot
in
state-space

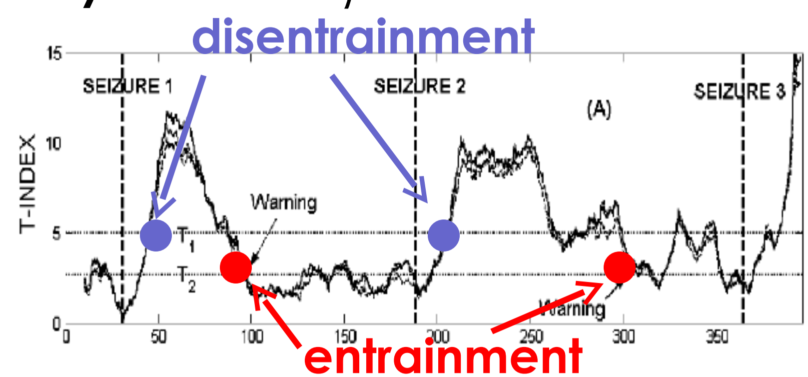
[Stam, 2005]

Dynamical Entrainment [Nonlinear, bivariate, statistical]



Short-term Lyapunov exponent (computed over 10sec) decreases (i.e. **stability of EEG trajectory increases**) **before seizure**





Prediction **horizon >1h**
Sensitivity 82%
1 FP every 8h
No statistical validation

[Iasemidis et al, 2005]

T-index = average **difference** of **STL between electrodes** in optimal **onset zone**

Nonlinear interdependence

Time-delay embedding
Of $x(t)$, $x(t-\tau)$, …, $x(t-d\tau)$ is $\mathbf{x}(t)$

EEG channel i and time series x_i
Time indices of K nearest neighbors of $\mathbf{x}_i(t)$

$$\{t_1^i, t_2^i, \ldots, t_K^i\}$$

EEG channel j and time series x_j
Time indices of K nearest neighbors of $\mathbf{x}_j(t)$

$$\{t_1^j, t_2^j, \ldots, t_K^j\}$$

$$R(t, x_i) = \frac{1}{K}\sum_{k=1}^{K}\left\|\mathbf{x}_\mathbf{i}(t) - \mathbf{x}_\mathbf{i}(t_k^i)\right\|_2^2$$

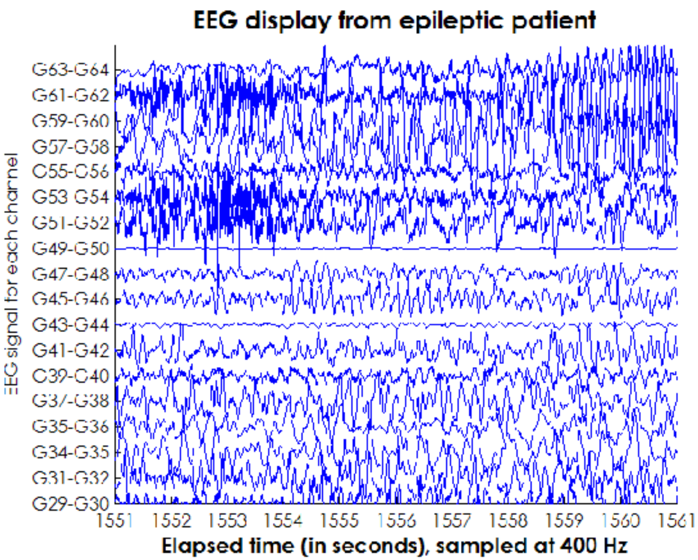
$$R(t, x_i | y_j) = \frac{1}{K}\sum_{k=1}^{K}\left\|\mathbf{x}_\mathbf{i}(t) - \mathbf{x}_\mathbf{i}(t_k^j)\right\|_2^2$$

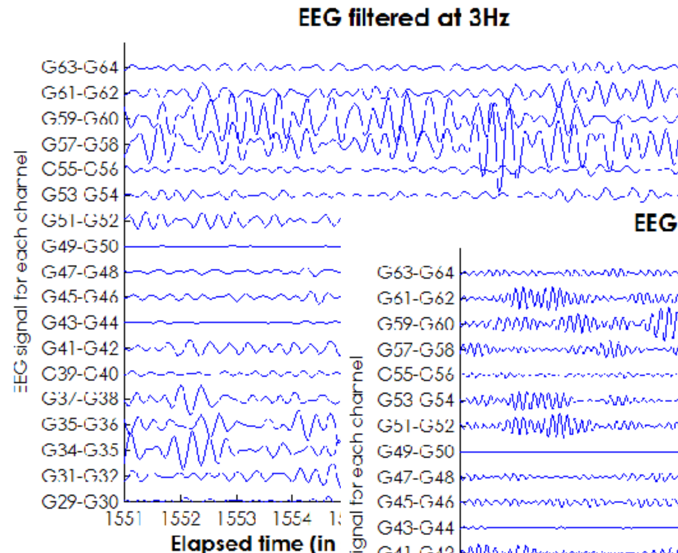
Similarity between the **trajectories** of channels i and j using the **reconstruction** error

