Advancing personalized aDBS with LAURA
predicting the dynamic nature of beta-power distributions

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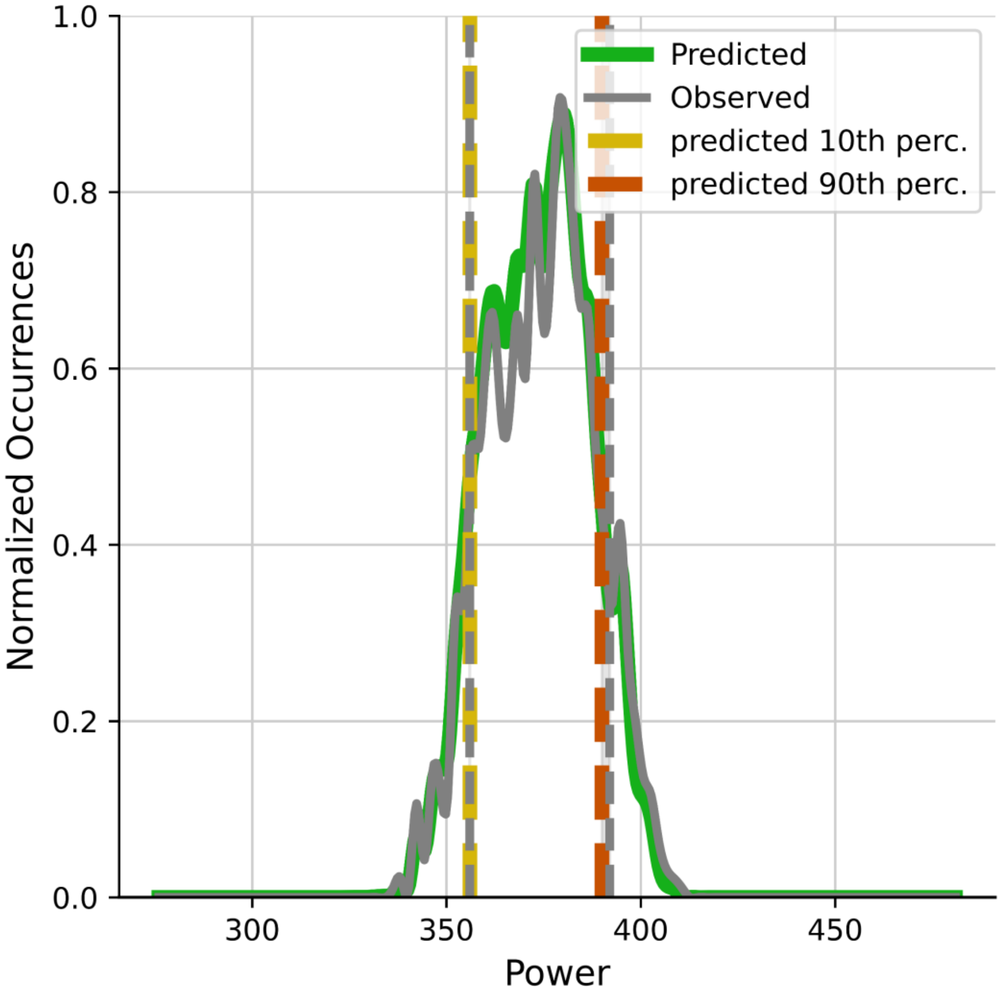
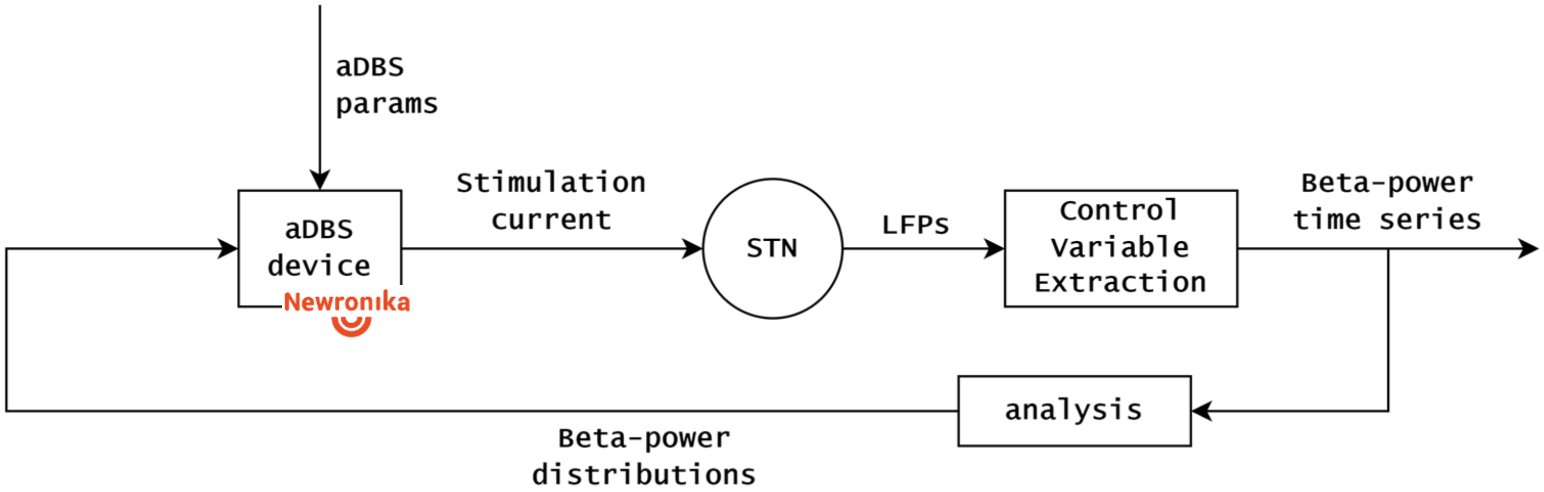
[4] Department of Excellence in Robotics and AI, Scuola Superiore Sant'Anna, Pisa, Italy



aDBS Workflow

Current state



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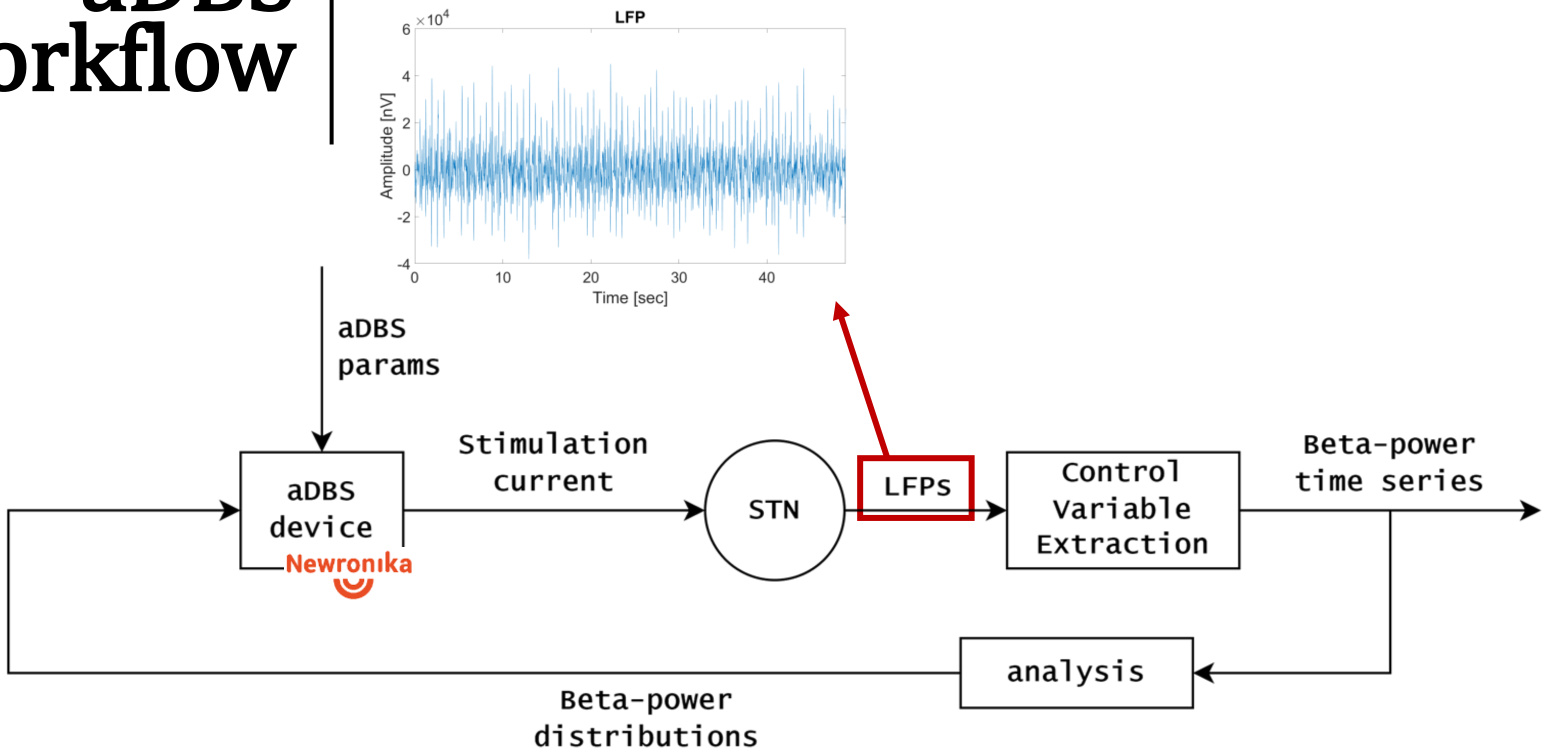

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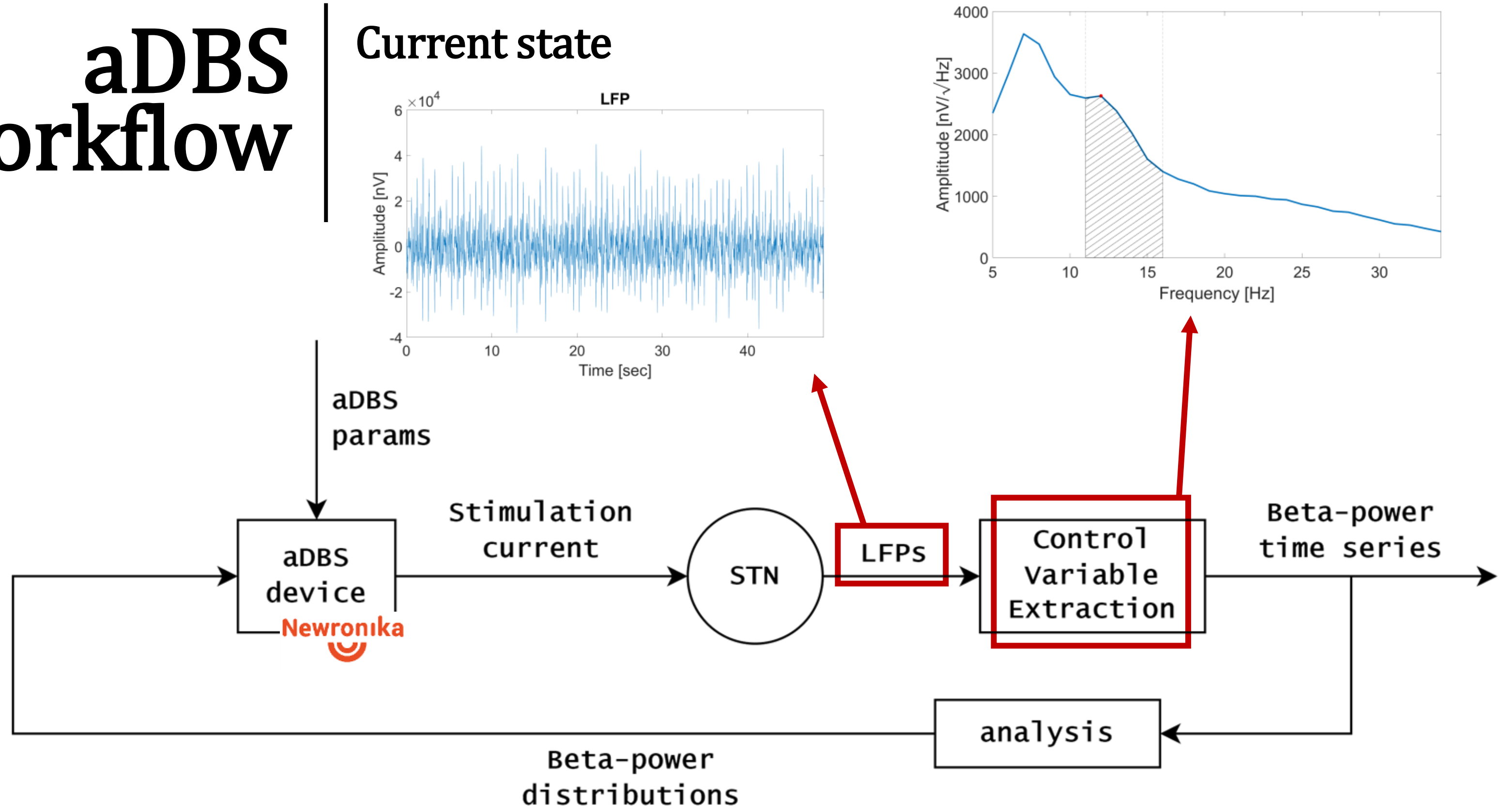

