Neuromimetic model of saccades for localizing deficits in an atypical eye-movement pathology

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Introduction

Eye movements of a **patient with unexplained neurological pathology** have been recorded. This patient exhibited **unusual ocular-motor disorders**:

1. **left-right asymmetrical increased saccadic peak velocities** (up to ∼1000 deg/s),
2. **dynamic saccadic overshoot**,
3. **left-right asymmetrical post-saccadic drift**,
4. **saccadic oscillations**.

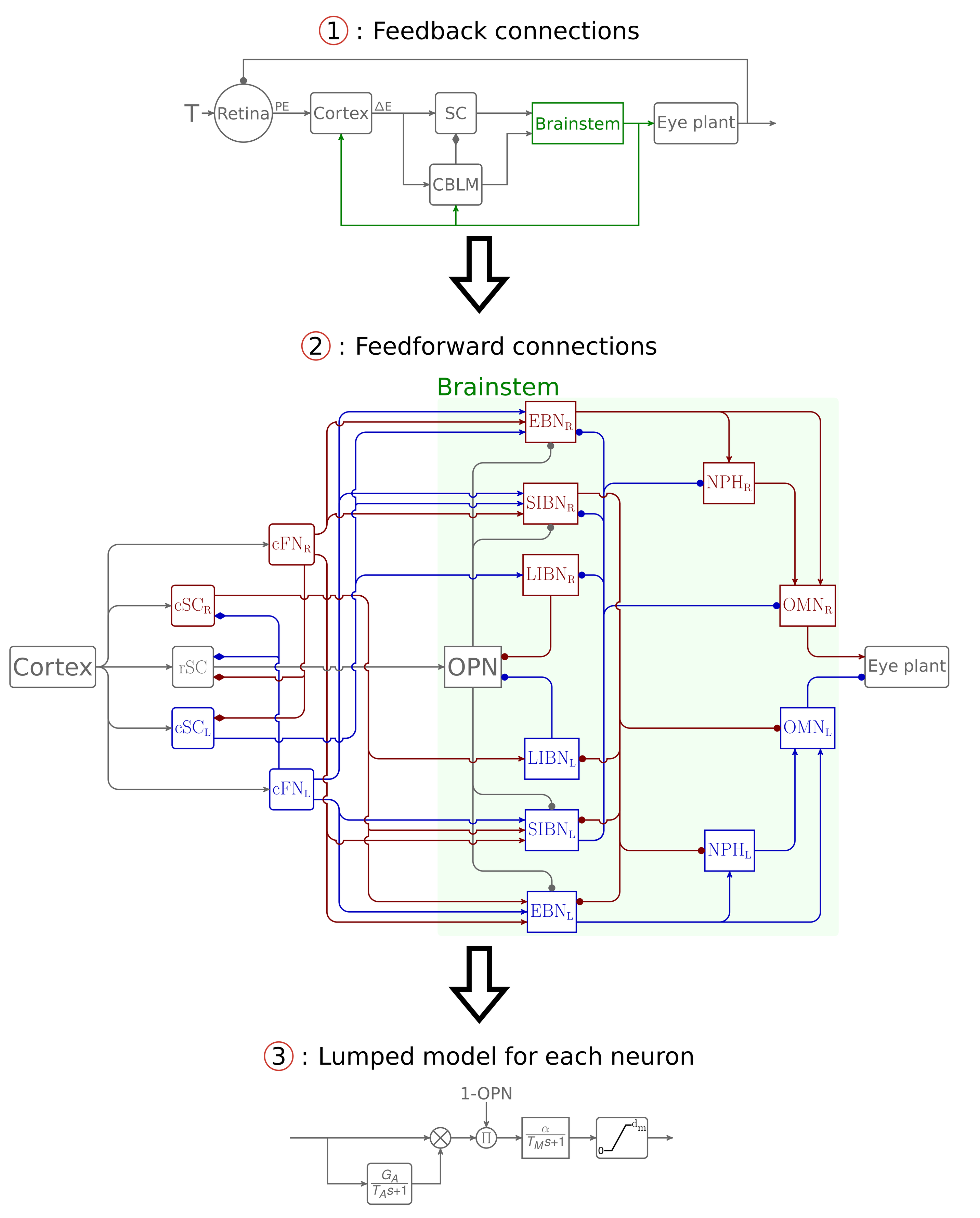
This study analyzes the patient's behavior in terms of a **neuromimetic model** to build a **pathophysiological hypothesis**.