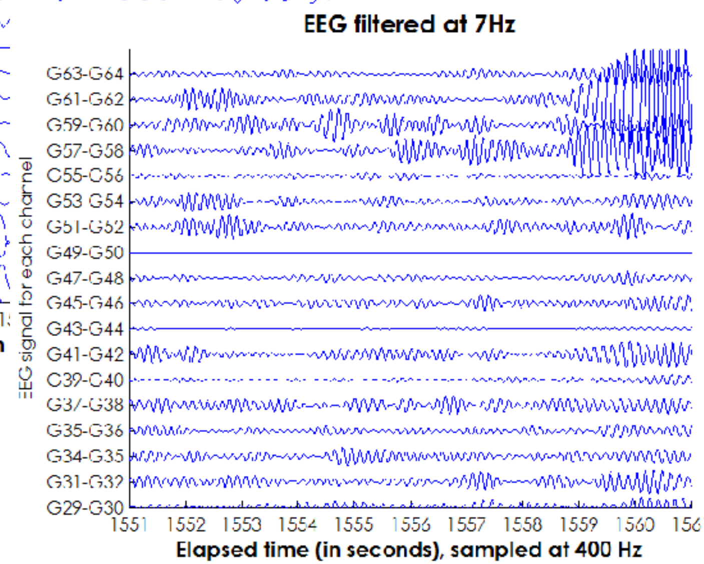
$$S(x_i | x_j) = \frac{1}{N}\sum_{t=1}^{N}\frac{R(t, x_i)}{R(t, x_i | x_j)}$$

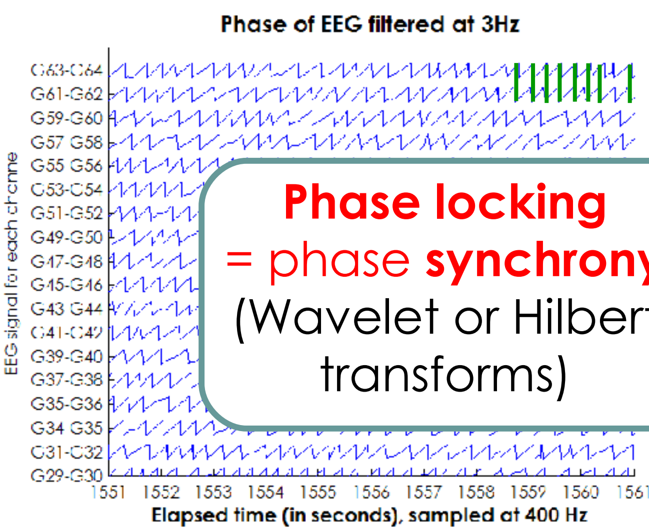
[Arhnold et al, 1999, Mormann et al, 2005, 2007]

Phase locking, synchrony

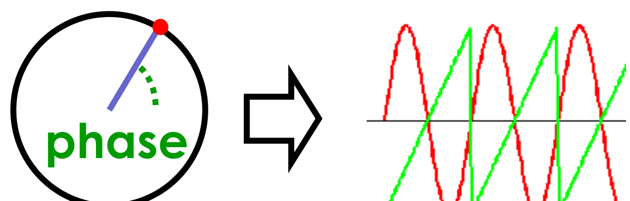








Phase locking
= phase **synchrony**
(Wavelet or Hilbert transforms)

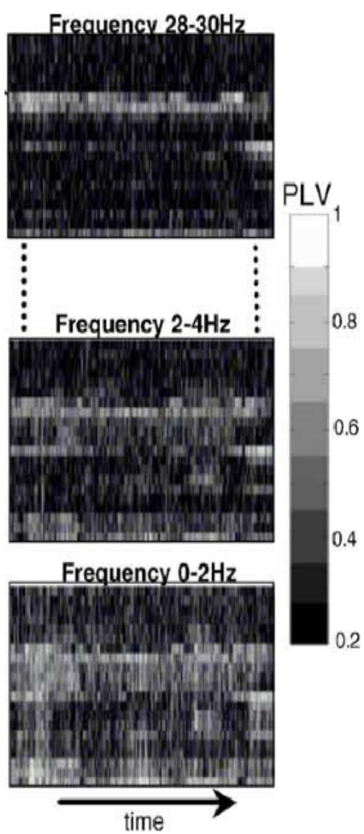


[Le Van Quyen et al, 2005], [Mormann et al, 2005]

Phase-locking value (synchrony) [nonlinear, bivariate, algorithmic]

Phase Locking Value
= average
phase difference

pairs of electrodes

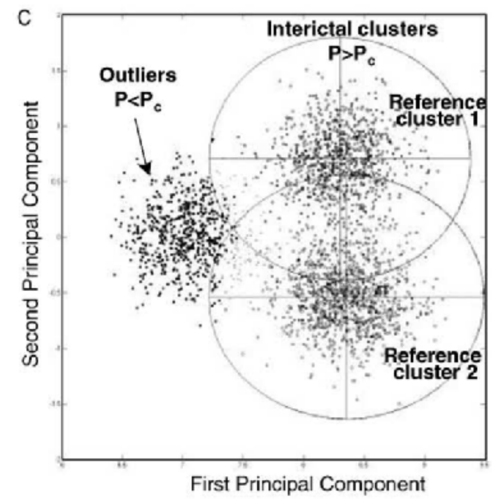


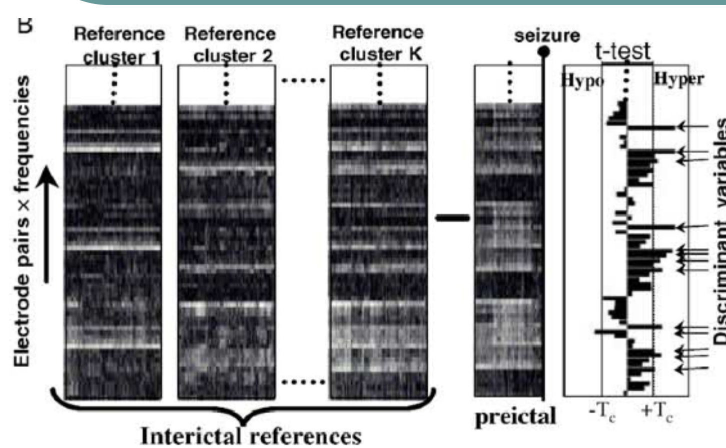
Feature vectors of **PLV**:
15 frequencies
× (20 × 19 / 2) electrodes

