# 뇌파를 통하여 알아보는 뇌의 동역학

# 2023 생명물리 여름학교

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https://www.dropbox.com/s/8g99hgudw6n8ydt/JoonYoungMoon\_SummerSchool\_2023.pdf?dl=0

# Research Motivation

Our work is motivated by the idea that understanding the dynamics of brain waves in the brain is critical to identify, monitor, and ultimately control brain states transitions.



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## **Research Themes**

#### I. Brain Waves

II. Phase Patterns in Brain States

III. Phase Dynamics of Brain States



~100 billion (~10<sup>11</sup>) neurons and ~100 trillion (10<sup>14</sup>) synapses in human brain. Recent estimate: 86 billion neurons, 16.3 billion in the cerebral cortex, and 69 billion in the cerebellum.



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http://www.schalklab.org/research/brain-computer-interfacing



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Richard Caton (1875): reported electrical activities of rabbits' and monkeys' brains

Adolf Beck (1890): published electrical activities of rabbits' and dogs' brains

Hans Berger (1924): recorded the first human EEG.





Hans Berger (1873-1941)

#### LFP (local field potential)

The Local Field Potential (LFP) is the electric potential recorded around neurons, typically using micro-electrodes (metal, silicon, etc).



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Besides their invasive aspect, LFPs also sample relatively localized populations of neurons, separated by a few hundred microns. In contrast, the EEG samples much larger populations of neurons.



http://www.scholarpedia.org/article/Local\_field\_potential

The electric potential generated by an individual neuron is far too small to be picked up by EEG.

EEG therefore reflects the group synchronous activities of the neurons.

Scalp EEG shows oscillations at a variety of frequencies (Fourier transform can be applied).













**Delta** 

Theta

Alpha

7- 12 Hz

**Beta** 12 - 30 Hz

**Gamma** 30 - 50 Hz

4 - 7 Hz

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https://sapienlabs.co//eyes-open-eyesclosed-and-variability-in-the-eeg

Delta: Deep, dreamless sleep (non-REM)



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**Theta**: Light sleep (REM), dream, deep meditation. "A person who has taken time off from a task and begins to daydream is often in a theta brainwave state. A person who is driving on a freeway, and discovers that they can't recall the last five miles, is often in a theta state."



Ned Herrmann, https://www.scientificamerican.com/article/what-is-the-function-of-t-1997-12-22/

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**Alpha**: eyes closed or brain not actively engaged to external stimuli, light meditation.

"A person who has completed a task and sits down to rest is often in an alpha state. A person who takes time out to reflect or meditate is usually in an alpha state. A person who takes a break from a conference and walks in the garden is often in an alpha state."



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#### Beta: engaged state.

"A person in active conversation would be in beta. A debater would be in high beta. A person making a speech, or a teacher, or a talk show host would all be in beta when they are engaged in their work."



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Alpha: eyes closed or brain not actively engaged to external stimuli, light meditation. May be a conduit for global brain communication. "A person who has completed a task and sits down to rest is often in an alpha state. A person who takes time out to reflect or meditate is usually in an alpha state. A person who takes a break from a conference and walks in the garden is often in an alpha state."

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Gamma: sensory processing. Local brain interaction.



#### Oscillation and Wave



#### Amplitude and Phase



A wave (oscillating signal) can be mapped to a circle on a complex plane (Hilbert transform).

 $\Theta$  is the phase of the oscillator, and |z| is the amplitude of the oscillator.



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How to Distinguish Consciousness from Unconsciousness?