Conclusion

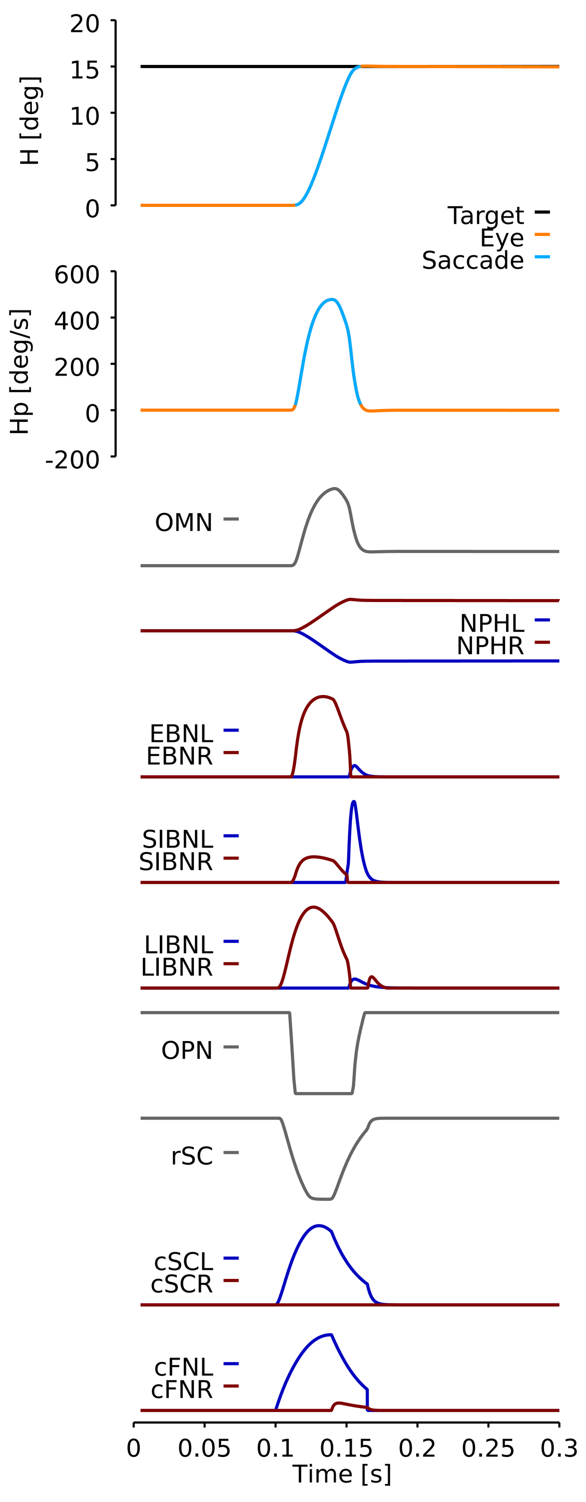
A lumped neuromimetic model of brainstem eye movement circuitry enabled us to propose that all of this **patient's diverse deficits** could be localized to a single structure, the **cerebellum**. Future work should be aimed at extending such models to include other functions in other parts of the brain, while maintaining the simplicity of interpretation given by the lumped circuitry. Such models would have further specificity and increase their utility in clinical diagnosis.

Model description

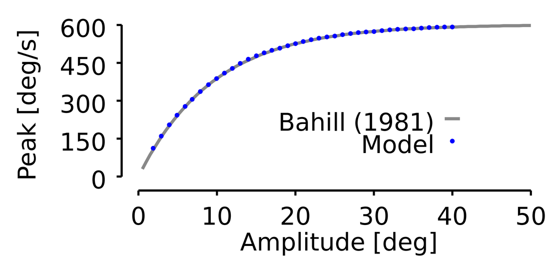
Model structure reflecting anatomical connections



Time course of neural activity



Main sequence



Model properties

Neural areas:

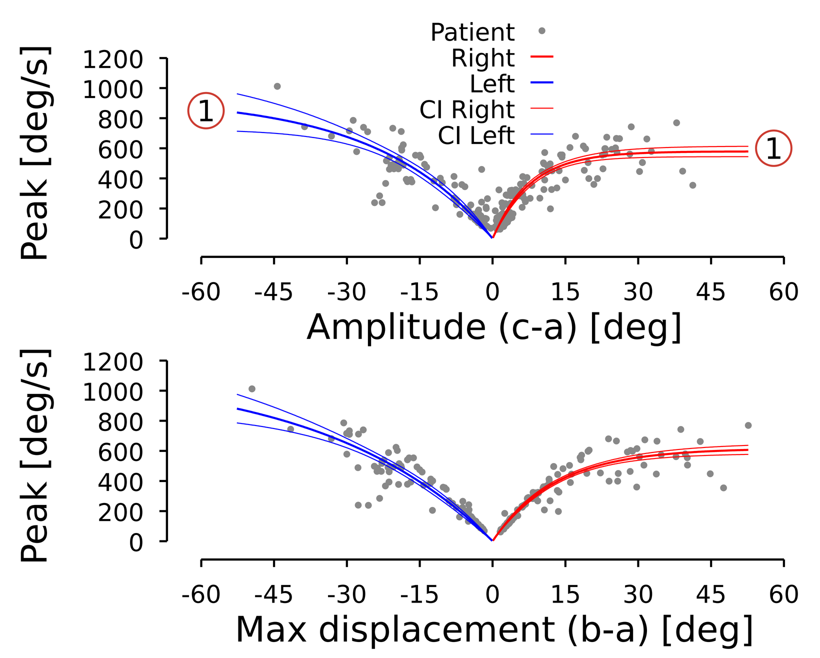
- **Retina:** Visual error
- **Cortex:** Trigger mechanism
- **SC:** Superior colliculus
- **CBLM:** Cerebellum
- **rSC:** Rostral superior colliculus (∼fixation zone)
- **$cSC_{R/L}$:** Caudal superior colliculus (burst+build-up)
- **$cFN_{R/L}$:** Caudal fastigial nucleus
- **$EBN_{R/L}$:** Excitatory burst neurons
- **$SIBN_{R/L}$:** Short lead inhibitory burst neurons
- **$LIBN_{R/L}$:** Long lead inhibitory burst neurons
- **OPN:** Omnipause neurons
- **$NPH_{R/L}$:** Nucleus prepositus hypoglossi
- **$OMN_{R/L}$:** Oculomotor motor neurons

Neurons population model

Model comprises three stages: ① Neuronal adaptation (gain: G_A, time constant: T_A). ② OPN modulation. ③ Membrane: saturated first order transfer function (gain: α, time constant: T_M, boundaries: $[0 \dots d_m]$).

Patient behavior

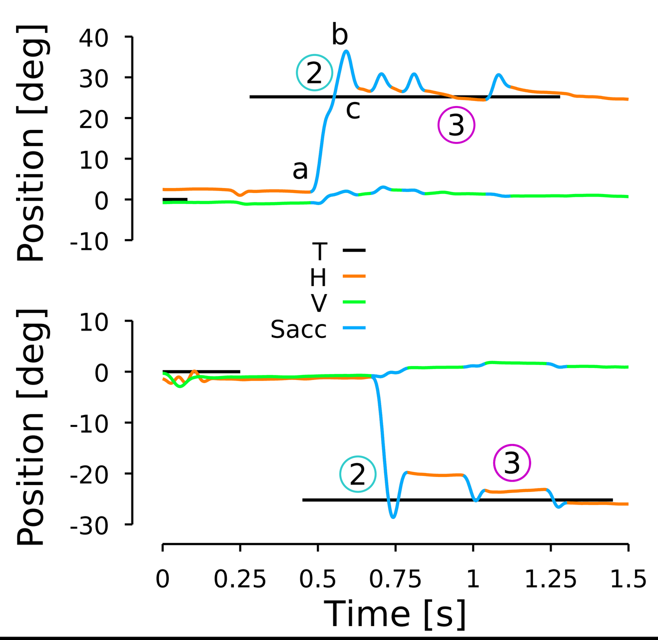
Average behavior



① **Main sequence fits**

$$V_{R,Max} = (579 \pm 35)\left(1 - e^{-(0.13\pm0.02)A_R}\right) \quad \text{MSE}=5643$$
$$V_{L,Max} = (938 \pm 237)\left(1 - e^{-(0.04\pm0.02)A_L}\right) \quad \text{MSE}=11562$$
$$V_{R,Max} = (617 \pm 35)\left(1 - e^{-(0.08\pm0.01)M_R}\right) \quad \text{MSE}=3517$$
$$V_{L,Max} = (1133 \pm 303)\left(1 - e^{-(0.03\pm0.01)M_L}\right) \quad \text{MSE}=7400$$

Typical horizontal saccades



② **Amplitude=f(Max displacement)**

$$A_R = (0.790 \pm 0.013)M_R - (0.698 \pm 0.2129)$$
$$R^2 = 0.96, \quad p < 0.001$$
$$A_L = (0.928 \pm 0.018)M_L - (0.528 \pm 0.086)$$
$$R^2 = 0.98, \quad p < 0.001.$$