Reference library
of 5 to 10 **clusters** of
PLV feature vectors
(interictal synchrony)

Outliers
= preictal PLV vectors

K-means





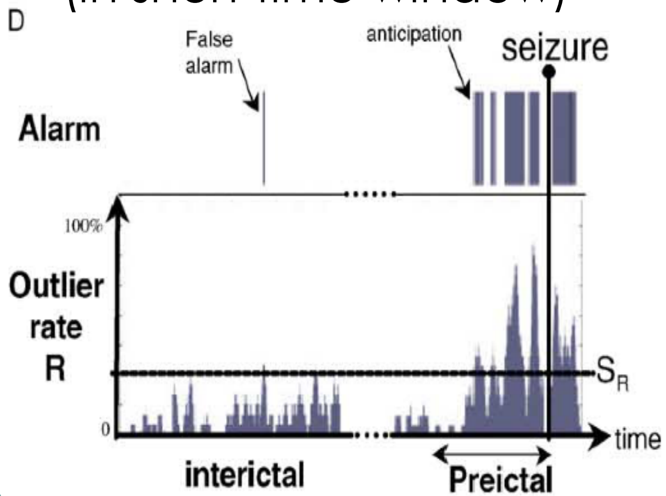
Student t-test for selection of **discriminant PLV features**

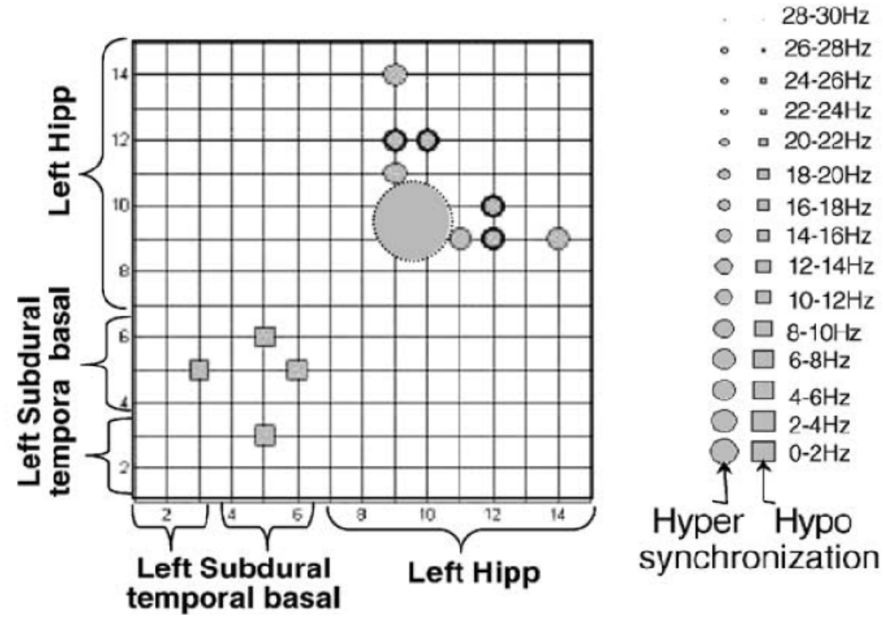
Chi-square test for **detection of outliers**

[Le Van Quyen et al, 2005]

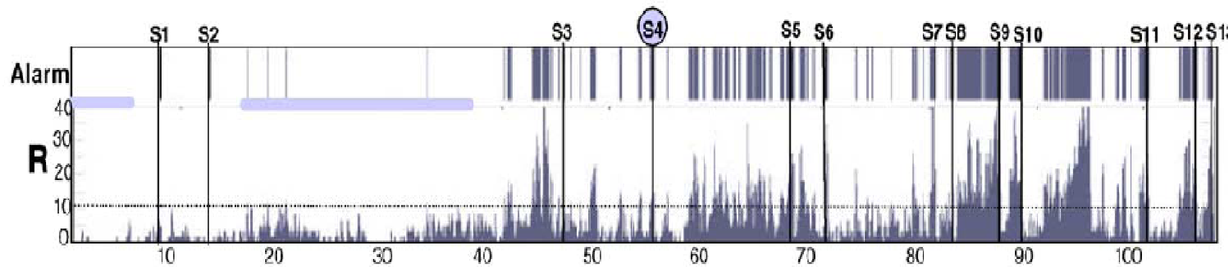
Phase-locking value (synchrony) [nonlinear, bivariate, algorithmic]

preictal alarm:
Outliers rate > threshold
(in short time window)





Prediction **horizon >3h**
Sensitivity 69%
Many FP
No statistical validation



[Le Van Quyen et al, 2005]

Outline

- Seizure prediction **problem**, **approaches**
- **International Seizure Prediction Group**:
  - actors
  - dataset (clinical facts, preprocessing)
  - goals
- How to ensure seizure **predictability**?
  - ROC, sensitivity, specificity
  - Statistical: Seizure Time Surrogates
  - Algorithmic: training vs. testing dataset
- **Linear univariate** techniques
  - (Accumulated) energy [Esteller, Harrison]
- **Linear bivariate** techniques
  - Fitting autoregressive model [Jouny]
  - Cross-correlation [Mormann]
- **Non-linear bivariate** techniques
  - Non-linear systems
  - Dynamical entrainment [Iasemidis]
  - Nonlinear interdependence [Arhnold]
  - Phase locking
  - Phase synchronization [Le Van Quyen]
- Our research: **classification of bivariate dynamical patterns**