#### Center for Consciousness Science, University of Michigan



Lee, UnCheol



Mashour, George

#### How to Distinguish Consciousness from Unconsciousness?

Patient State	Device	Features	Reading	Frontal Electroencephalography (EEG) Trace
Wakeful	EEG	$ \uparrow f, ↓ Amp, blinks $	↑γ,β,α↓θ,δ	
	SEF95	Twenties	26 Hz.	EEG with the burn with the second second
	BIS	High β ratio	96	ware war ware have a me and have a second and have a second and the se
	Entropy	High entropy	97	50µV
	AAI	↓lat, ↑∆amp	81	
	NI	EEG f band analysis	Α	
	ETAG	Age-adjusted MAC	0 MAC	
Sedated	EEG	$\alpha$ oscillations	$\downarrow \gamma, \beta, \uparrow \alpha, \theta, \delta$	
	SEF95	High teens	19 Hz.	EEG Anterna die Marca
	BIS	Low β ratio	78	
	Entropy	High entropy	85	
	AAI	† ing lat, ↓ ing ∆Amp	45	γ <sub>50µ</sub> γ γ
	NI	EEG f band analysis	B/C	
	ETAG	Age-adjusted MAC	0.4 MAC	
Unresponsive	EEG	Spindles, K, $\downarrow f$	<b>↑ α,θ,δ</b>	
	SEF <sub>95</sub>	Low teens	14 Hz.	
	BIS	Bispectral coherence	52	Féc a second sec
	Entropy	Entropy drop	43	Thanks made blackson my and all a
	AAI	î ing lat, ↓ing ∆Amp	30	. And all at the the head by sound by
	NI	EEG $f$ band analysis	D	A>nin A
	ETAG	Age-adjusted MAC	0.8 MAC	
Surgically	EEG	Slow $\delta$ waves, $\downarrow f$	δ dominance	
Anesthetized	SEF95	< 12 Hz.	10 Hz.	enter and the top off all all as
	BIS	Bispectral coherence	42	E SEPERA AND AND SUBARIAN DO AN ARCHIN, BANDAR
	Entropy	Low entropy	38	ארע האנגענגענאלא אונראיצענאיי איינאעראיי אאנגענעראי אוונאיצענאעראיי
	AAI	† ing lat, ↓ ing ∆Amp	22	A A A A A A A A A A A A A A A A A A A
	NI	EEG f band analysis	E	. A A A A A A A A A A A A A A A A A A A
	ETAG	Age-adjusted MAC	1.3 MAC	
Deeply	EEG	BS, isoelectricity	Bursts & flat	
Anesthetized	SEF95	< 2 Hz. (BS corrected)	2 Hz.	FFG
	BIS	High BSR	9	
	Entropy	Burst suppression	8	and the second
	AAI	† latency, ↓∆amp	11	2.upV
	NI	EEG $f$ band analysis	F	
15	ETAG	Age-adjusted MAC	2 MAC	

#### How to Prevent Intraoperative Awareness?

Anesthesia awareness rate may approach 1% in high risk patients. BIS (Bi-Spectral Index) is a popular monitoring tool, but not always accurate.



## Directionality Changes in EEG Functional Networks

Front-Back directionality may be a neural correlate of consciousness.



UC Lee et al., Anesthesiology 2013

## Model: Brain as a Coupled Oscillator System





# Model: Brain as a Coupled Oscillator System





We consider neural masses as oscillators





#### Coupled Oscillator System



Arthur T. Winfree, 1967 Yoshiki Kuramoto, 1975

# Model: Brain as a Coupled Oscillator System





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# メトロノーム同期 (72個) Synchronization of 72 metronomes

#### 2014年2月8日,池口研究室にて撮影 Recorded by Ikeguchi Laboratory, on February 8, 2014.

## **Canonical Coupled Oscillator Models**



Wilson-Cowan Model  

$$\dot{E}_{j}(t) = -E_{j} + F \left[ C_{EE}E_{j} - C_{IE}I_{j} + P_{j} + S \sum_{k=1}^{N} K_{jk}E_{k} \right]$$
  
 $\dot{I}_{j}(t) = -I_{j} + F \left[ C_{EI}E_{j} - C_{II}I_{j} + Q_{j} \right], \quad F[x] = (1 - e^{-x}), \quad j = 1, 2, ..., N.$ 