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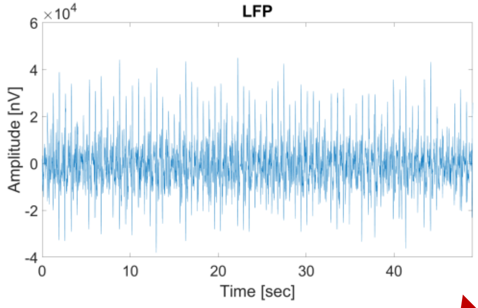
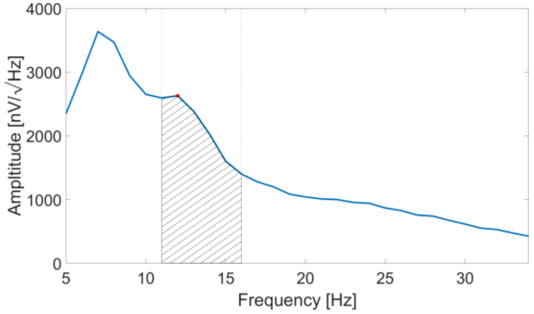
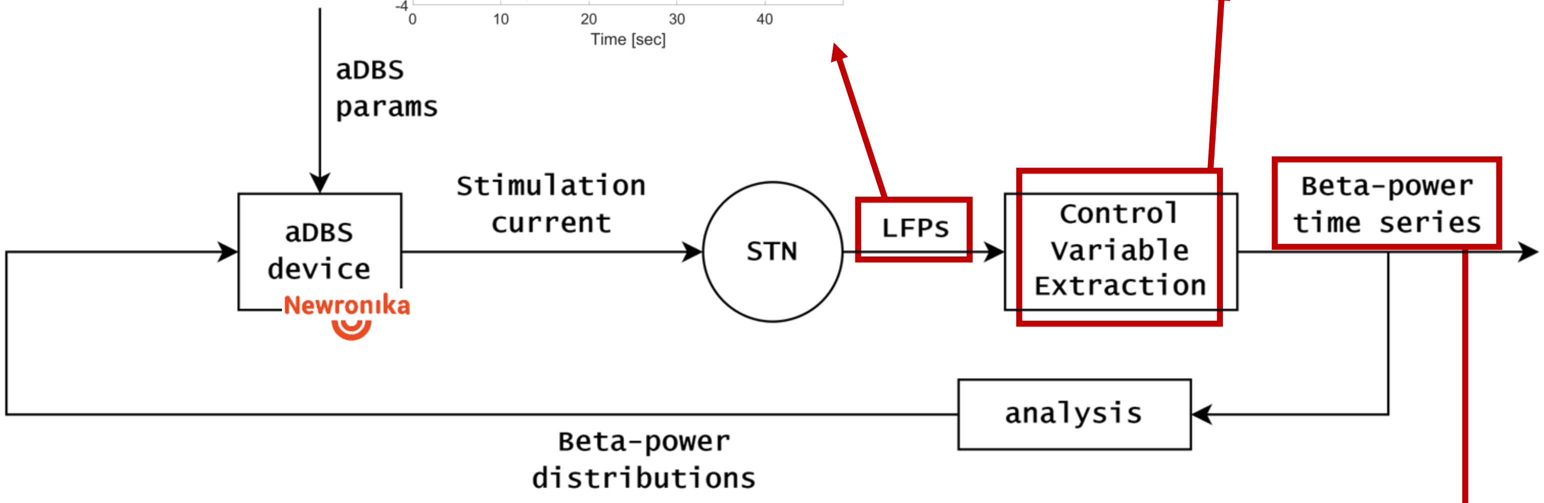
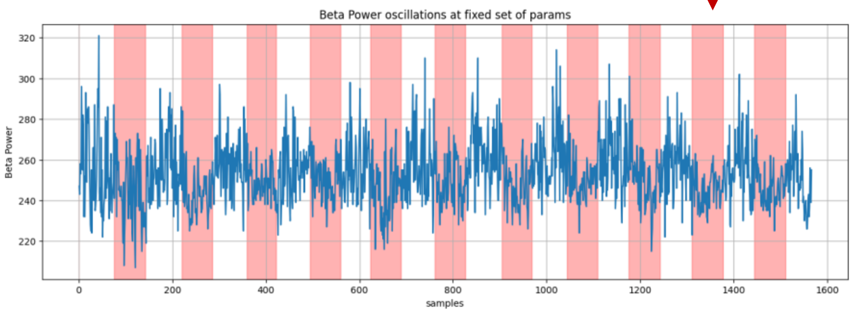






Biomarker: **subthalamic beta-power**

- Positively correlated with **bradykinesia** and **rigidity** (UPDRS-III)
- Reduced by **levodopa** and **stimulation**



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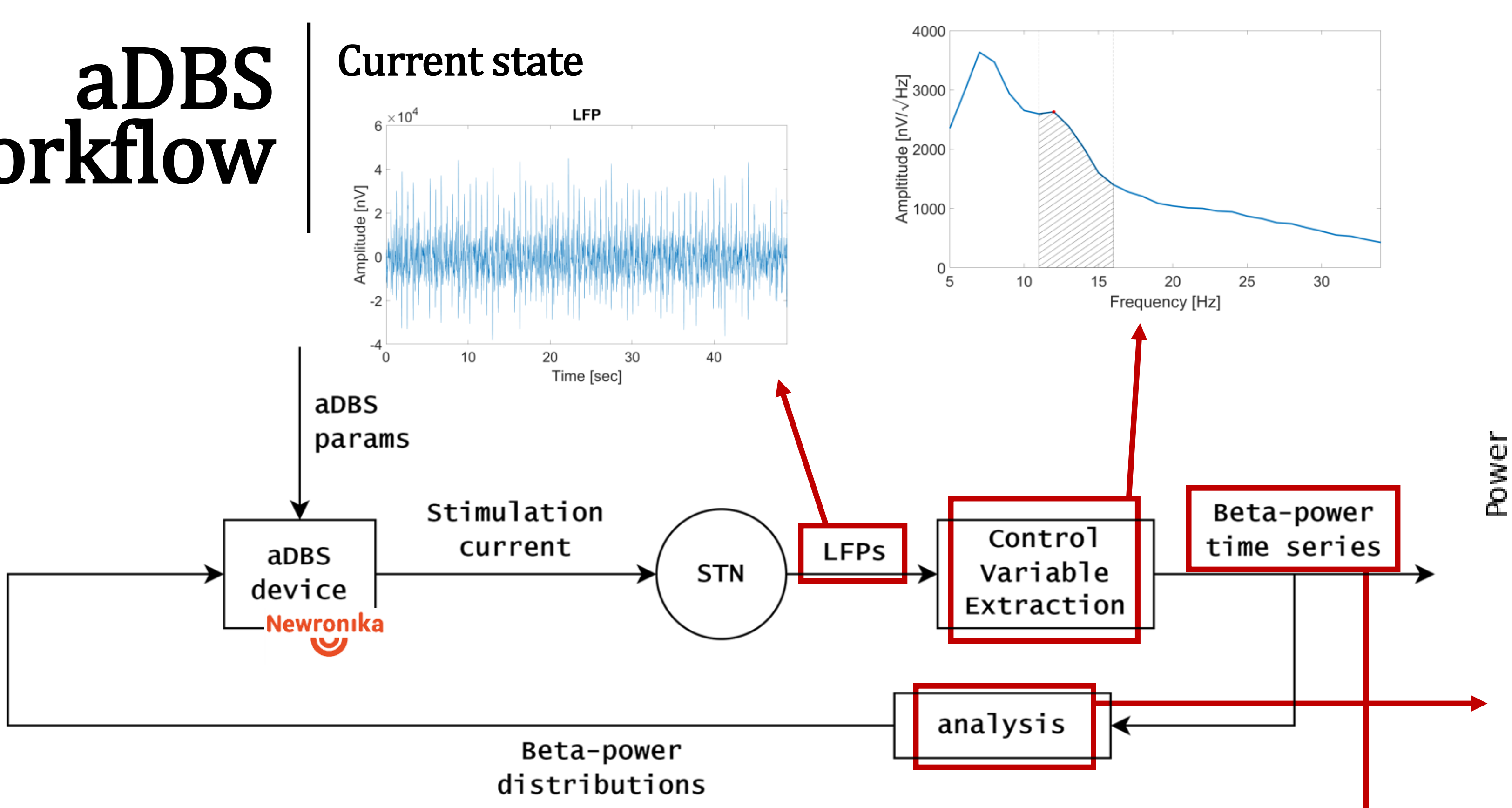

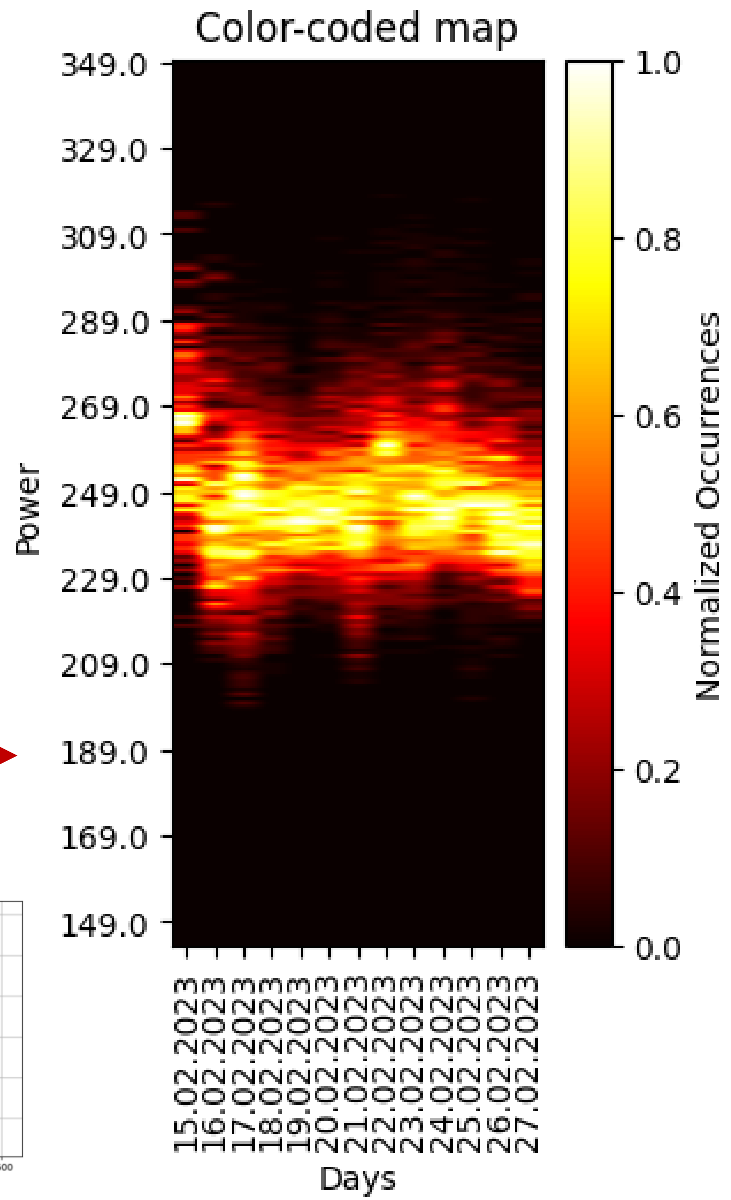

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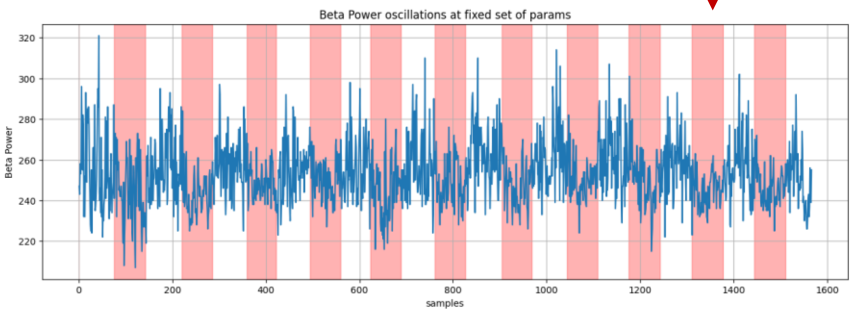

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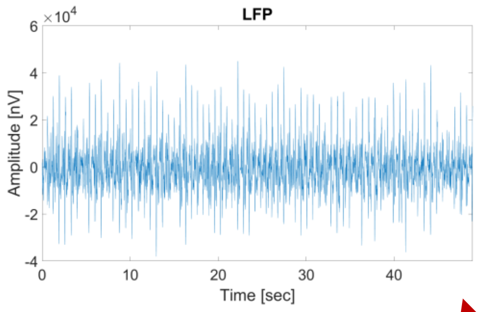