③ **Drift: time constant and amplitude**

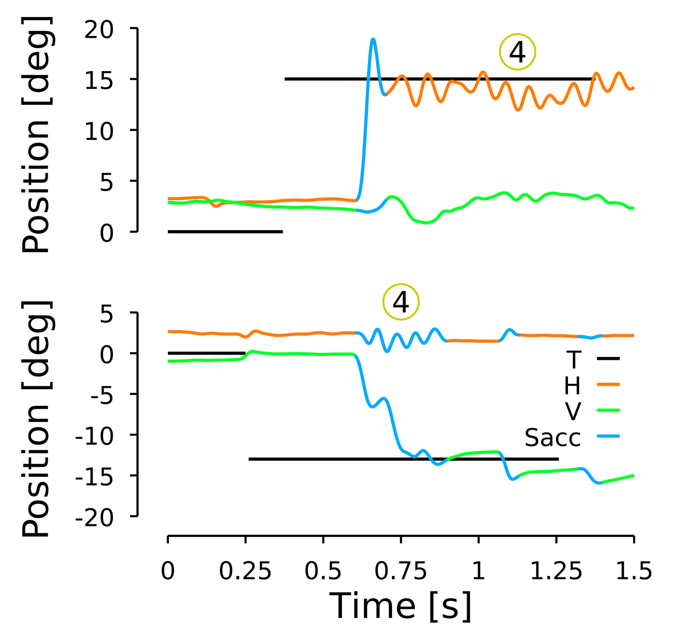
$$\tau_{D,R} = (90 \pm 75) \text{ [ms]}$$
$$A_{D,R} = (3.4 \pm 1.9) \text{ [deg]}$$
$$\tau_{L,R} = (142 \pm 171) \text{ [ms]}$$
$$A_{L,R} = (-0.5 \pm 0.9) \text{ [deg]}$$

④ **Oscillations freqency**

$$f_{H,H} = (14.5 \pm 3.4) \text{ [Hz]}$$
$$f_{H,V} = (13.1 \pm 3.1) \text{ [Hz]}$$