Stuart-Landau Model

$$\dot{Z}_{j}(t) = \left\{\lambda_{j} + i\omega_{j} - \left|Z_{j}(t)\right|^{2}\right\} Z_{j}(t) + S \sum_{k=1}^{N} K_{jk} Z_{k}(t - \tau_{jk}), \quad j = 1, 2, ..., N$$

Kuramoto Model

$$\dot{\theta}_j(t) = \omega_j + S \sum_{k=1}^N K_{jk} \sin\left(\theta_k (t - \tau_{jk}) - \theta_j(t)\right), \qquad j = 1, 2, \dots, N$$

Kuramoto/Stuart-Landau models are general/canonical models of the oscillators, and have general properties which more complex models also have.

J-Y Moon, PLOS Comp. Biol. 2015



There exists mappings from all oscillators to the Kuramoto model, as a first-order approximation. There exists mappings from some oscillators to the Stuart-Landau model, as the next-order appx.

> Kuramoto/ Stuart-Landau model are the canonical models of oscillators. If we can show that the K. model and S.-L. model yield *a specific property*, it suggests that other oscillators can possibly yield *that property*.

Hoppensteadt and Izhikevich, Springer, 1997



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# Kuramoto Model



$$\dot{\theta}_j(t) = \omega_j + K \sum_{k=1}^N A_{jk} \sin\left(\theta_k(t-\tau) - \theta_j(t)\right), j = 1, 2, \dots, N.$$

https://hdietert.github.io/static/kuramoto-animation/kuramoto.html

https://gereshes.com/2018/02/26/modeling-fireflies-in-sync/




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$$\dot{r}_j(t) = \left\{ \lambda_j - \left| r_j(t) \right|^2 \right\} r_j(t) + K \sum_{k=1}^N A_{jk} r_k \cos\left(\theta_k(t-\tau) - \theta_j\right),$$
  
$$\dot{\theta}_j(t) = \omega_j + K \sum_{k=1}^N A_{jk} \frac{r_k}{r_j} \sin\left(\theta_k(t-\tau) - \theta_j\right), \quad j = 1, 2, \dots, N$$

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 $\dot{r}_j(t) = \left\{ \lambda_j - \left| r_j(t) \right|^2 \right\} r_j(t) \qquad \Longrightarrow \qquad \dot{r}_j(t) = \left\{ \lambda_j - \left| r_j(t) \right|^2 \right\} r_j(t)$  $\dot{\theta}_j(t) = \omega_j$ 





$$\dot{Z}_{j}(t) = \left\{\lambda_{j} + i\omega_{j} - \left|Z_{j}(t)\right|^{2}\right\}Z_{j}(t)$$

 $\dot{r}_{j}(t) = \left\{\lambda_{j} - \left|r_{j}(t)\right|^{2}\right\}r_{j}(t)$  $\dot{\theta}_{j}(t) = \omega_{j}$ 



$$\dot{Z}_{j}(t) = \left\{\lambda_{j} + i\omega_{j} - |Z_{j}(t)|^{2}\right\}Z_{j}(t) + S\sum_{k=1}^{N} K_{jk}Z_{k}(t - \tau_{jk}) \xrightarrow{\dot{r}_{j}(t)} \left\{\lambda_{j} - |r_{j}(t)|^{2}\right\}r_{j}(t) + S\sum_{k=1}^{N} K_{jk}r_{k}\cos\left(\theta_{k}(t - \tau_{jk}) - \theta_{j}(t)\right), \\ \dot{\theta}_{j}(t) = \omega_{j} + S\sum_{k=1}^{N} K_{jk}\frac{r_{k}}{r_{j}}\sin\left(\theta_{k}(t - \tau_{jk}) - \theta_{j}(t)\right).$$