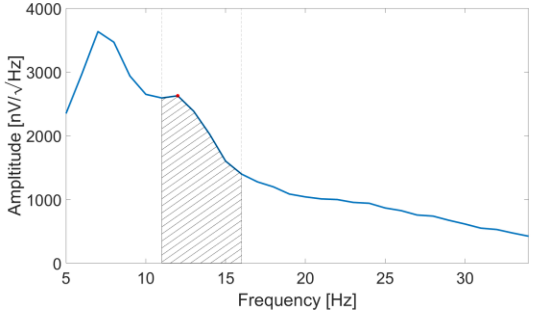

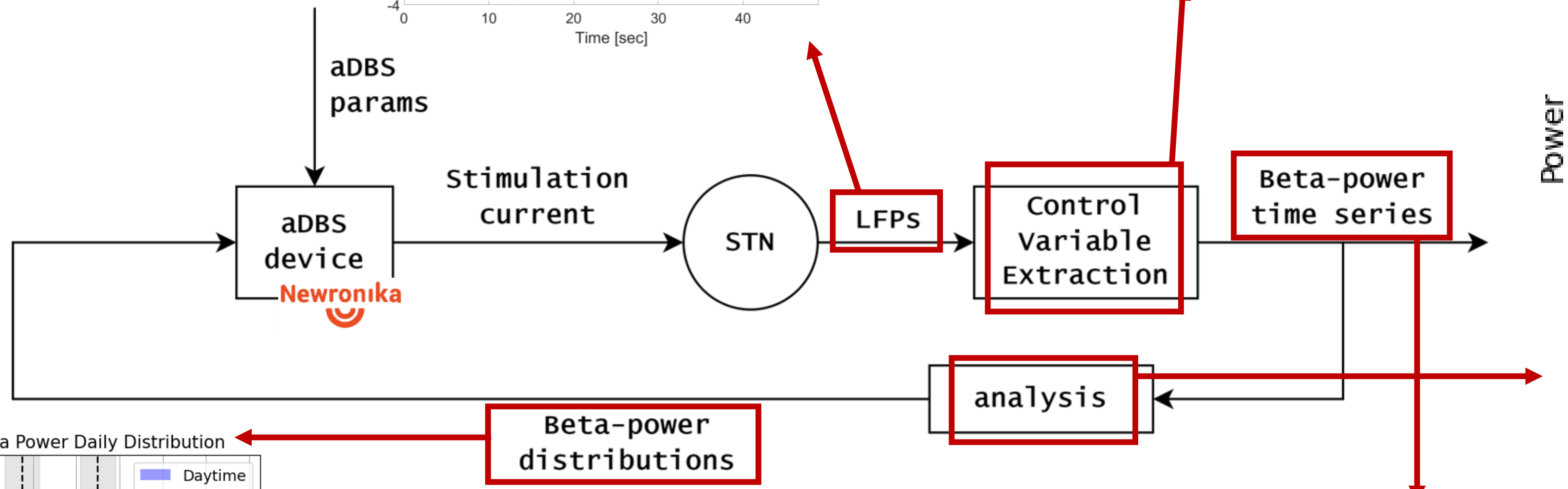

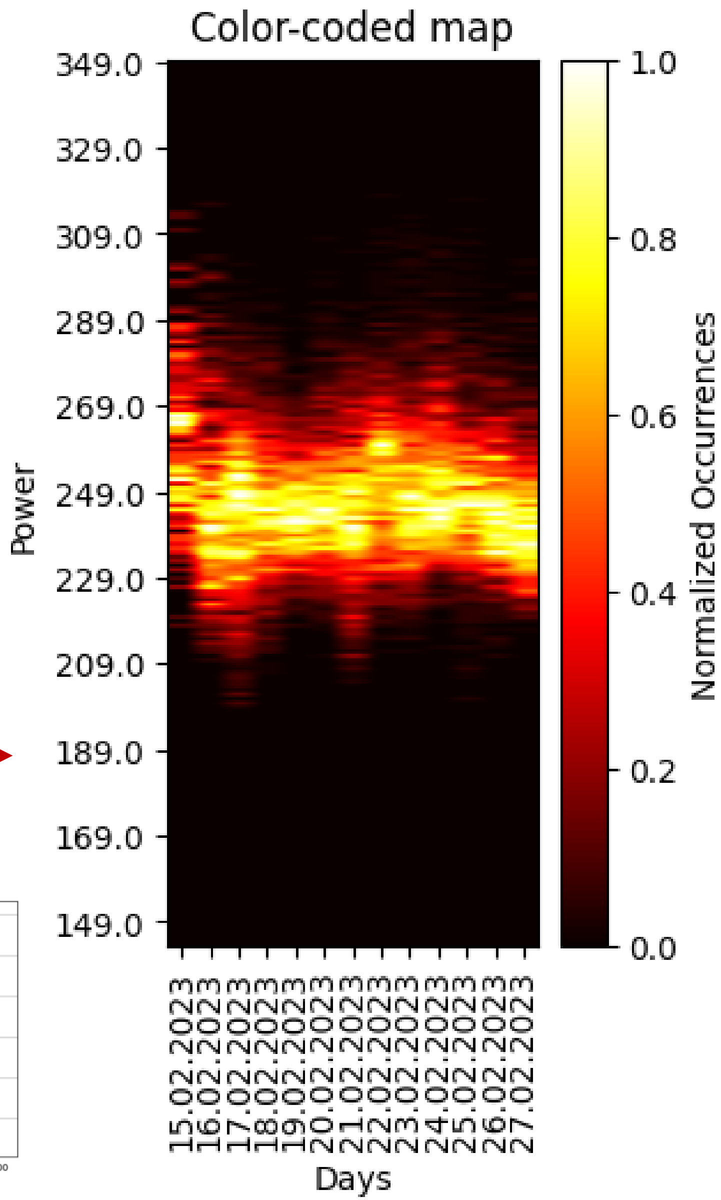

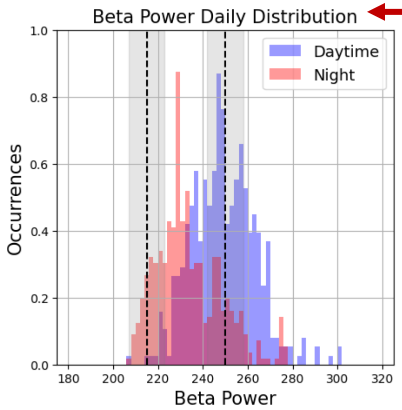

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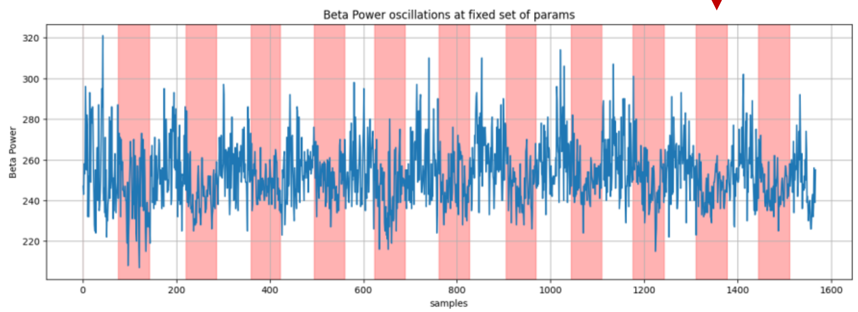

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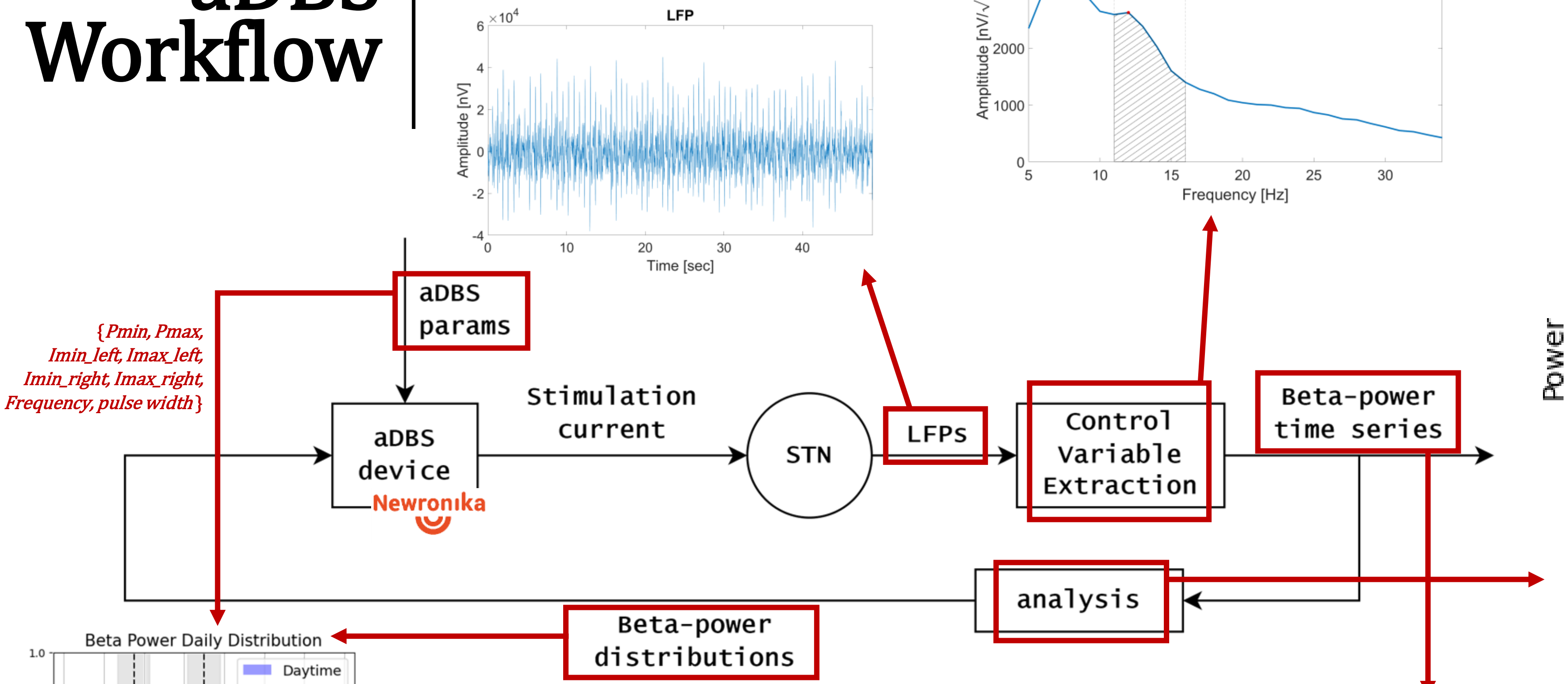

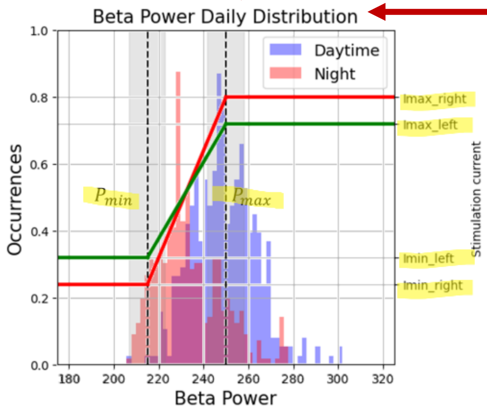

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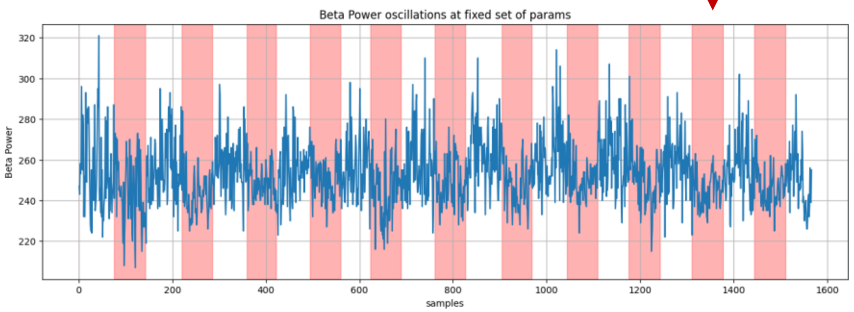
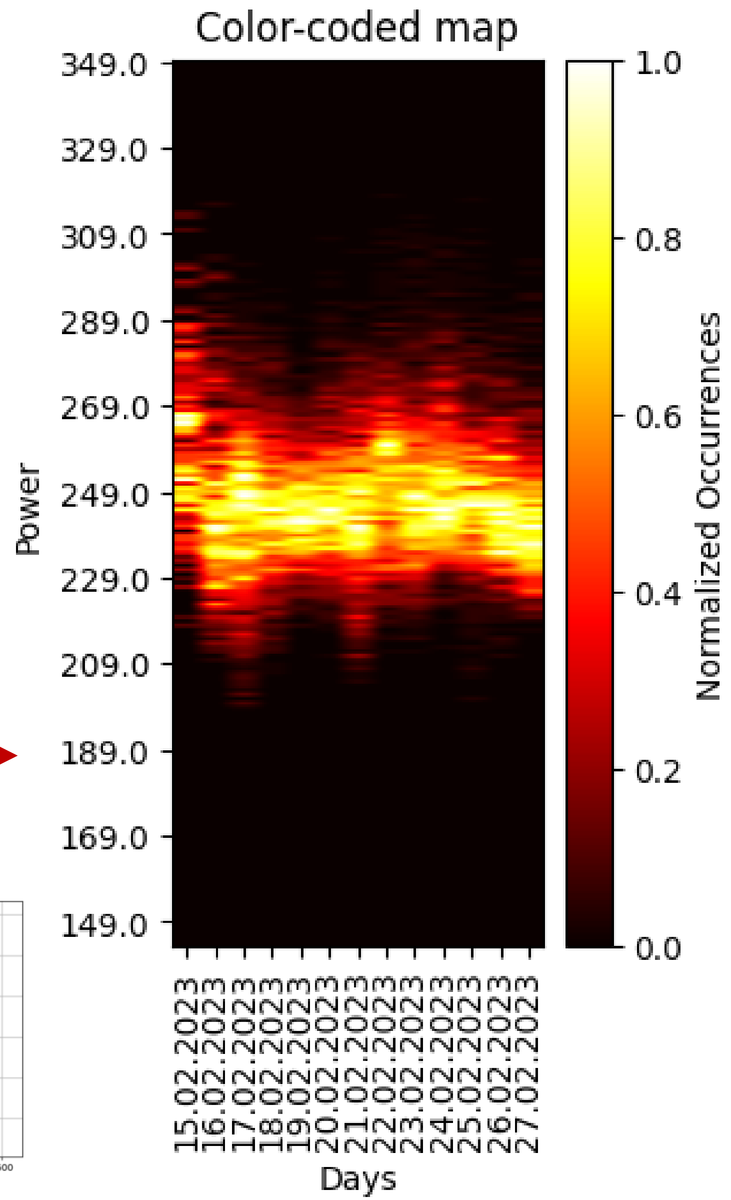
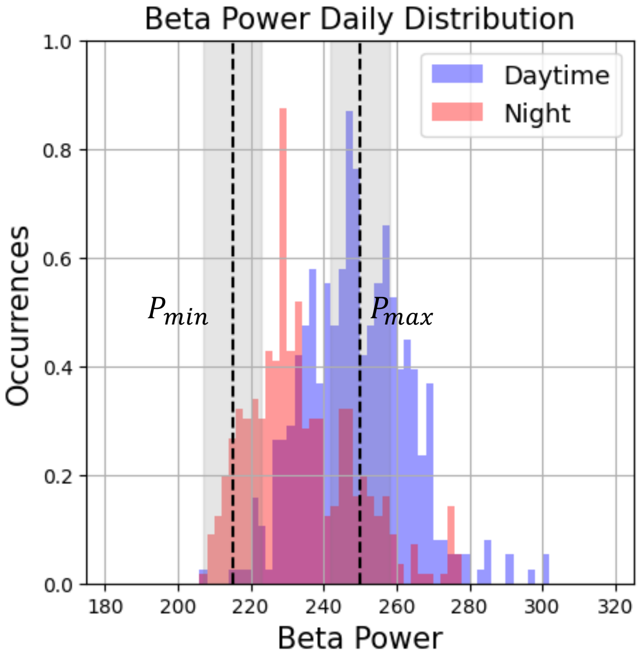