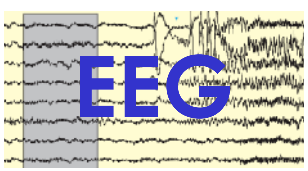
Classification of dynamical bivariate features (1)

EEG data

- **Public EEG database** at Albert-Ludwigs-Universität in **Freiburg**
  - **21 patients**
- **NYUMed EEG database** (supplied by Vanessa Arnedo, Ruben Kuzniecky)
  - So far **4 patients**

Patient 1	112 iEEG (56 in bipolar)	5 days	4 seizures	Left frontal epilepsy focus
Patient 2	126 iEEG (63 in bipolar)	12 days	7 seizures	Lateral frontal epilepsy focus

Step 1:



Generate from EEG, every 5sec, **bivariate features**

Maximal **cross-correlation**

Dynamical **entrainment**

Phase-locking **synchrony**

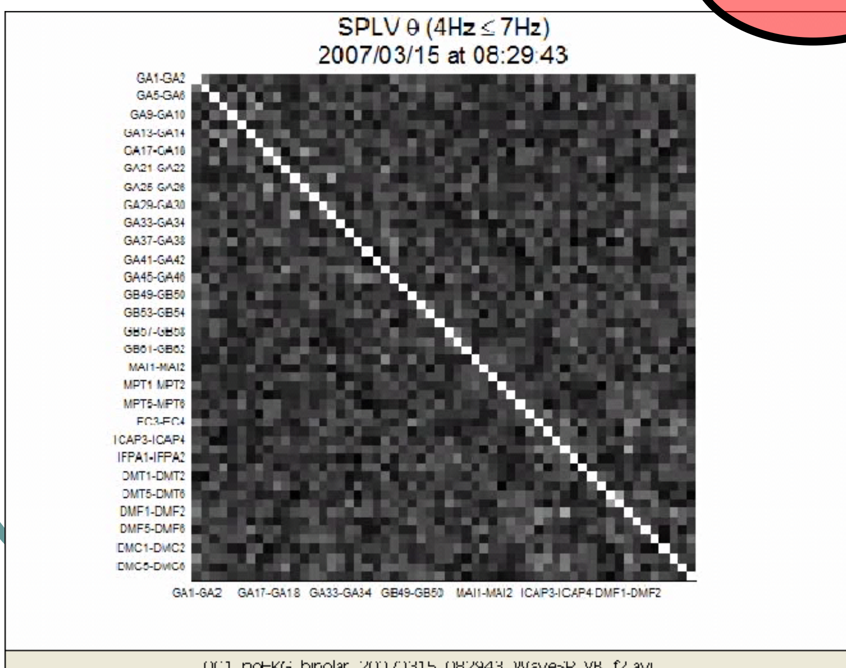
Nonlinear **interdependence**

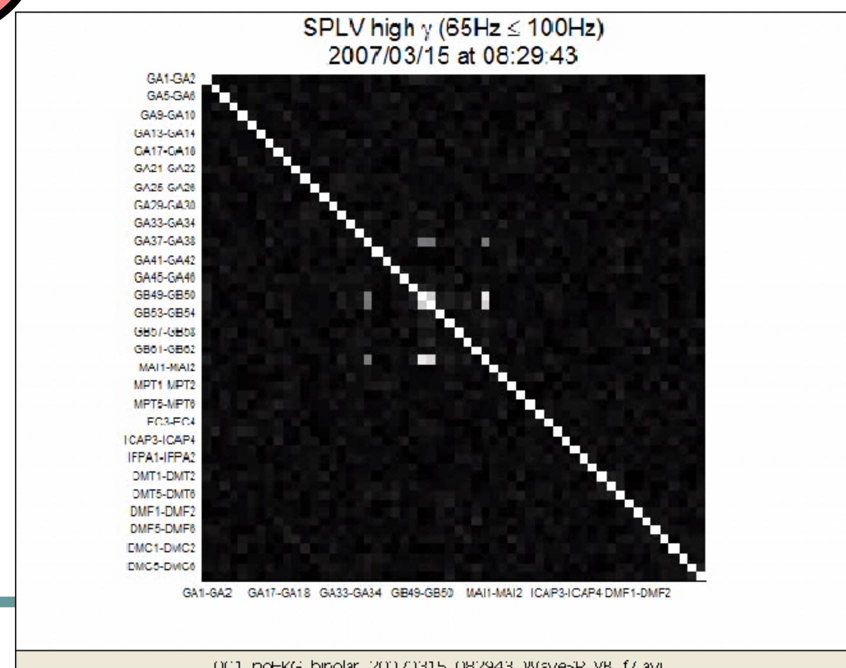
Classification of dynamical bivariate features (2)

Step 2:

Phase-locking **synchrony** → Group **bivariate features** into **short "movies"** (1min or 5min) → **Dynamical Bivariate Features**