Moon et al., PLOS Comp. Biol. 2015



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Hoppensteadt and Izhikevich, Springer, 1997

## Model: Results on Human Structural Brain Networks



## Model: Results on Human Structural Brain Networks

➡ Kuramoto Model



# Every Oscillations Are Represented by Phase and Amplitude



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## **Relative Phase**

1. Summarize phase of each oscillator in the system and define the system's phase  $\Theta$  :

$$Re^{i\Theta} = \frac{1}{N} \sum_{j=1}^{N} e^{i\theta_j}$$

2. We subtract the system's phase from each oscillator's phase, and define it as relative phase  $\varphi_i$ :

$$\varphi_j = \theta_j - \Theta$$

## Model: Results on Human Structural Brain Networks



# Model Analysis, Simulations, and Experimental Confirmations



# Mathematical Results 1: Mean-Field Method

Using mean-field technique, we show the degreephase relationship.

$$\dot{\theta}_j(t) = \omega_j + \frac{S}{N} \sum_{k=1}^N K_{jk} \sin\left(\theta_k (t - \tau_{jk}) - \theta_j(t)\right), \qquad j = 1, 2, \dots, N$$

$$\approx \omega_j + \frac{S}{N} \sum_{k=1}^{N} K_{jk} [\sin(\theta_k - \theta_j - \beta)]$$

$$\approx \omega_j + \frac{SK_j}{N^2} \sum_{k=1}^{N} [\sin(\theta_k - \theta_j - \beta)]$$

 $\therefore$  S(homogeneous)  $\rightarrow \frac{SK_j}{N}$ (inhomogeneous)

$$\theta_j = \sin^{-1}\left(\frac{N}{K_j}\frac{\Delta_j}{SR}\right) + \Theta - \beta$$

$$\Delta_j \equiv \omega_j - \Omega$$
  $Re^{i\Theta} \equiv \frac{1}{N} \sum_{j=1}^N e^{i\theta_j}$ 

For  $z_j(t)$  on networks with sufficient coupling strength S and small time delay  $\tau_{jk}$ ,

degree(m) > degree(n),

then

if

phase(m) < phase(n).

T-W Ko, PRE 2008. J-Y Moon, PLOS Comp. Biol. 2015.

# Information Flow Analysis across Different Species



# Patterns Strongest at the Peak Frequency



Each species has a peak in its frequency distribution: 10~11 Hz for human, 8~9 Hz for macaque, 7~8 Hz for mouse. The observed patterns were strongest at the peak frequency, suggesting that the global inter-regional communication may be strongest at the peak frequency of each species.

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**III. Phase Dynamics of Brain States** 

## Current Research: Identification of Internal/External Modes

Hypothesis: The majority of time windows will match the internal or external template.



## Identification of Internal/External Modes in EEG and ECoG Recordings

Hypothesis: The majority of time windows will match the internal or external template.





Validate Electrophysiologically Defined Modes against fMRI Reference States

Hypothesis: EEG-defined modes are be associated with fMRI defined states





Kim, HyoungKyu

Internal/External Brain Modes Transitions May Be a Crucial Mechanism

**Hypothesis:** Transitions between two dominant modes, internal & external mode, can be the crucial mechanism facilitating learning and memory.



Honey et al., Network Neurosci. 2017

Internal/External Brain Modes Transitions May Be a Crucial Mechanism

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In external mode, we are biased towards external world.

In internal mode, we process information, and construct an internal model.

Internal/External Brain Modes Transitions May Be a Crucial Mechanism

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In external mode, we are biased towards external world. In internal mode, we process information, and construct an internal model.