Clinical Problem

STN beta power distributions of a patient may change over time



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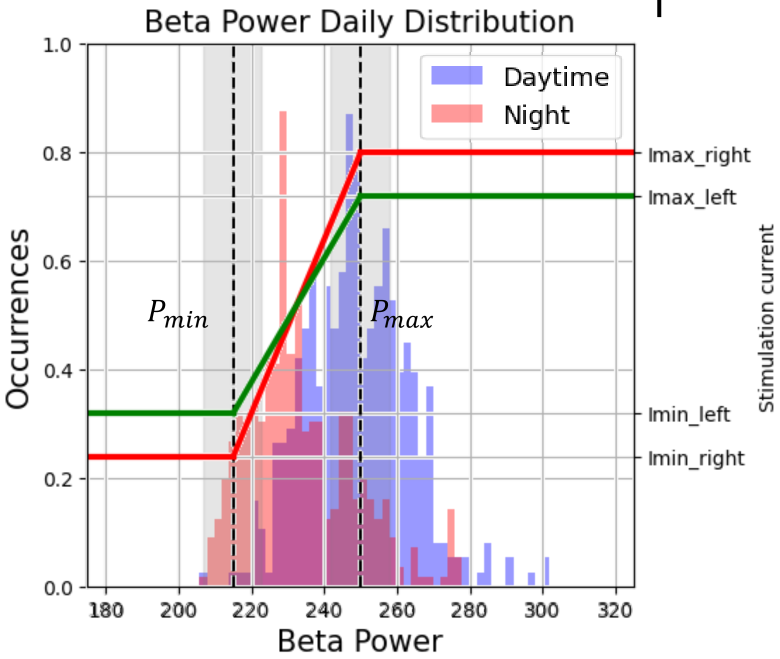

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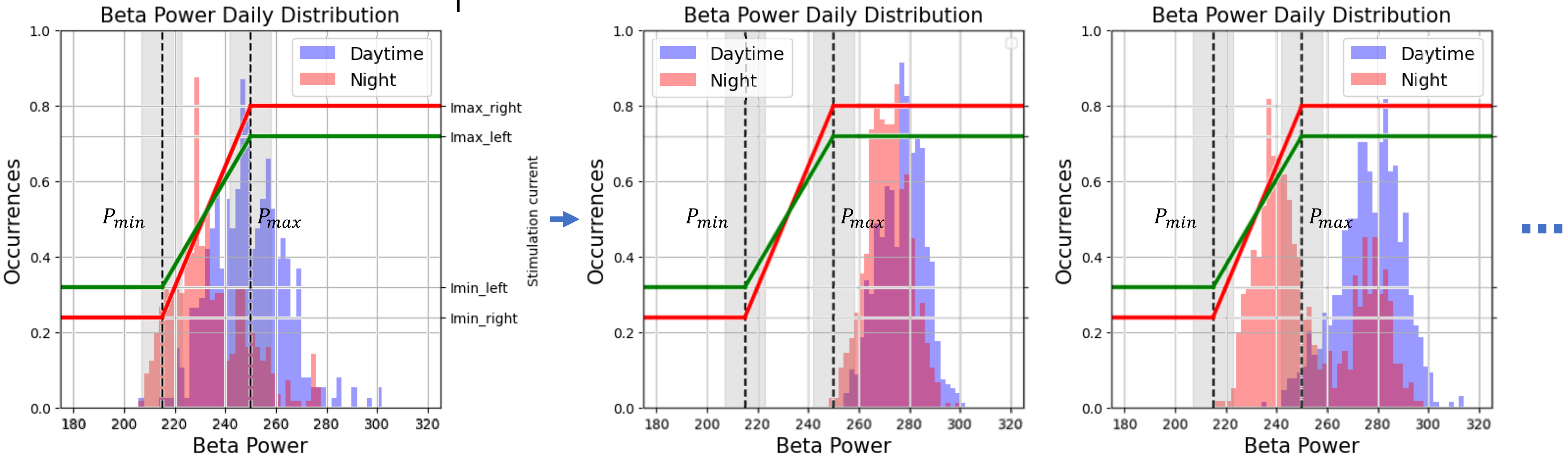
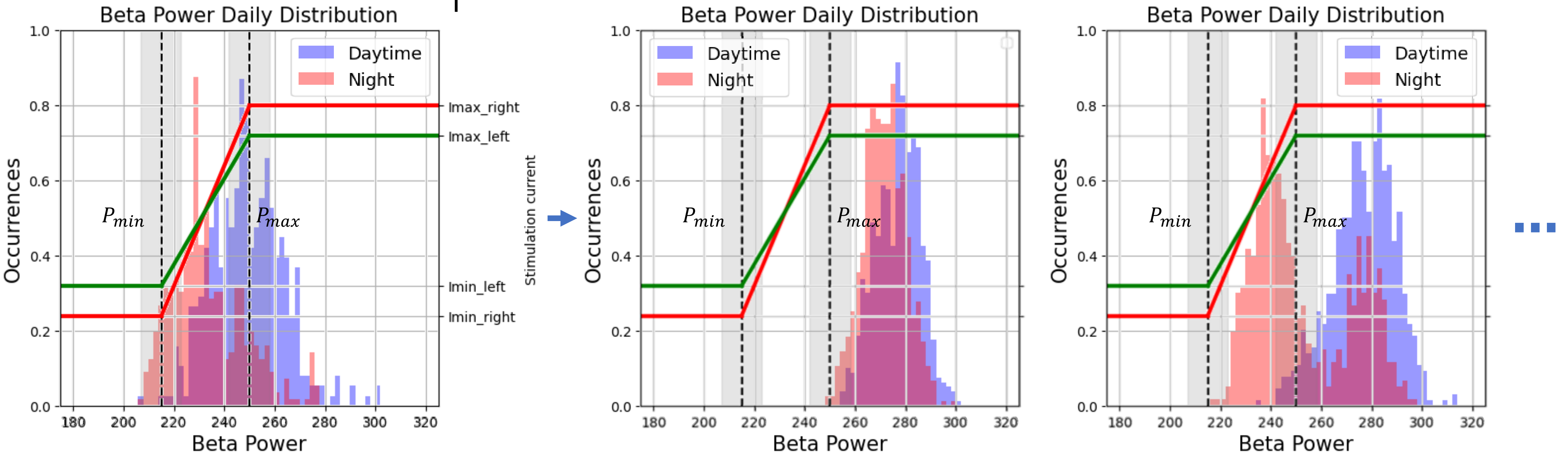


Need to adapt to the evolution of the disease

Clinical Problem

STN beta power distributions of a patient may change over time



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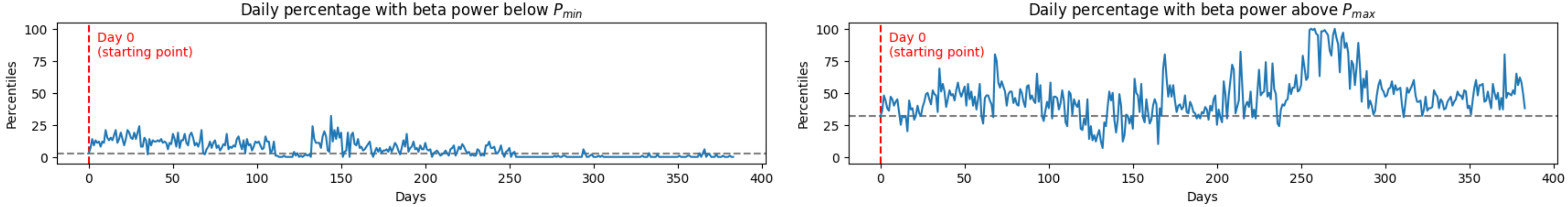
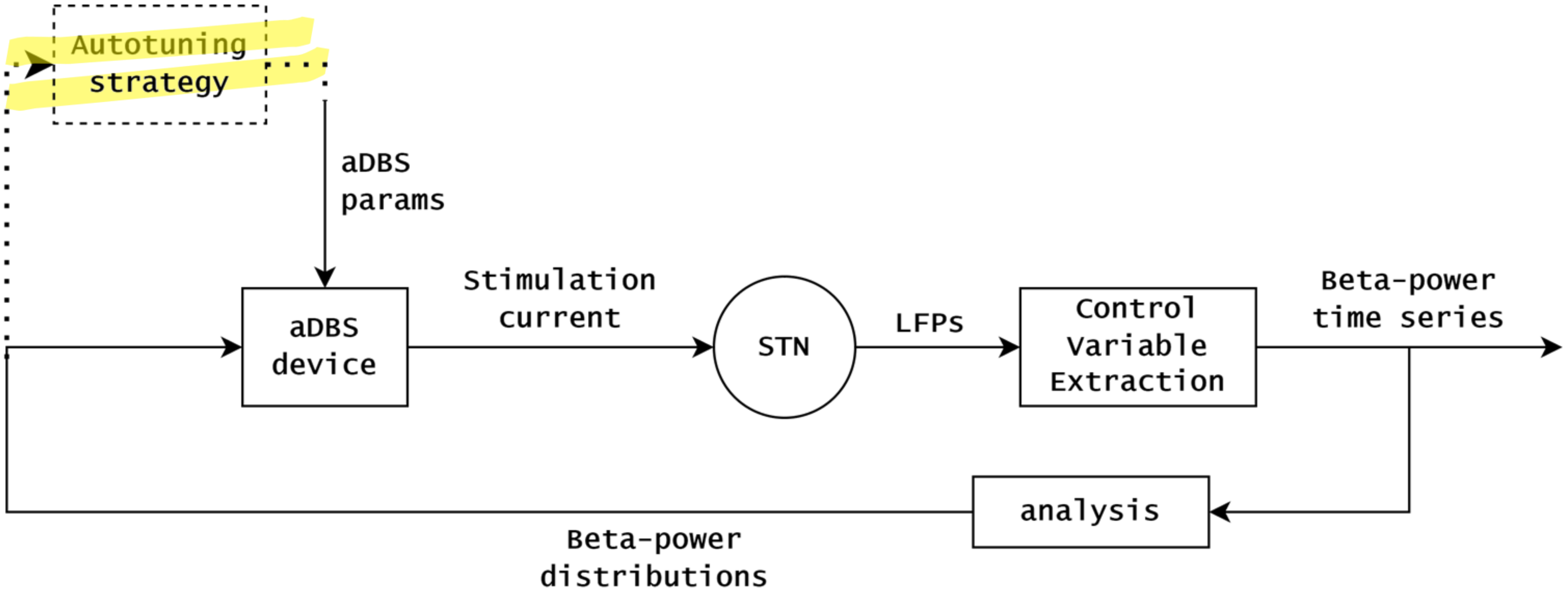


Clinical Question

Is there any way of **predicting when** the beta power distribution will be outside a safe range around the fixed aDBS params $\boldsymbol{P_{min}}$ and $\boldsymbol{P_{max}}$?