Examples of **Ictal** synchrony movies



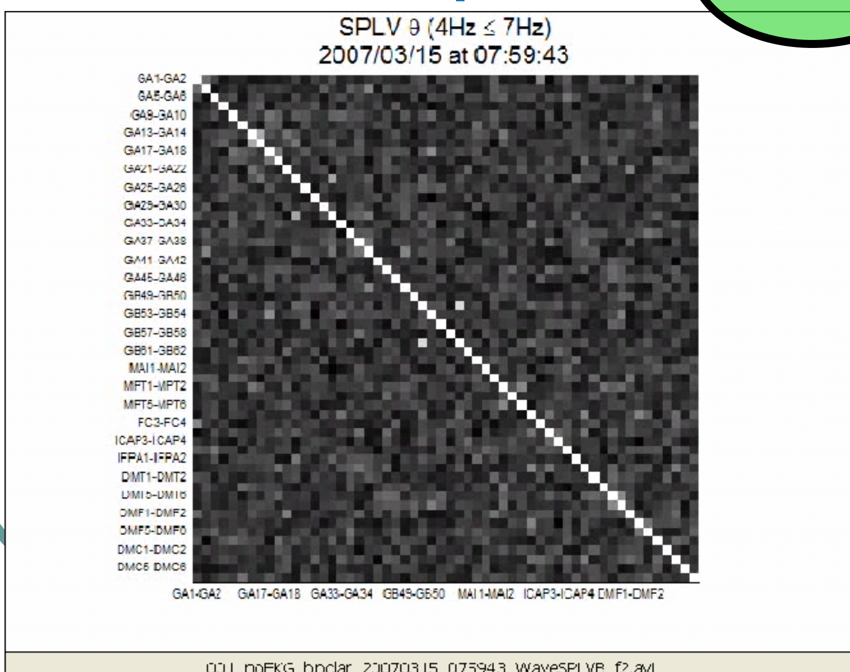


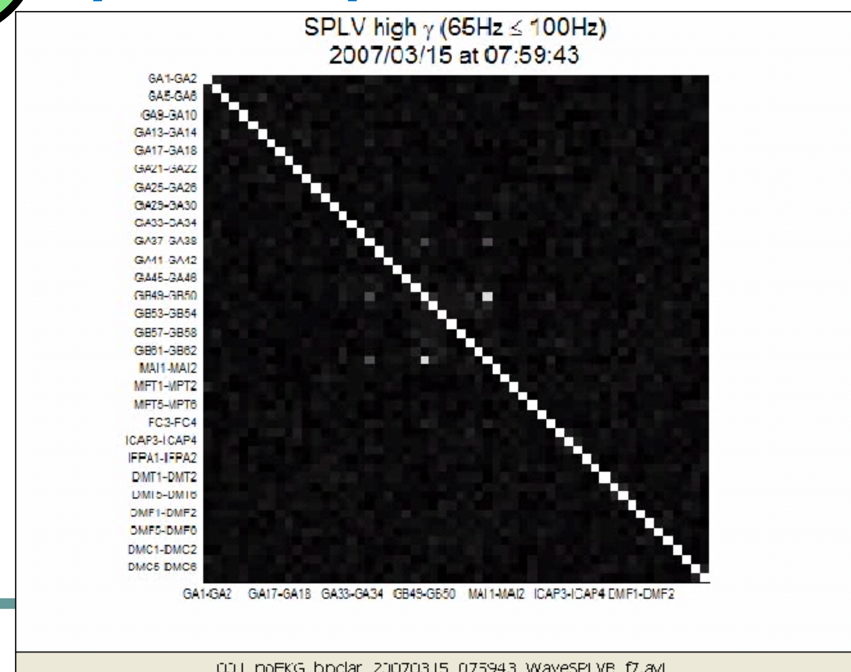
Classification of dynamical bivariate features (2)

Step 2:

Phase-locking **synchrony** → Group **bivariate features** into **short "movies"** (1min or 5min) → **Dynamical Bivariate Features**