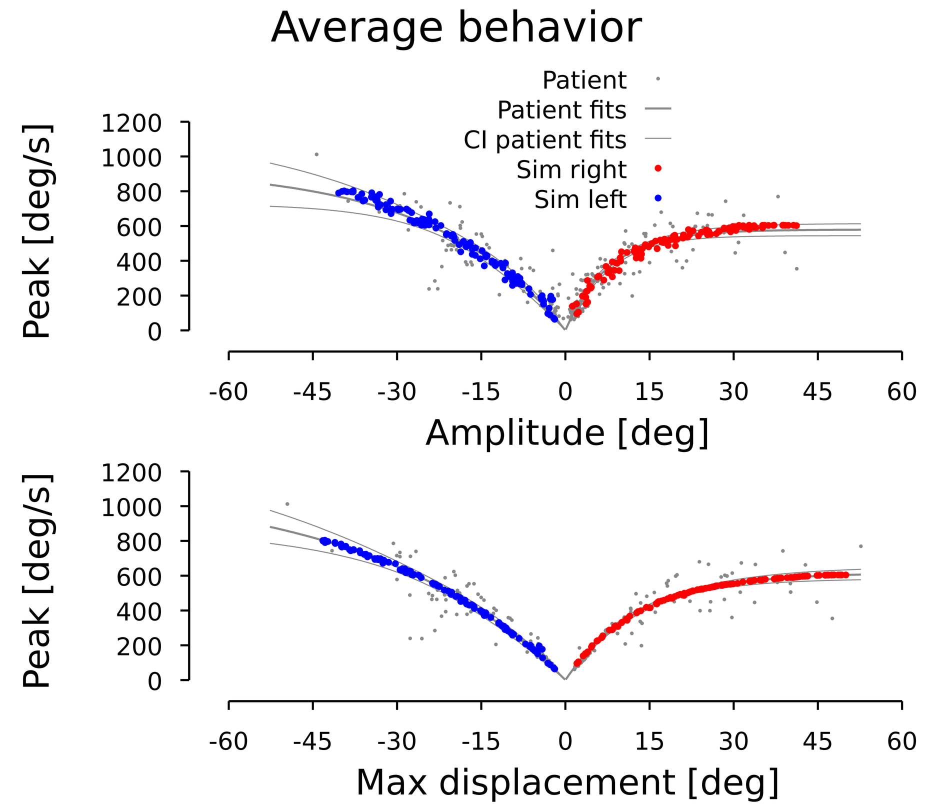
No oscillation vertical channel

Saccadic oscillations



Model simulations

Average behavior



Model modifications

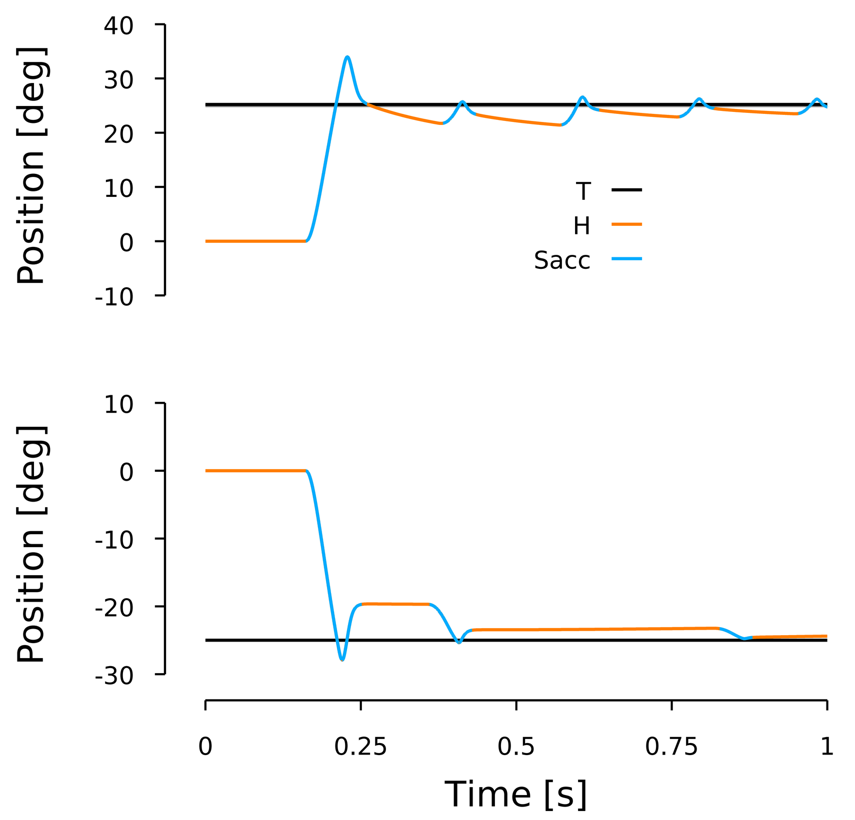
Increase in peak velocity: Increase activity contralateral cFN and cSC

Asymmetrical drift: Increase the time constant on both sides (20→22.5 [s]) + Increase the step gain right side (0.15→0.185)

Dynamic overshoot: Increase activity ipsilateral cFN + Trigger ipsilateral FN sooner

Noise: 25% gaussian noise added to ipsilateral cFN

Extreme conditions

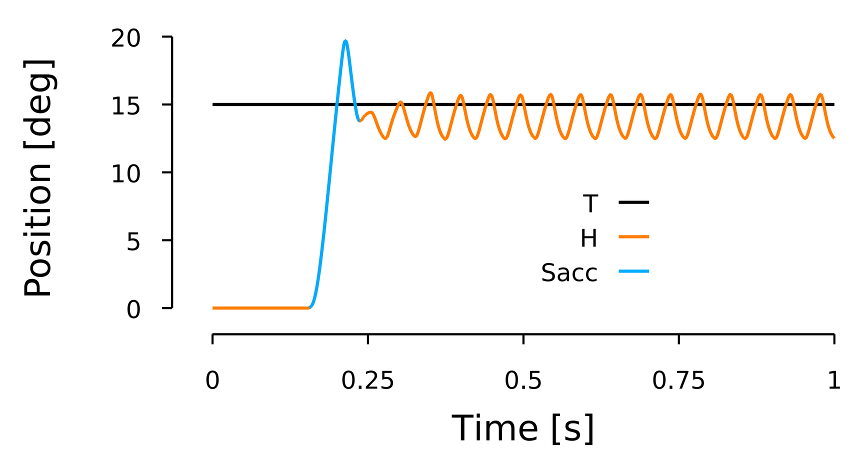


Extreme conditions: The model must reproduce extreme conditions and show its limitations

Observations:

- Large overshoot compared to the average behavior
- Marked left-right asymmetrical drift
- "Visual overshoot" (see patient example) → Calibration problem vs neural deficit?

Saccadic oscillations



OPN input gain decreased → The loop $SIBN_L - SIBN_R$ can oscillate similarly to Ramat et al. (2005).

long sustained oscillations: Harder to maintain long oscillations. To stop the oscillations, reactivate the OPN input.

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