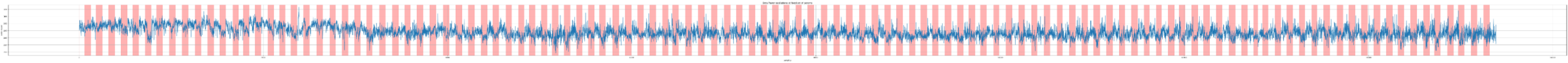


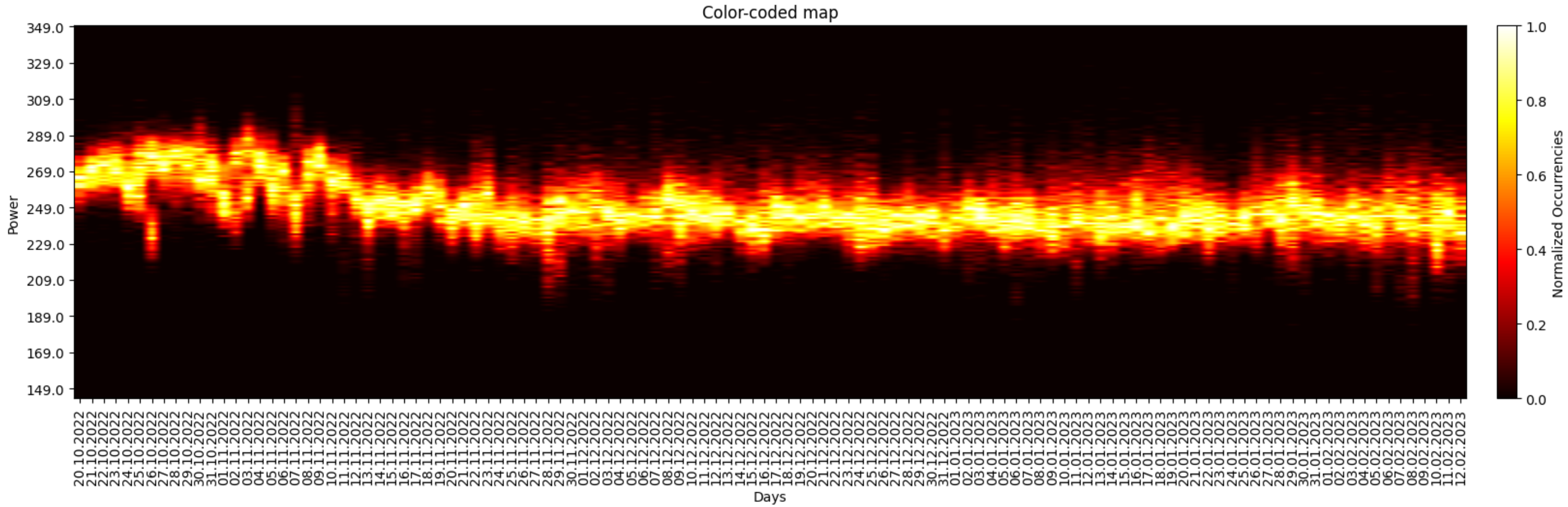
Do we have enough data?

Analysis conducted for one single patient

Patient	Available number of segments	Length of segments (Days)
LS	11	| 30 | 17 | 22 | 9 | 6 | 29 | 24 | 51 | **116** | 13 | 57 |

set of aDBS parameters kept constant for **~ 4 months.**





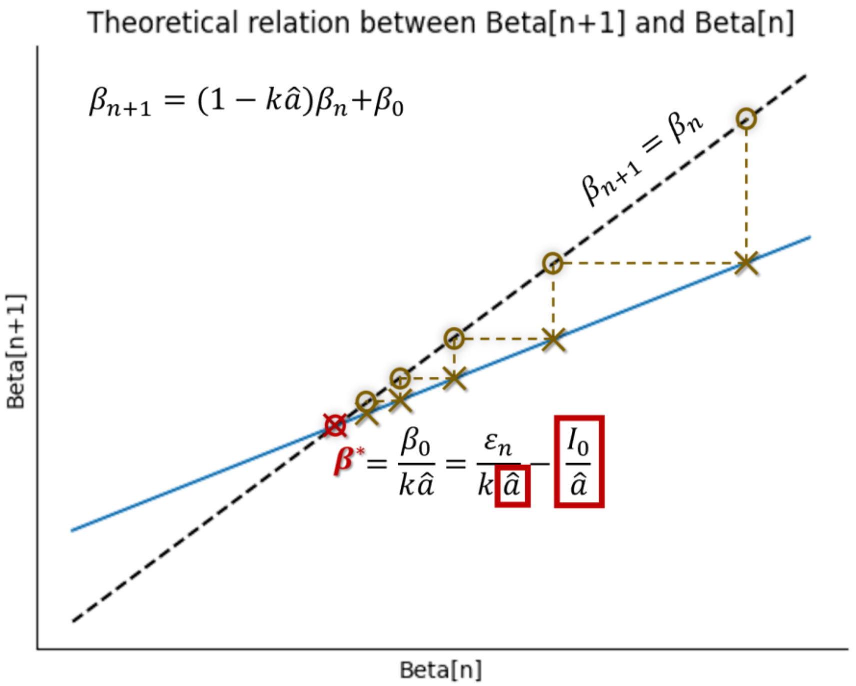
Linear evidence of beta power memory

Analysis conducted for one single patient

Newronika

Beta-Stimulus relation (input) | $I_n = \hat{a}\beta_n + \widehat{I_0}$

Beta-Beta relation (output) | $\beta_{n+1} = \beta_n - \mathrm{k}I_n + \varepsilon_n$



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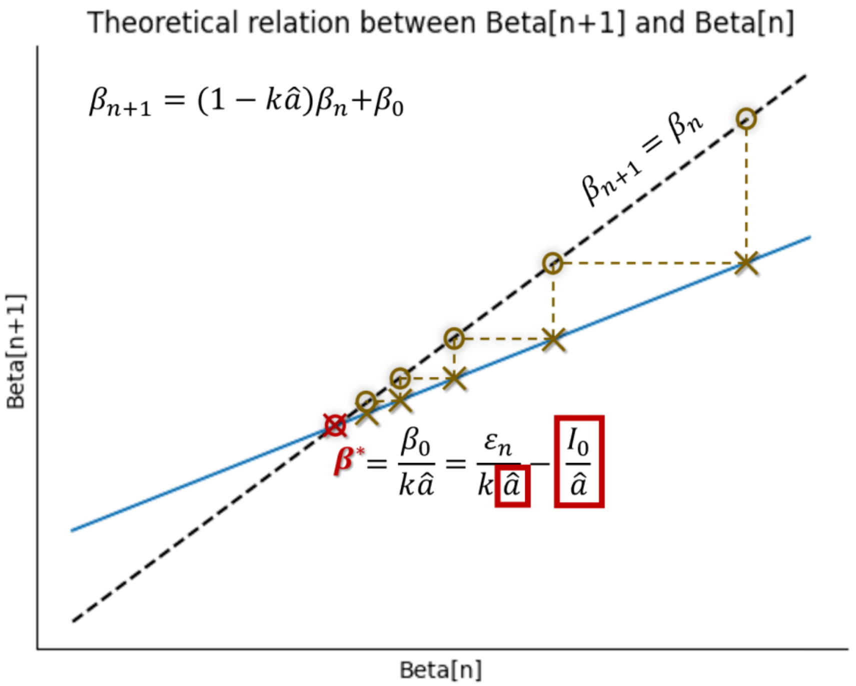

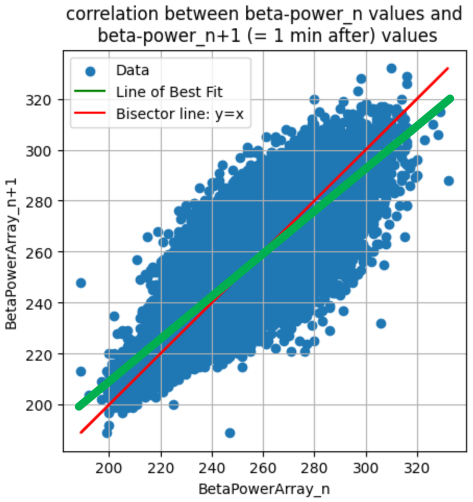

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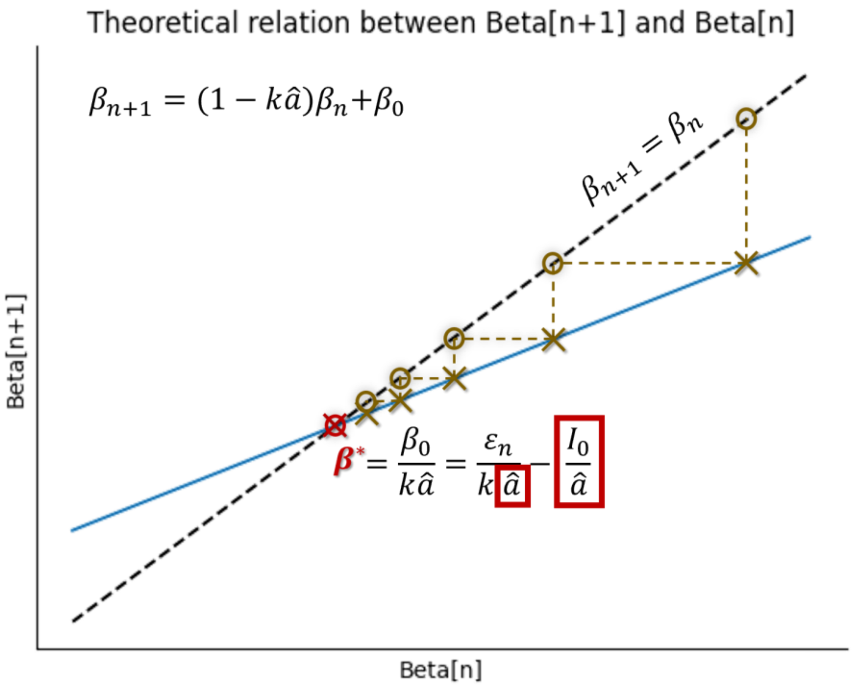