Examples of **Pre-ictal** synchrony movies



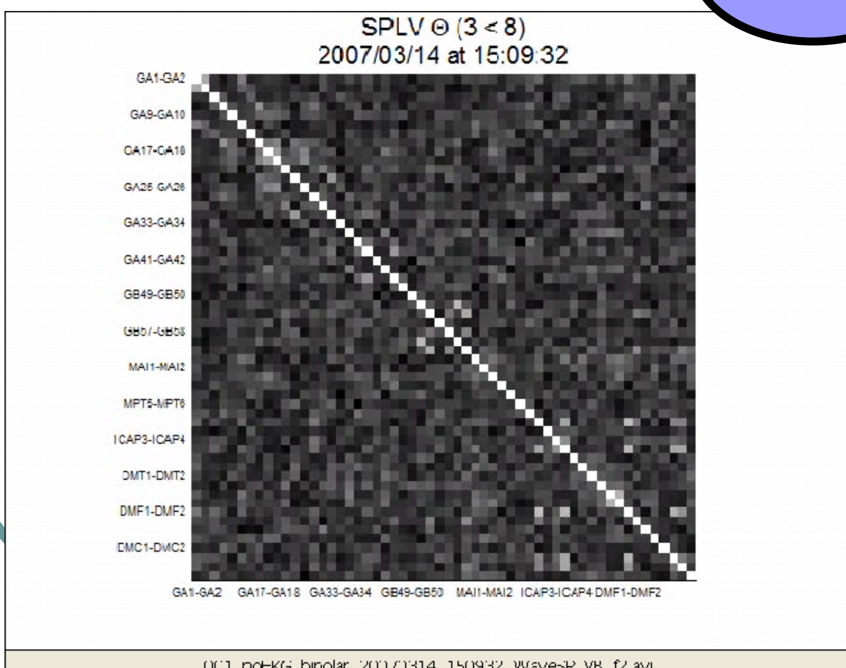


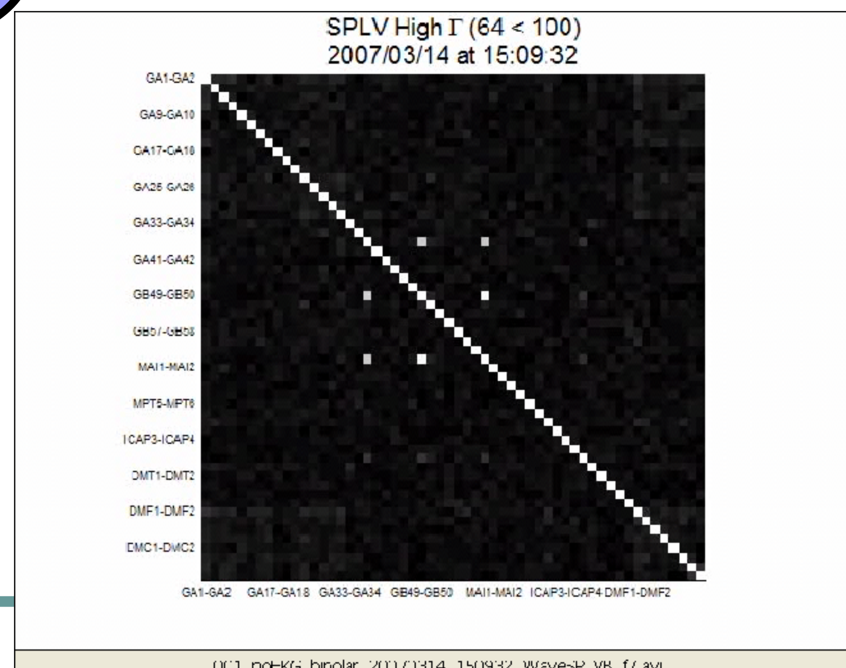
Classification of dynamical bivariate features (2)

Step 2:

Phase-locking **synchrony** → Group **bivariate features** into **short "movies"** (1min or 5min) → **Dynamical Bivariate Features**

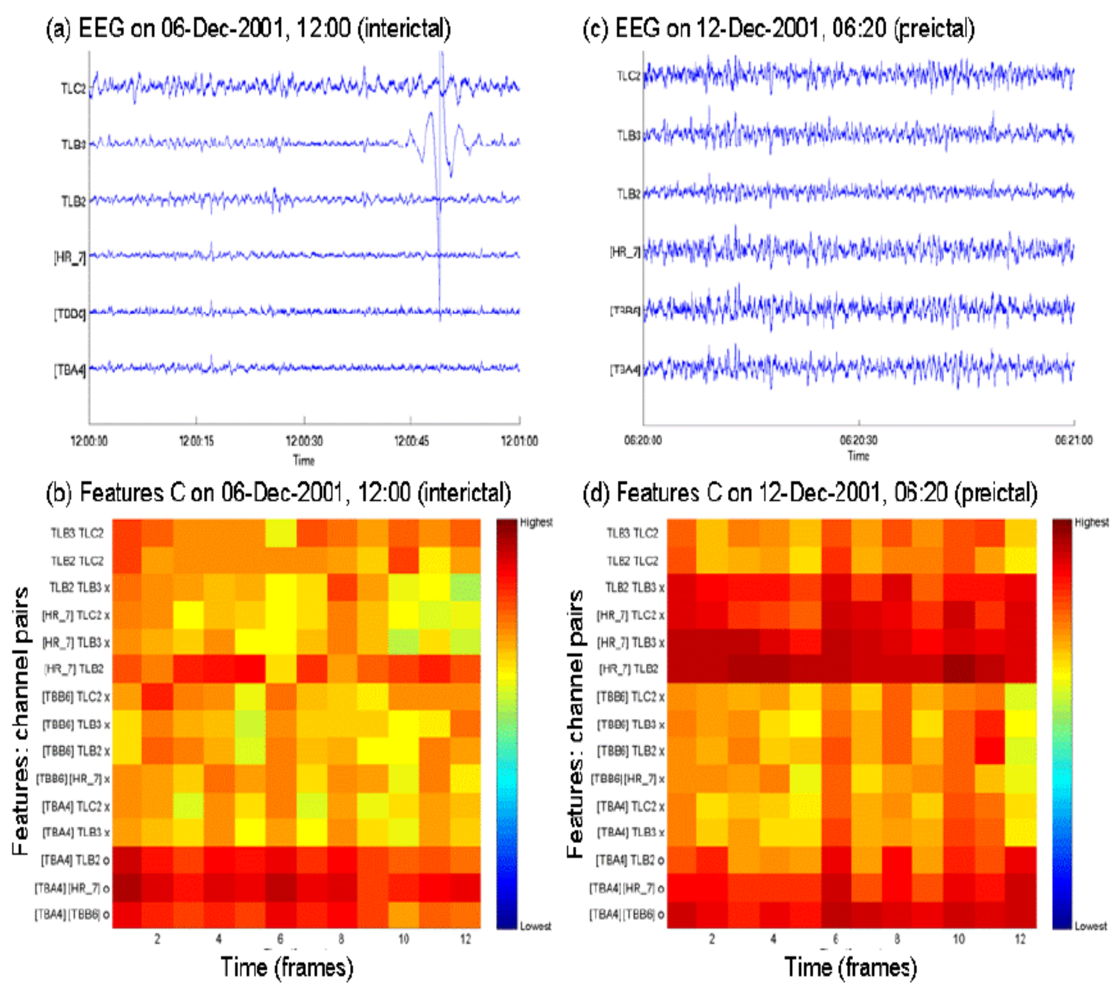
Examples of **Interictal** synchrony movies