Again in external mode, we compare our model against external world. Again in internal mode, we modify our model, triggered by the "mismatch". Characterize Internal (top-down) /External (Bottom-up) Modes Using EEG

**Hypothesis:** Large-scale cortical dynamics transition between two dominant modes, internal & external mode.



Characterize Internal (top-down) /External (Bottom-up) Modes in Our Model

**Idea:** we can map how amplitude/phase dynamics are affected by diffusive coupling term in our model.



Stuart-Landau model with diffusive term

$$\dot{Z}_{j}(t) = \left\{\lambda_{j} + i\omega_{j} - \left|Z_{j}(t)\right|^{2}\right\} Z_{j}(t) + S \sum_{k=1}^{N} A_{jk} \left[Z_{k}(t)e^{-i\beta} - Z_{j}(t)ge^{-i\alpha}\right],$$
  
$$j = 1, 2, \dots, N$$

equivalent to

$$\dot{r}_{j}(t) = \left\{\lambda_{j} - \left|r_{j}(t)\right|^{2}\right\}r_{j}(t) + S\sum_{k=1}^{N}A_{jk}r_{k}\left[\cos\left(\theta_{k} - \beta - \theta_{j}\right) - r_{j}g\cos\alpha\right],$$
$$\dot{\theta}_{j}(t) = \omega_{j} + S\sum_{k=1}^{N}A_{jk}\frac{r_{k}}{r_{j}}\left[\sin\left(\theta_{k} - \beta - \theta_{j}\right) + g\sin\alpha\right],$$
$$j = 1, 2, ..., N$$

Woo et al., Chaos 2020

Characterize Internal (top-down) /External (Bottom-up) Modes in Our Model

**Hypothesis:** Both internal and external states will allow for both high & low-amplitude oscillations.



# **Current Research**

#### 1. Characterize Internal and External Brain Modes

- Characterize internal vs external modes in model
- Identify internal/external modes in EEG/ECoG, and against fMRI reference states



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- 2. Determine Mechanisms and Targets for Triggering Mode Switches
- Determine conditions for mode transitions from model
- Determine triggers for internal-external mode transitions from experiments

# **Current Research**

### 1. Characterize Internal and External Brain Modes

- Characterize internal vs external modes in model
- Identify internal/external modes in EEG/ECoG, and against fMRI reference states



- 2. Determine Mechanisms and Targets for Triggering Mode Switches
- Determine conditions for mode transitions from model
- Determine triggers for internal-external mode transitions from experiments
- 3. Compare Mode Transition Properties against Non-General Populations.

# General Population vs. ADHD (inattentive type)







0.01 S



# Experiments Utilizing Simultaneous EEG/fMRI











Lee, YeJi



Cho, MinSeo







# Experiments Utilizing Simultaneous EEG/fMRI: gradCPT



# Experiments Utilizing Simultaneous EEG/fMRI: gradCPT



# Experiments Utilizing Simultaneous EEG/fMRI: gradCPT







#### **Members**

## Collaborations





Research Research Professor, Fellow, Kim, HyoungKyu Park, YoungJae

Researcher, Cha, YoungHwa



Researcher, Lee, YeJi







Intern, Cho, MinSeo

Lee, HaeSung

Ph.D. Candidate, Ph.D. Candidate, Nam, SeonHo





Professor, Kang, Min-Suk Professor, Hong, Seok-Jun Professor, Sohn, Hansem

Research Fellow, Kim, Dongho (KBSI) Senior Researcher, Han, SoHyun Ph.D. Candidate, Oh, Younghyun

# Thank you

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# Directionality Change as a Common Metric for General Anesthesia

#### Table 2. Select Characteristics of Three Major Classes of General Anesthetics

Explanatory Level		Group 1 (e.g., Propofol)	Group 2 (e. <i>g.,</i> Ketamine)	Group 3 (e. <i>g.,</i> Sevoflurane)
Molecular Neuroanatomic target Systems neuroscience Neurophysiology	Major GABA receptor agonist? Depression of the thalamus? VLPO activation? Increased alpha power?	Yes Yes Yes Yes	No No No	Yes Yes Yes Yes
Information theory	Inhibition of cortical feedback connectivity?	Yes	Yes	Yes