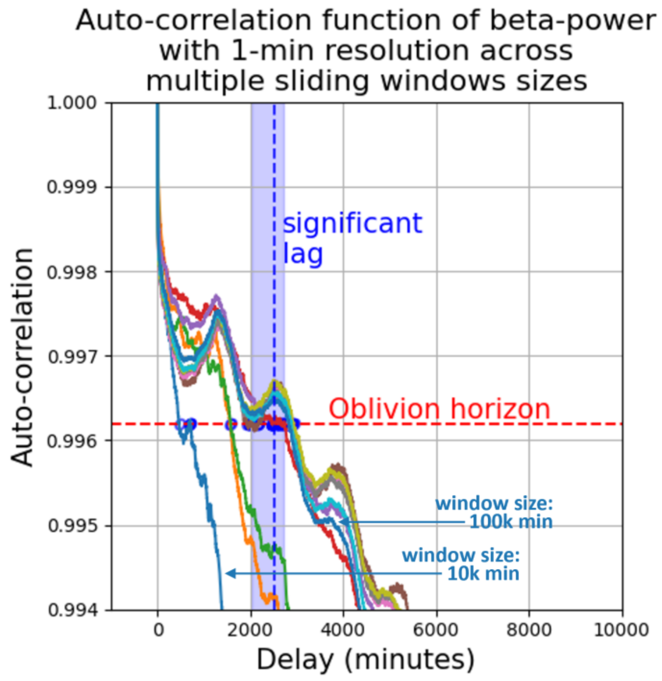

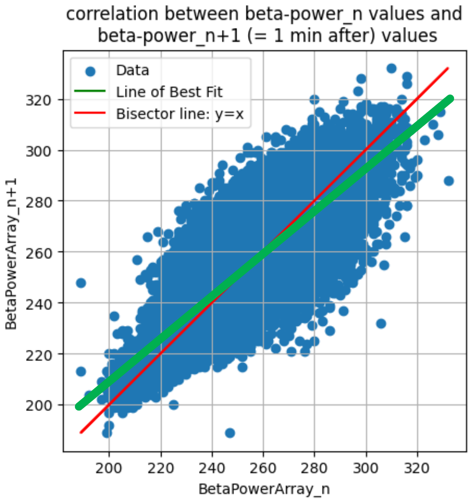

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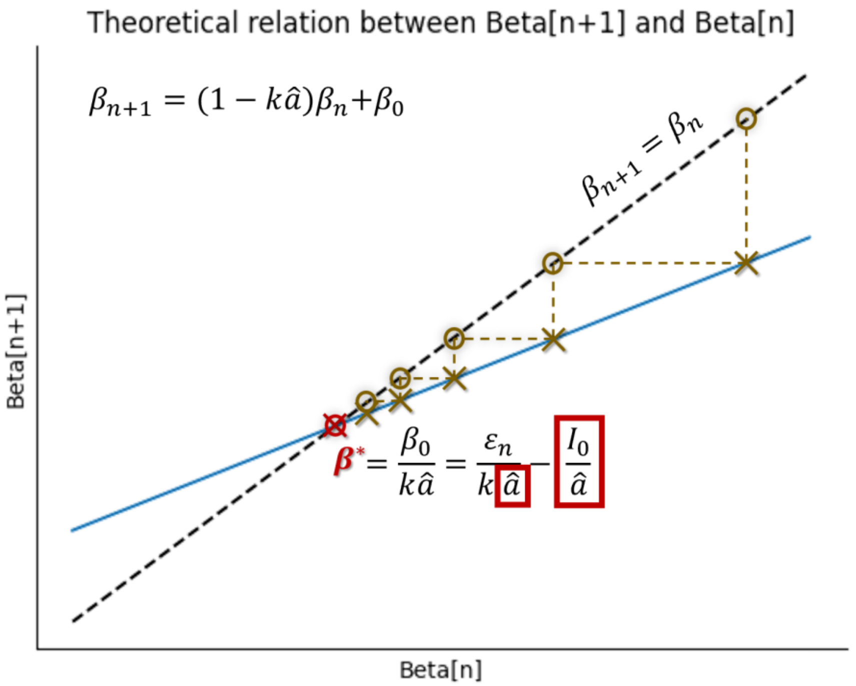
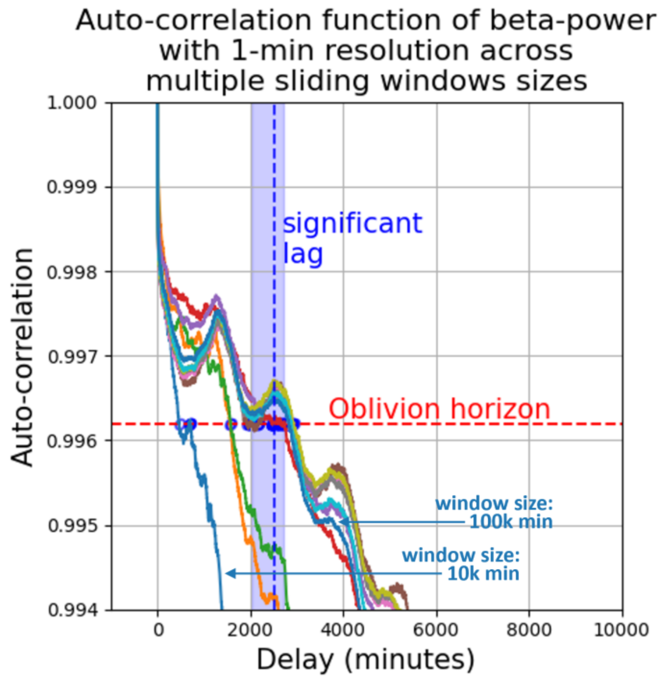
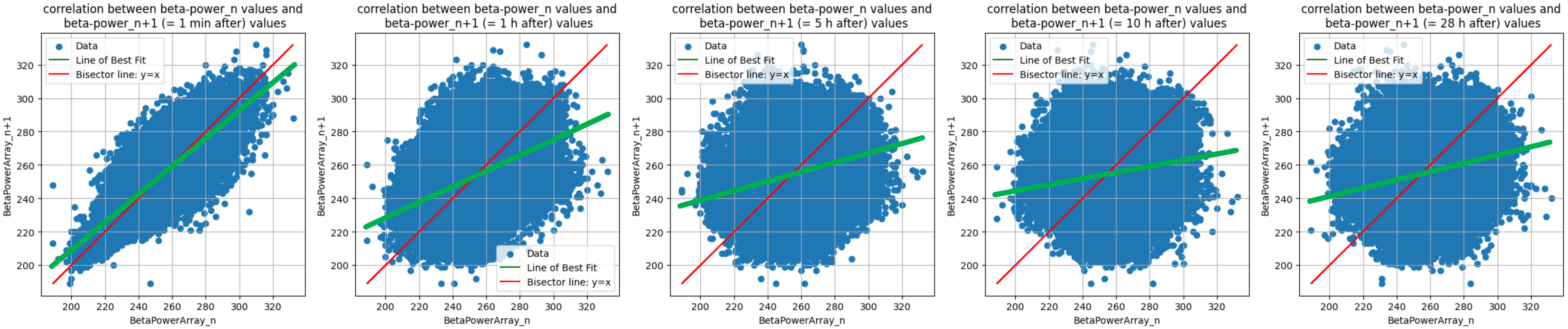
We can see the *Beta power decreasing* effect for *~41 hours (34-45)*

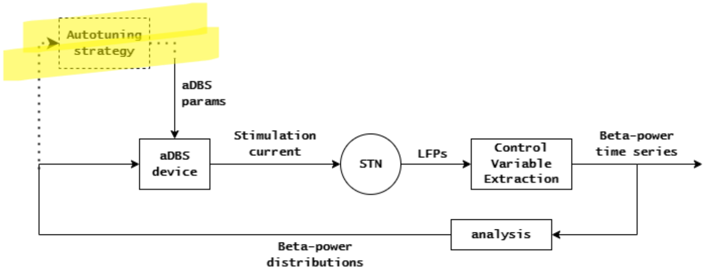


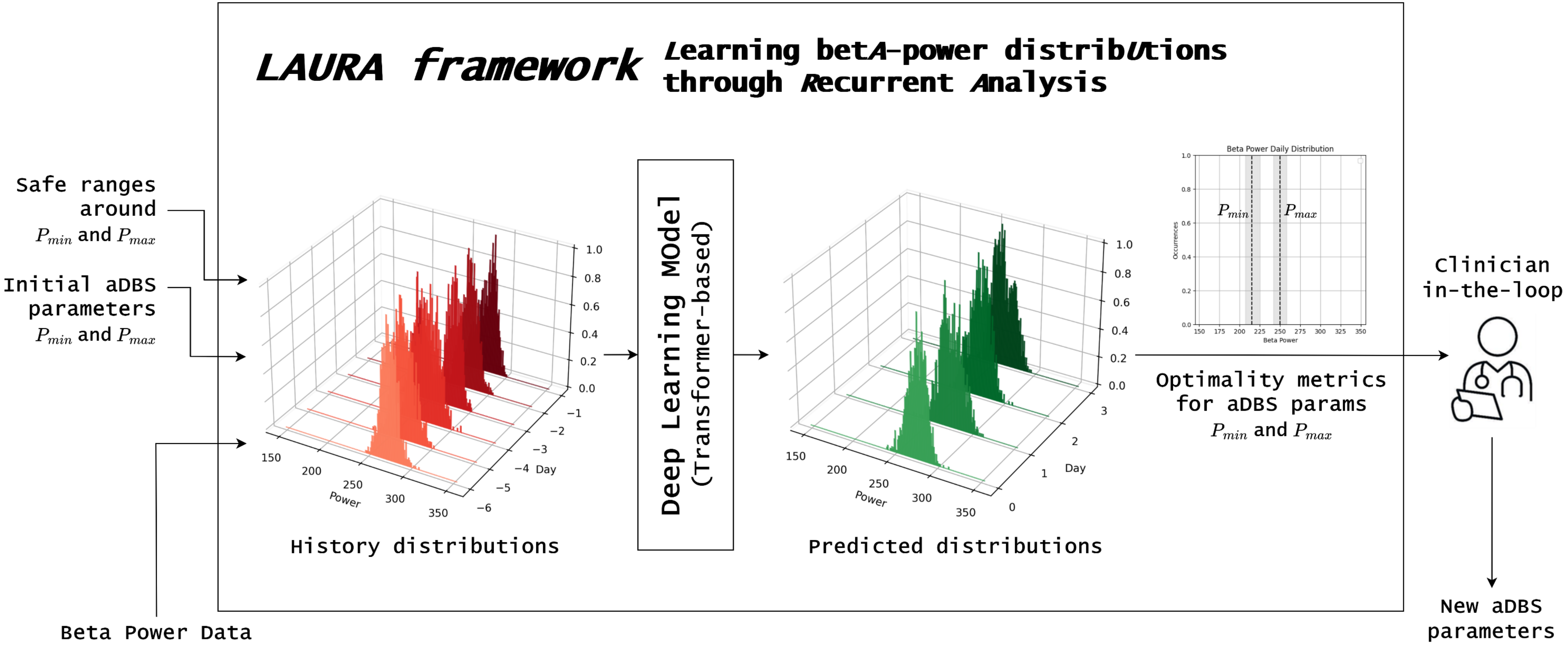




Our answer

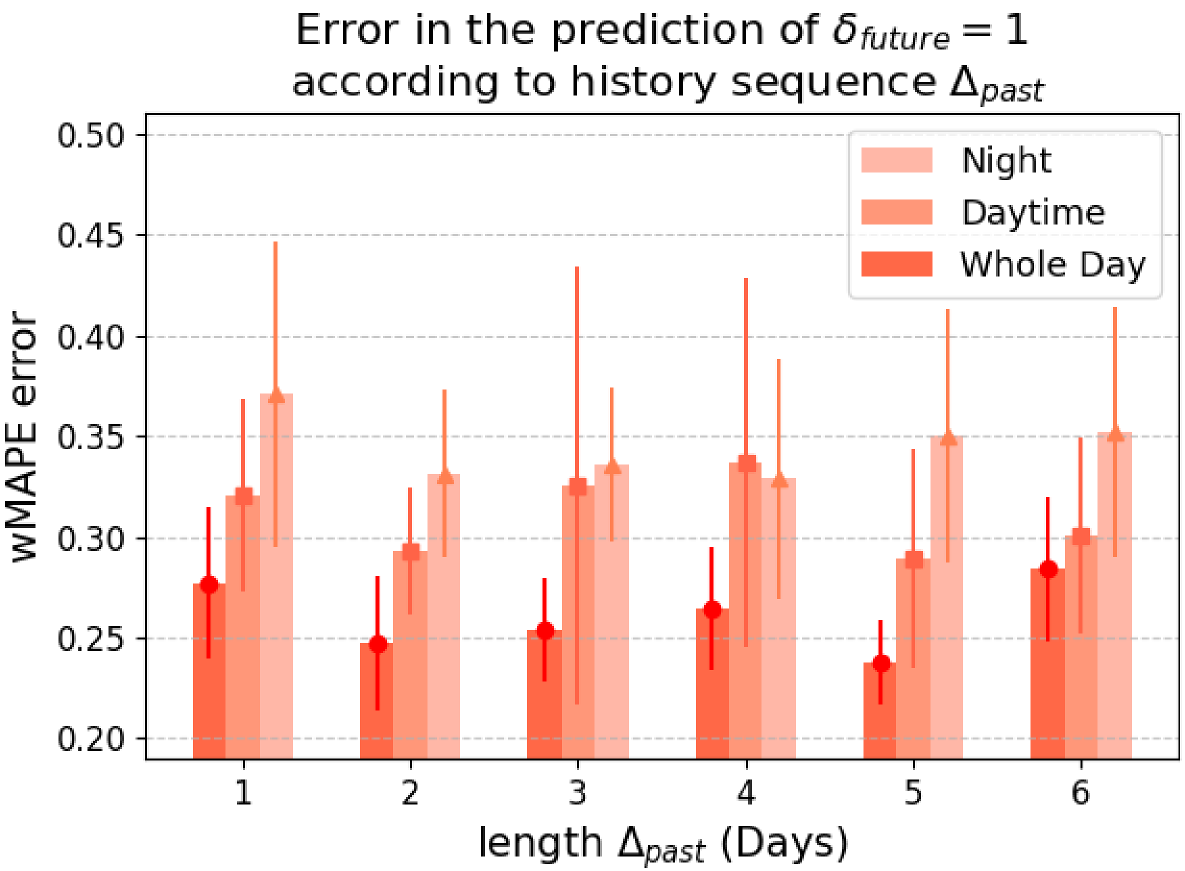
LAURA framework – *towards the Autotuning strategy*