Classification of dynamical bivariate features (2)

- Example from **Freiburg** using:
  - 1min patterns
    (12 frames of 5sec)
  - Cross-correlation
  - 6 channels
    (3 onset zone, 3 outside)
    i.e. 6*5/2=15 pairs
- **Freiburg** data:
  4 types of patterns
- Non-frequential features:
  - Cross-correlation
  - Nonlinear interdependence
  - Difference of Lyapunov exponents
  - 1min: 12*15=180 features
  - 5min: 60*15=900 features
- Frequency-specific features (7 freq bands):
  - Phase locking synchrony
  - Entropy of phase difference
  - Wavelet coherence
  - 1min: 12*15*7=1260 features
  - 5min: 60*15*7=6300 features



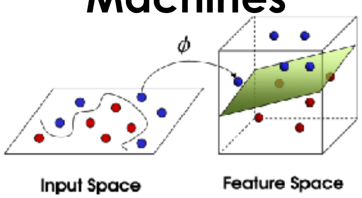
Classification of dynamical bivariate features (3)

Step 3:

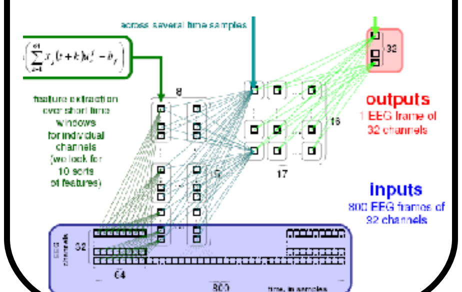
Dynamical Bivariate Features

Train and test **nonlinear classifiers** using **Machine Learning**

Support Vector Machines



Time-Delay Neural Networks



Locally Linear Embedding

Optimally Sparse Codes

Unsupervised clustering

1. Uncover unique clusters
2. Optimize choice of features, movie length...

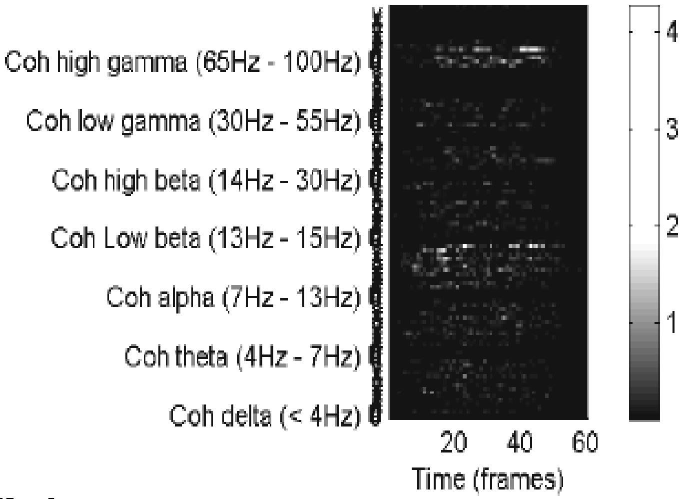
Supervised classification

Interictal **Pre-ictal**

[Mirowski, Madhavan, LeCun, Kuzniecky, 2006]

Machine learning classification

- Neural networks:
  - Logistic regression
    - L1 regularization
    - Feature selection by looking at weights
  - Convolutional networks
    - L1 regularization
    - Feature selection by input sensitivity analysis
- SVM



Results on Freiburg dataset

		pat 1		pat 2		pat 3			pat 4			pat 5			pat 6		pat 7		pat 8		pat 9			pat 10			pat 11	
		fpr	ts1	fpr	ts1	fpr	ts1	ts2	fpr	ts1	ts2	fpr	ts1	ts2	fpr	ts1	fpr	ts1	fpr	ts1	fpr	ts1	ts2	fpr	ts1	ts2	fpr	ts1
C	log	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	0	46	x	x	x	x	x	0	79	73	x	x
	lenet5	0	68	0	40	x	x	x	0	54	61	0	25	52	x	x	0	56	x	x	x	x	x	x	x	x	x	x
	svm	0.23	68	0	40	x	x	x	x	x	x	x	x	x	0.12	66	0	36	x	x	x	x	x	0.12	79	73	x	x
S	log	x	x	x	x	0	48	3	0	54	61	x	x	x	x	x	0	56	x	x	x	x	x	x	x	x	x	x
	lenet5	0	68	0	40	0	48	3	0	54	61	x	x	x	x	x	0	56	x	x	0	51	78	x	x	x	0	67
	svm	0.23	68	0	40	x	x	x	0.13	39	61	0	45	52	0.12	16	0	56	0	9	0.13	51	43	0.12	79	73	0.25	67
DSTL	svm	x	x	x	x	x	x	x	0	39	51	x	x	x	x	x	x	x	x	x	x	x	x	0.24	9	3	x	x
SPLV	log	0	68	0	40	0	48	3	0	54	61	x	x	x	0	66	0	56	x	x	0	51	78	x	x	x	0	57
	lenet5	0	68	0	40	0	48	3	0	54	61	x	x	x	x	x	0	56	0	39	0	51	78	0	79	73	0	67
	svm	0.12	68	0	40	0	48	3	0	54	41	x	x	x	0.12	66	0	56	x	x	0	51	78	0.24	79	73	0	27
H	log	x	x	0	40	0	48	3	0	54	61	x	x	x	x	x	0	56	x	x	0	51	78	x	x	x	0	67
	lenet5	0	68	0	40	0	48	3	0	54	61	x	x	x	x	x	0	56	x	x	0	51	78	x	x	x	0	67
	svm	0.23	68	0	40	0	48	3	0	54	61	x	x	x	0.12	66	0	56	x	x	0	51	78	0.24	79	73	0	27
Coh	log	0	68	0	40	0	48	3	0	54	61	x	x	x	0	66	0	56	x	x	0	51	78	x	x	x	0	37
	lenet5	0	68	0	40	0	48	3	0	54	61	0	45	52	0	71	0	56	0	44	0	51	78	0	79	73	0	67
	svm	0.12	68	0	40	0	48	3	0	54	61				0.12	66	0	56	x	x	0	51	78	0.24	79	73	0	32