Group 1 anesthetics include primarily GABA<sub>A</sub> agonists such as propofol, etomidate, and thiopental. These drugs tend to be strong hypnotics, but weak immobilizers and analgesics. Group 2 anesthetics include non-GABAergic drugs (such as ketamine, nitrous oxide) that may antagonize the *N*-methyl-D-aspartate glutamatergic receptor. These drugs tend to be strong analgesics, but weak hypnotics and immobilizers. Groups 3 anesthetics have a mixed profile of GABA<sub>A</sub> agonism, two-pore potassium channel agonism, and excitatory neurotransmitter antagonism. These drugs—such as sevoflurane, isoflurane, and desflurane—are strong hypnotics and immobilizers. Inhibition of cortical feedback connectivity is potentially a common mechanism of anesthetic-induced unconsciousness across all three groups. VLPO contains neurons that are active during sleep.

GABA =  $\gamma$ -aminobutyric acid; VLPO = ventrolateral preoptic nucleus.

## Directionality Analysis across Different Species

Human	Macaque	Mouse
Structural network:	Structural network:	Structural network:
80 subjects/78 parcels (Gong et al. 2009)	11 studies/71 parcels (Young 1993)	8 subjects/74 parcels (constructed from Wu et al. 2013)
Experimental data:	Experimental data:	Experimental data:
6 subjects/128 ch. EEG (U of Michigan)	4 subjects/128 ch. ECoG (http://neurotycho.org/)	9 subjects/38 ch. ECoG (Choi et al. from KIST)

# 2-Mean Clustering of Human Resting State Example



# 4-Mean Clustering of Human Resting State Example



## Directional phase-lag index: *dPLI*

### *dPLI* of two signals *i* and *j*:

1. Instantaneous Phase Difference (IPD): phase difference at t.

 $\Delta \varphi_{ij}(t) = \varphi_i(t) - \varphi_j(t)$ 

2. Directional Phase Lag Index  $(dPLI_{jj})$ : time average of sign of *IPD* captures the phase lead/lag relationship between *i* and *j*.

$$dPLI_{ij} = \langle sign(\Delta \varphi_{ij}(t)) \rangle_t$$

If 0<*dPLI*≤1, *i* lead *j*. If -1≤*dPLI*<0, *i* lag *j*. In *dPLI*=0, neither *i* or *j* lead/lag.

CJ Stam et al. NeuroImage 2012



## Phase Relationship Is Equivalent to Other Measures



## Characterize Internal/External Modes in Our Oscillator Model

**Hypothesis:** Both internal and external states will allow for both high & low-amplitude oscillations.



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Lee, HaeSung

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equivalent to

$$\dot{r}_{j}(t) = \left\{\lambda_{j} - \left|r_{j}(t)\right|^{2}\right\}r_{j}(t) + S\sum_{k=1}^{N}A_{jk}r_{k}\left[\cos\left(\theta_{k} - \beta - \theta_{j}\right) - r_{j}g\cos\alpha\right]$$
$$\dot{\theta}_{j}(t) = \omega_{j} + S\sum_{k=1}^{N}A_{jk}\frac{r_{k}}{r_{j}}\left[\sin\left(\theta_{k} - \beta - \theta_{j}\right) + g\sin\alpha\right],$$
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Woo et al., Chaos 2020



# Collaborations

### **Data Collection and Analysis**



### University of Michigan

George Mashour Anthony Hudetz UnChoel Lee Joseph Lee



#### **University of Toronto** Taufik Valiante Araceli Cárdenas



#### Nathan Kline Institute Charles Schroeder Qawi Telesford Ting Xu



**KIST** Jee-Hyun Choi Eun-Jin Hwang



### **Yonsei Severance Hospital** Bon-Nyeo Koo Eun Jung Kim

### **Data Analysis and Modeling**

### Johns Hopkins University

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