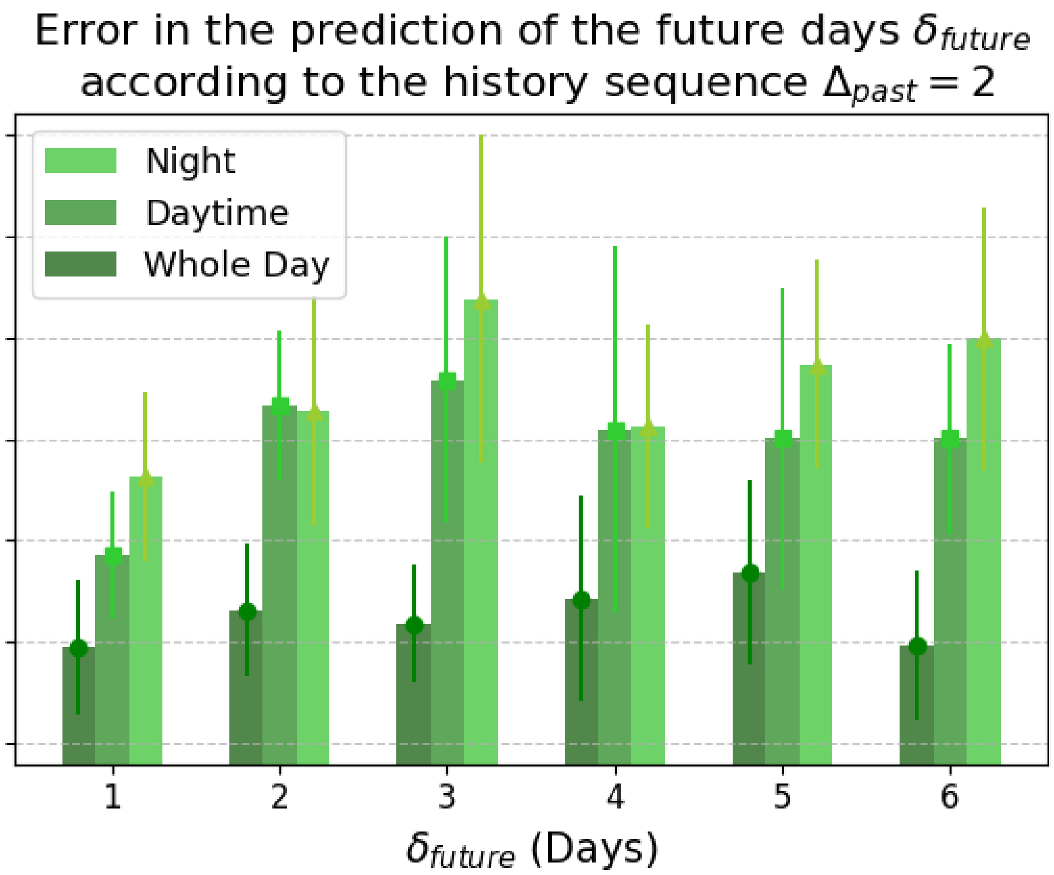




LAURA framework

Performance – *fixed set_of_aDBS_params*

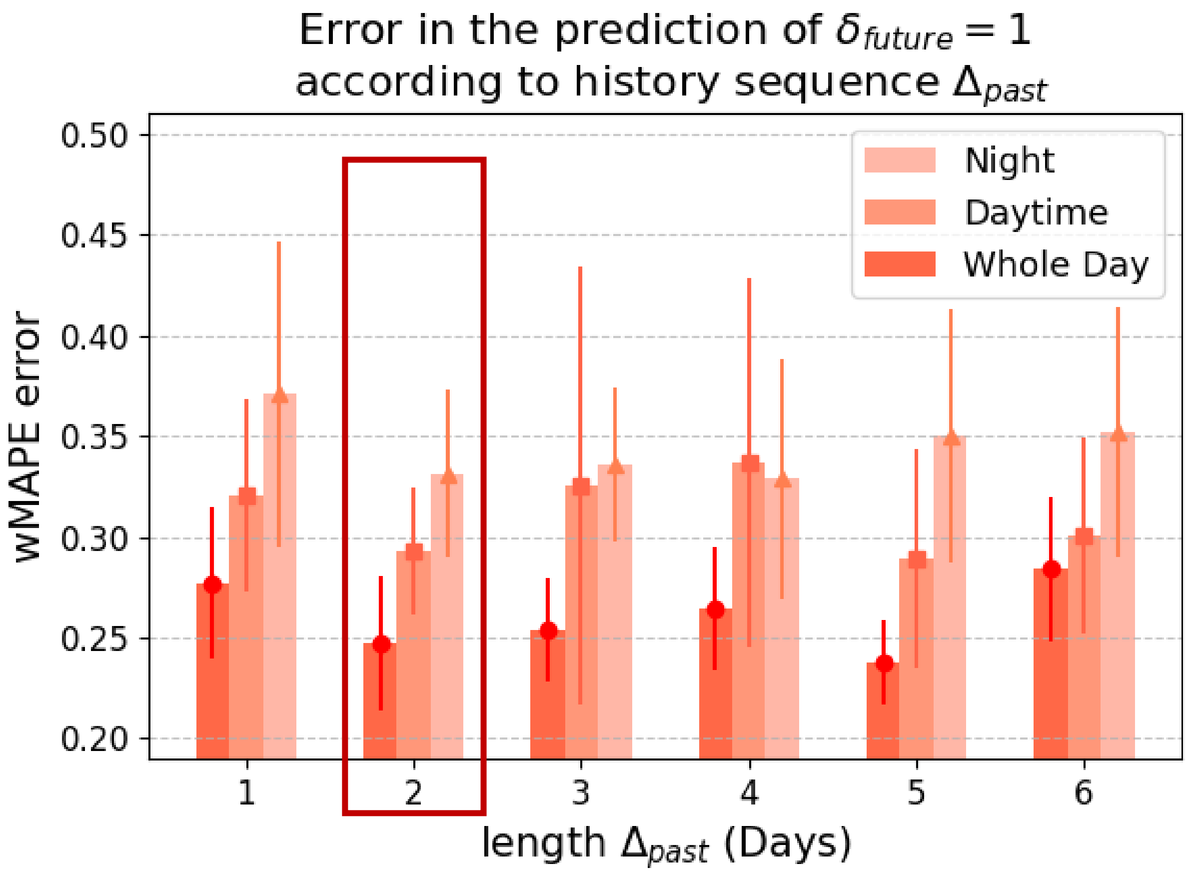


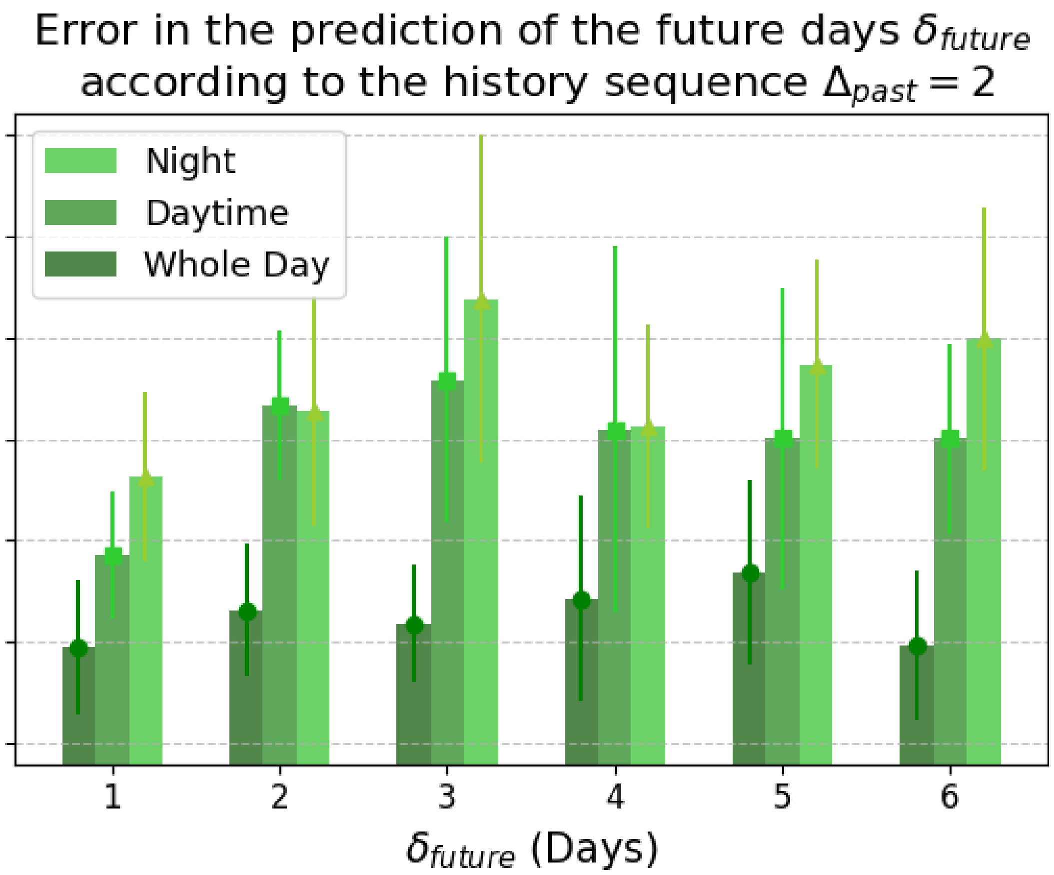


LAURA framework

Performance – *fixed set_of_aDBS_params*

Results reveal that, for this patient,
i) **a 2-day history is sufficient to forecast the next day up to 6 days later**





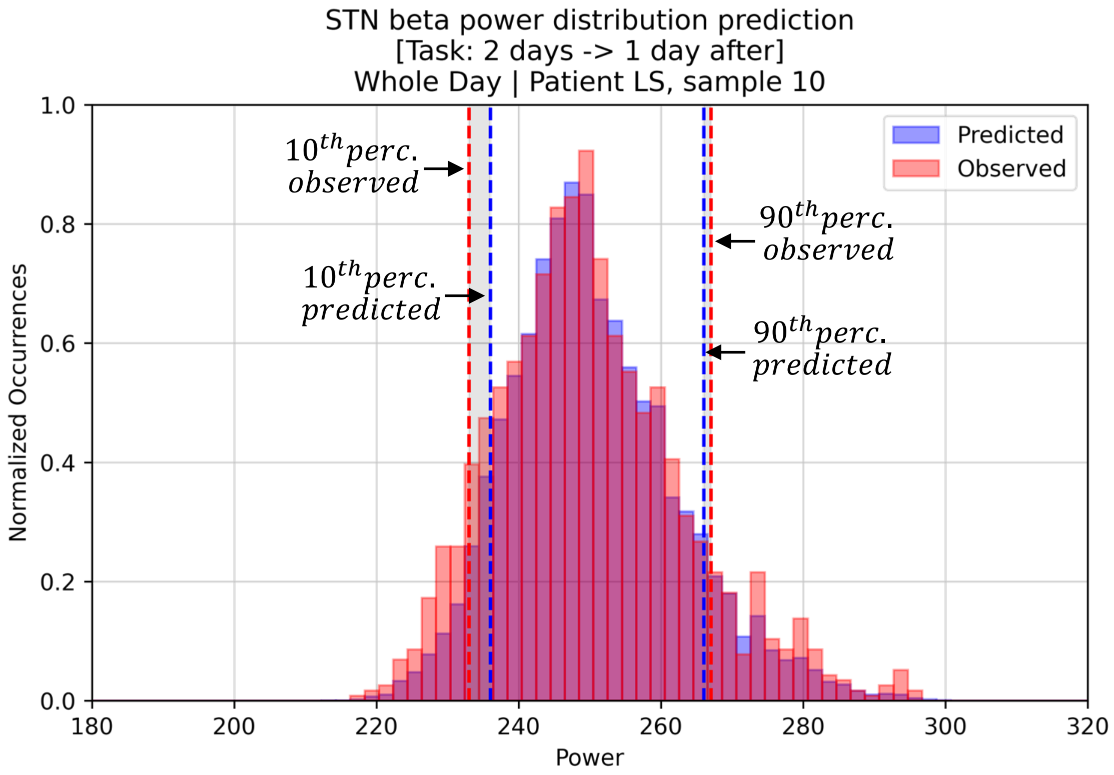
LAURA framework

Performance – *fixed set_of_aDBS_params*

Results reveal that, for this patient,

i) a 2-day history is sufficient to forecast the next day up to 6 days later

ii) The inaccuracy in identifying the 10th and 90th percentiles of the distribution is less than 1%



Error in individuating the 10^{th} and 90^{th} percentiles

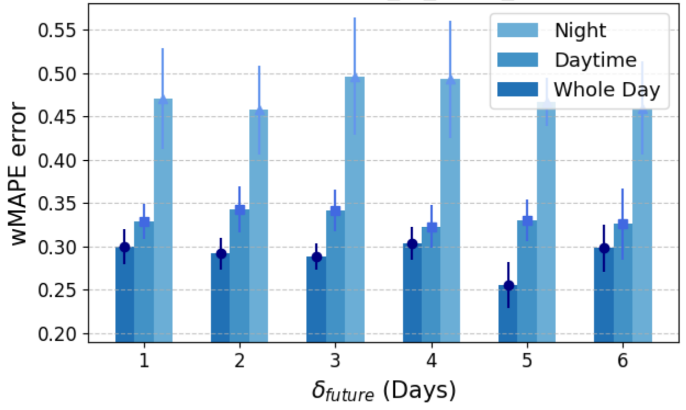
length Δ_{past} (Days) with $\delta_{future} = 1$		1	2	3	4	5	6
90^{th} perc [P_{max}]	Whole Day	± 4.51 bins (± 0.5 %)	± 4.21 bins (± 0.6 %)	± 3.67 bins (± 0.7 %)	± 3.63 bins (± 0.7 %)	± 4.16 bins (± 0.7 %)	± 4.16 bins (± 0.6 %)
	Daytime	± 3.33 bins (± 0.5 %)	± 2.73 bins (± 0.5 %)	± 3.24 bins (± 0.5 %)	± 3.34 bins (± 0.6 %)	± 2.49 bins (± 0.5 %)	± 3.04 bins (± 0.5 %)
	Night	± 3.90 bins (± 0.5 %)	± 3.33 bins (± 0.5 %)	± 3.49 bins (± 0.5 %)	± 2.94 bins (± 0.5 %)	± 2.52 bins (± 0.5 %)	± 3.33 bins (± 0.5 %)
10^{th} perc [P_{min}]	Whole Day	± 3.92 bins (± 0.5 %)	± 2.81 bins (± 0.5 %)	± 33.82 bins (± 0.6 %)	± 2.98 bins (± 0.5 %)	± 3.40 bins (± 0.5 %)	± 3.14 bins (± 0.6 %)
	Daytime	± 3.32 bins (± 0.4 %)	± 3.12 bins (± 0.4 %)	± 3.38 bins (± 0.5 %)	± 3.77 bins (± 0.4 %)	± 3.32 bins (± 0.3 %)	± 3.44 bins (± 0.3 %)
	Night	± 3.10 bins (± 0.3 %)	± 2.27 bins (± 0.4 %)	± 2.75 bins (± 0.4 %)	± 2.99 bins (± 0.3 %)	± 2.57 bins (± 0.4 %)	± 3.17 bins (± 0.2 %)