		pat 12		pat 13		pat 14		pat 15		pat 16			*pat 17*			pat 18			*pat 19*		pat 20			*pat 21*		
		fpr	ts1	fpr	ts1	fpr	ts1	fpr	ts1	fpr	ts1	ts2	fpr	ts1	ts2	fpr	ts1	ts2	fpr	ts1	fpr	ts1	ts2	fpr	ts1	ts2
C	log	0	25	0	2	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	lenet5	0	25	0	7	x	x	x	x	0	65	25	x	x	x	x	x	x	x	x	*0*	*91*	*96*	x	x	x
	svm	0	25	x	x	x	x	x	x	0	60	20	x	x	x	x	x	x	x	x	x	x	x	0.12	99	70
S	log	0	25	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	lenet5	0	25	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	*0*	*28*	0	91	96	x	x	x
	svm			x	x	0.13	33	0.12	90	0	55	55	x	x	x	x	x	x	x	x	x	x	x	x	x	x
DSTL	svm			x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
SPLV	log	0	25	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	*0*	*99*	*75*
	lenet5	0	25	x	x	x	x	0	90	x	x	x	x	x	x	0	20	70	*0*	*28*	x	x	x	x	x	x
	svm			x	x	0.26	33	0	80	x	x	x	x	x	x	x	x	x	x	x	x	x	x	0.12	99	80
H	log	0	25	x	x	0	33	0	70	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	lenet5	0	25	x	x	0	33	0	90	x	x	x	*0*	*73*	##	x	x	x	x	x	x	x	x	x	x	x
	svm			x	x	0.13	33	0	85	x	x	x	x	x	x	x	x	x	x	x	x	x	x	0.12	14	75
Coh	log	0	25	x	x	x	x	0	45	0	60	10	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	lenet5	0	25	x	x	x	x	0	90	x	x	x	x	x	x	*0*	*25*	*90*	x	x	0	99	20	x	x	x
	svm			x	x	0.26	28	0	85	0	60	5	x	x	x	0.23	15	90	x	x	x	x	x	0.12	99	75

An innovative approach

1. **Integrate dynamical data**
   i.e. evolution of synchronization
2. **Nonlinear classification**
   learnt from data (**machine learning**)
   (instead of simple threshold-based decision)
3. **Feature selection**
   which **channels** at which **frequencies** are discriminative of seizures?
4. **Remaining** problem:
   - **Time to seizure: what is the preictal duration?**
   - (Instead of interictal vs. preictal **classification**)

- Epilepsy Foundation grant proposal (August 2008)

Thank You

- **Andrzejak R.G.**, Mormann F., Kreuz T., et al, Testing the null hypothesis of the non-existence of the pre-seizure state, *Physical Review E* **2003**
- **D'Alessandro M.**, Esteller R., Chaovalitwongse W., et al, Adaptive epileptic seizure prediction system, *IEEE Transactions in Biomedical Engineering* **2003**
- **D'Alessandro M.**, Vachtsevanos G., Esteller R., et al, A multi-feature and multi-channel univariate selection process for seizure prediction, *Clinical Neurophysiology* **2005**
- **Esteller R.**, Echauz J., D'Alessandro M., et al, Continuous energy variation during the seizure cycle: towards an online accumulated energy, *Clinical Neurophysiology* **2005**
- **Harrison M.A.**, Frei M.G., Osorio I., Accumulated energy revisited, *Clinical Neurophysiology* **2005**
- **Iasemidis L.D.**, Shiau D.S., Pardalos P.M., et al, Long-term prospective online real-time seizure prediction, *Clinical Neurophysiology* **2005**
- **Jerger K.K.**, Weinstein S.L., Sauer T., et al, Multivariate linear discrimination of seizures, *Clinical Neurophysiology* **2005**
- **Jouny C.**, Franaszczuk P., Bergey G., Signal complexity and synchrony of epileptic seizures: is there an identifiable preictal period, *Clinical Neurophysiology* **2005**
- **Lehnertz K.**, Litt B., The first international collaborative workshop on seizure prediction: summary and data description, *Clinical Neurophysiology* **2005**
- **Lehnertz K.**, Mormann F., Osterhage H., et al, State-of-the-art seizure prediction, *Journal of Clinical Neurophysiology* **2007**
- **Le Van Quyen M.**, Soss J., Navarro V., et al, Preictal state identification by synchronization changes in long-term intracranial recordings, *Clinical Neurophysiology* **2005**
- **Litt B.**, Echauz J., Prediction of epileptic seizures, *The Lancet Neurology* **2002**
- **Mormann F.**, Kreuz T., Rieke C., et al, On the predictability of epileptic seizures, *Clinical Neurophysiology* **2005**
- **Mormann F.**, Elger C.E., Lehnertz K., Seizure anticipation: from algorithms to clinical practice, *Current Opinion in Neurology* **2006**