δ_{future} (Days) with $\Delta_{past} = 2$		1	2	3	4	5	6
90^{th} perc [P_{max}]	Whole Day	± 3.71 bins (± 0.7 %)	± 3.65 bins (± 0.7 %)	± 4.04 bins (± 0.7 %)	± 3.96 bins (± 0.7 %)	± 4.12 bins (± 0.6 %)	± 4.21 bins (± 0.7 %)
	Daytime	± 3.27 bins (± 0.5 %)	± 3.48 bins (± 0.5 %)	± 3.69 bins (± 0.6 %)	± 3.26 bins (± 0.5 %)	± 3.46 bins (± 0.5 %)	± 3.23 bins (± 0.5 %)
	Night	± 3.24 bins (± 0.5 %)	± 3.32 bins (± 0.6 %)	± 2.94 bins (± 0.5 %)	± 2.96 bins (± 0.6 %)	± 3.83 bins (± 0.5 %)	± 3.07 bins (± 0.6 %)
10^{th} perc [P_{min}]	Whole Day	± 3.26 bins (± 0.6 %)	± 3.17 bins (± 0.6 %)	± 3.71 bins (± 0.5 %)	± 2.94 bins (± 0.5 %)	± 3.36 bins (± 0.6 %)	± 3.78 bins (± 0.5 %)
	Daytime	± 3.99 bins (± 0.3 %)	± 4.04 bins (± 0.3 %)	± 3.84 bins (± 0.4 %)	± 3.64 bins (± 0.3 %)	± 3.41 bins (± 0.4 %)	± 3.94 bins (± 0.4 %)
	Night	± 2.64 bins (± 0.3 %)	± 2.77 bins (± 0.3 %)	± 2.85 bins (± 0.3 %)	± 3.09 bins (± 0.3 %)	± 2.68 bins (± 0.3 %)	± 2.52 bins (± 0.3 %)

LAURA framework

Performance – *Multi-period with varying sets_of_aDBS_params*

Error in the prediction of the future days δ_{future} according to the history sequence $\Delta_{past} = 2$ on the left out *set_of_aDBS_params*



Error in individuating the 10^{th} and 90^{th} percentiles

		1	2	3	4	5	6
$90^{th}perc$ [P_{max}]	Whole Day	± 6.09 bins (± 0.3 %)	± 4.99 bins (± 0.3 %)	± 6.89 bins (± 0.3 %)	± 5.56 bins (± 0.3 %)	± 5.18 bins (± 0.2 %)	± 4.76 bins (± 0.2 %)
	Daytime	± 3.55 bins (± 0.2 %)	± 3.45 bins (± 0.3 %)	± 3.63 bins (± 0.2 %)	± 3.39 bins (± 0.2 %)	± 3.33 bins (± 0.2 %)	± 3.32 bins (± 0.2 %)
	Night	± 5.13 bins (± 0.1 %)	± 5.27 bins (± 0.0 %)	± 4.73 bins (± 0.1 %)	± 5.70 bins (± 0.1 %)	± 4.20 bins (± 0.1 %)	± 5.59 bins (± 0.1 %)
$10^{th}perc$ [P_{min}]	Whole Day	± 3.99 bins (± 0.3 %)	± 4.45 bins (± 0.2 %)	± 4.84 bins (± 0.3 %)	± 4.71 bins (± 0.3 %)	± 4.78 bins (± 0.3 %)	± 4.99 bins (± 0.2 %)
	Daytime	± 3.51 bins (± 0.2 %)	± 3.71 bins (± 0.2 %)	± 3.38 bins (± 0.3 %)	± 3.03 bins (± 0.3 %)	± 3.54 bins (± 0.2 %)	± 3.61 bins (± 0.2 %)
	Night	± 3.32 bins (± 0.1 %)	± 3.03 bins (± 0.1 %)	± 3.35 bins (± 0.1 %)	± 2.81 bins (± 0.1 %)	± 2.83 bins (± 0.1 %)	± 3.17 bins (± 0.1 %)

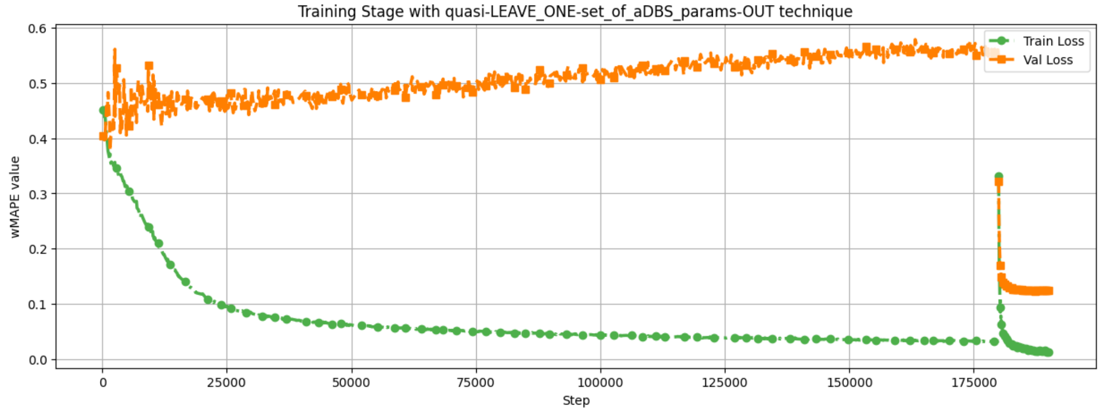
length Δ_{past} (Days) with $\delta_{future} = 1$

Training with quasi-LEAVE-ONE-*set_of_aDBS_params*-OUT

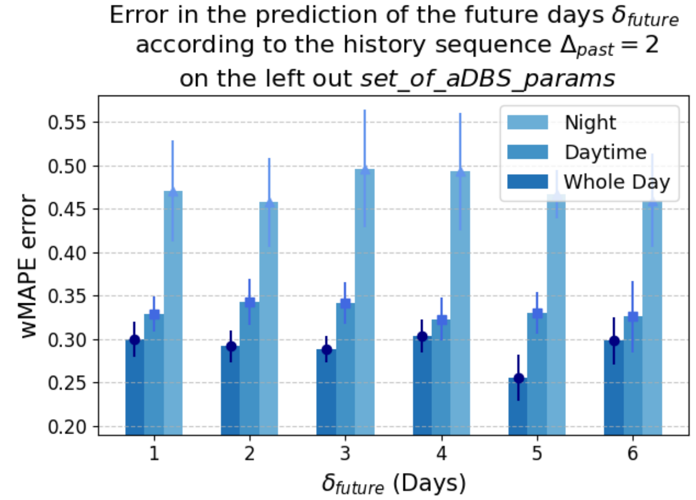
i) Train the model on several *sets_of_aDBS_params*, leaving one *set_of_aDBS_params* out

ii) Fine-tuning on the left out *set_of_aDBS_params*

- Train on the 50% of these data (usually it is 80-85%)
- Test on the other 50% of these data



LAURA framework | Performance – *Multi-period with varying sets_of_aDBS_params*



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	Daytime	± 3.55 bins (± 0.2 %)	± 3.45 bins (± 0.3 %)	± 3.63 bins (± 0.2 %)	± 3.39 bins (± 0.2 %)	± 3.33 bins (± 0.2 %)	± 3.32 bins (± 0.2 %)
	Night	± 5.13 bins (± 0.1 %)	± 5.27 bins (± 0.0 %)	± 4.73 bins (± 0.1 %)	± 5.70 bins (± 0.1 %)	± 4.20 bins (± 0.1 %)	± 5.59 bins (± 0.1 %)
10thperc [P_{min}]	Whole Day	± 3.99 bins (± 0.3 %)	± 4.45 bins (± 0.2 %)	± 4.84 bins (± 0.3 %)	± 4.71 bins (± 0.3 %)	± 4.78 bins (± 0.3 %)	± 4.99 bins (± 0.2 %)
	Daytime	± 3.51 bins (± 0.2 %)	± 3.71 bins (± 0.2 %)	± 3.38 bins (± 0.3 %)	± 3.03 bins (± 0.3 %)	± 3.54 bins (± 0.2 %)	± 3.61 bins (± 0.2 %)
	Night	± 3.32 bins (± 0.1 %)	± 3.03 bins (± 0.1 %)	± 3.35 bins (± 0.1 %)	± 2.81 bins (± 0.1 %)	± 2.83 bins (± 0.1 %)	± 3.17 bins (± 0.1 %)

length Δ_{past} (Days) with $\delta_{future} = 1$

Results reveal that, for this patient,

i) **The wMAPE between the observed and predicted distributions is comparable to that obtained with fixed aDBS params**

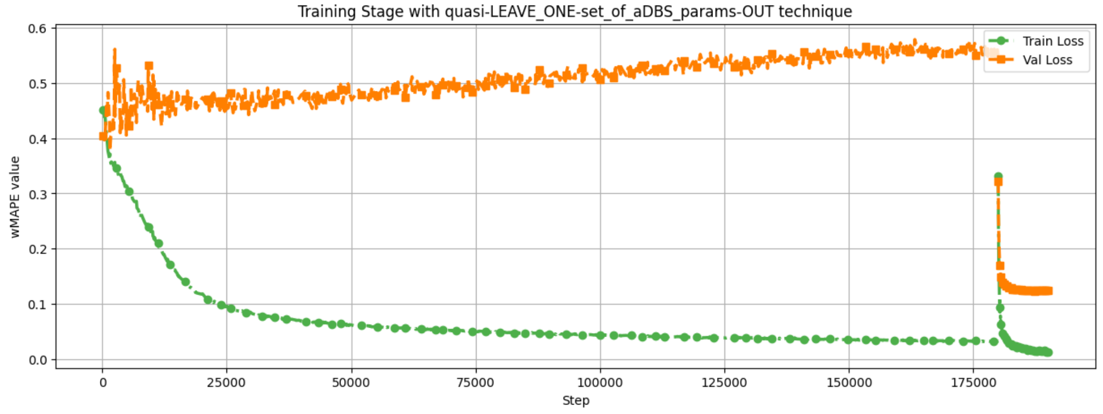
ii) **Inaccuracies in identifying the 10th and 90th percentiles of the distribution remain below 1%**

Training with quasi-LEAVE-ONE-*set_of_aDBS_params*-OUT

i) Train the model on several *sets_of_aDBS_params*, leaving one *set_of_aDBS_params* out

ii) Fine-tuning on the left out *set_of_aDBS_params*

- Train on the 50% of these data (usually it is 80-85%)
- Test on the other 50% of these data



Advancing personalized aDBS with LAURA: predicting the dynamic nature of beta-power distributions

S. Falciglia [1,4], L. Caffi[1,2,3,4], C. Palmisano[2,3], I.U. Isaias[2,3*] and A. Mazzoni[1,4*]

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[4] Department of Excellence in Robotics and AI, Scuola Superiore Sant'Anna, Pisa, Italy

Novelty in the scientific community

Personalized system designed to:
i) **predict the beta-power distributions of a patient** within a *fixed set of aDBS params*
ii) **extract the fluctuations characteristics of a patient**

*Integration of the **LAURA framework** with **clinician-mediated aDBS therapy** appears feasible, thereby enhancing its efficacy as a **long-term treatment strategy for PD**.*

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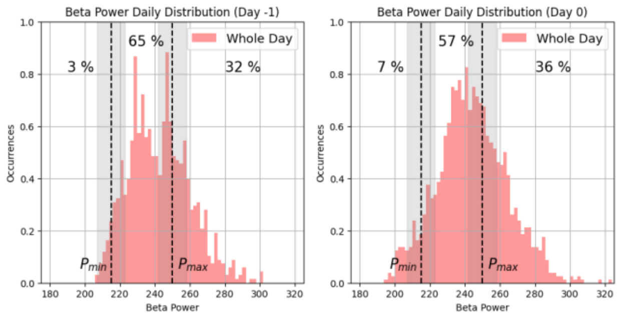
2-day history



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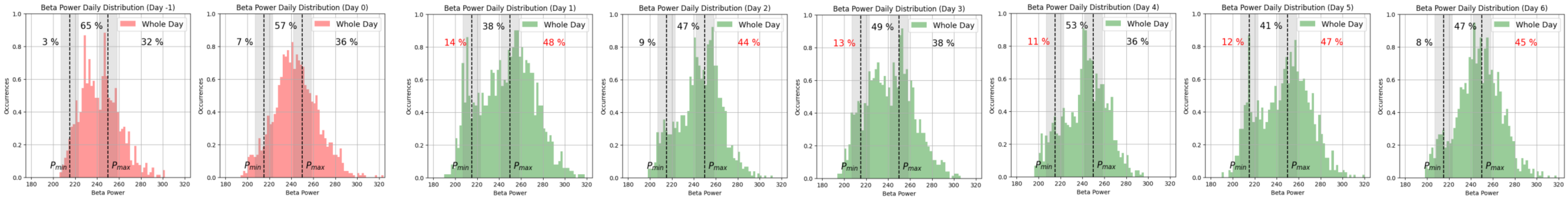
2-day history → **LAURA framework** → 6 days prediction



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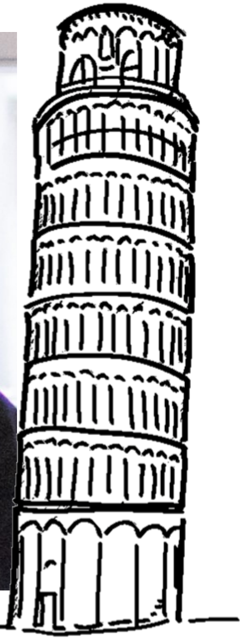
Our Research Team



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