



Accounting for Sleep Inertia in the Differential Equation Framework of a Biomathematical Model of Fatigue

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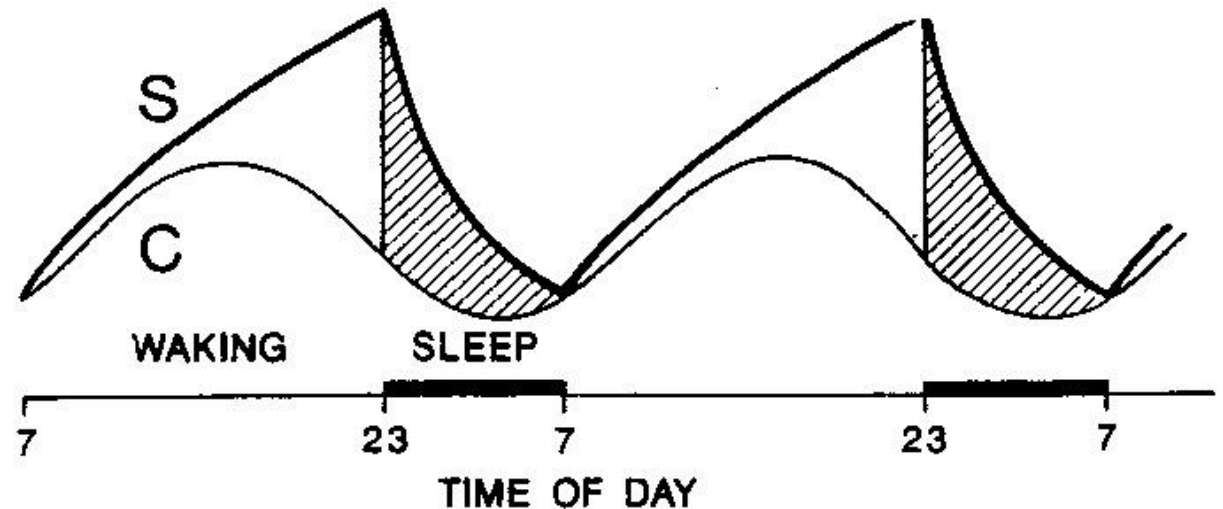
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Two-Process Model of Sleep

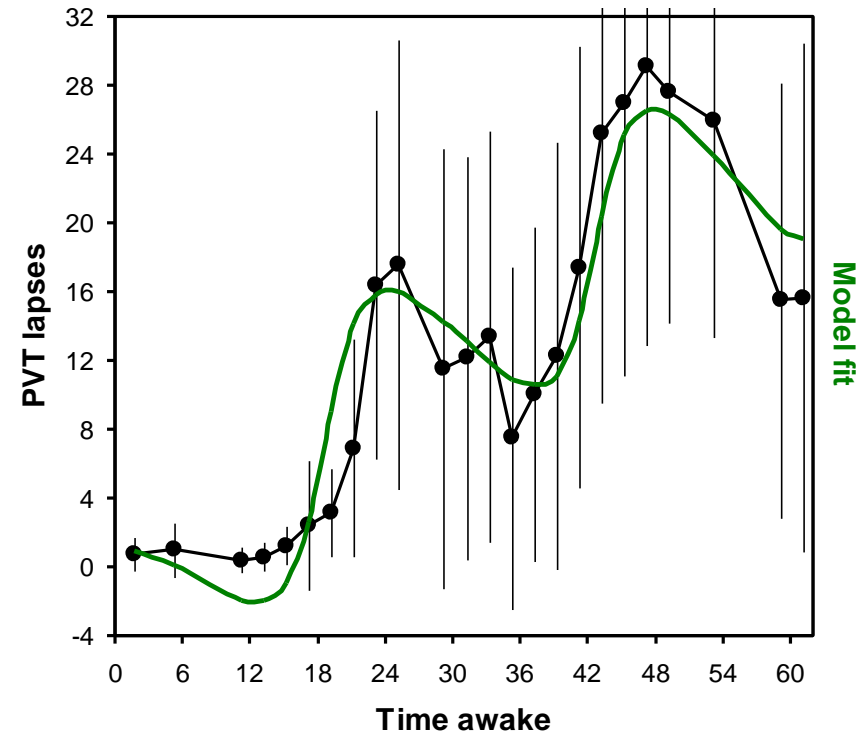
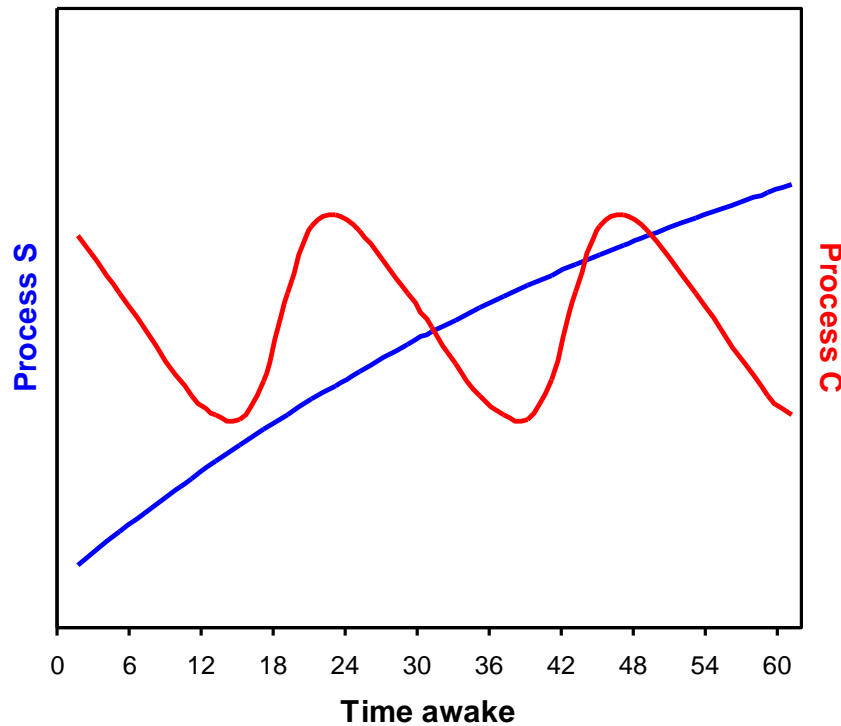
- Sleep and wakefulness governed by *biological* mechanisms
- Two-process model of sleep regulation:
 - *Homeostatic process*: builds up pressure for sleep during wakefulness and dissipates pressure during sleep
 - *Circadian process*: modulates sleep pressure as a function of time of day



Borbély AA (1982). A two process model of sleep regulation. Hum Neurobiol 1: 195-204.



Two Basic Processes for Modeling Performance: Homeostatic Process and Circadian Process

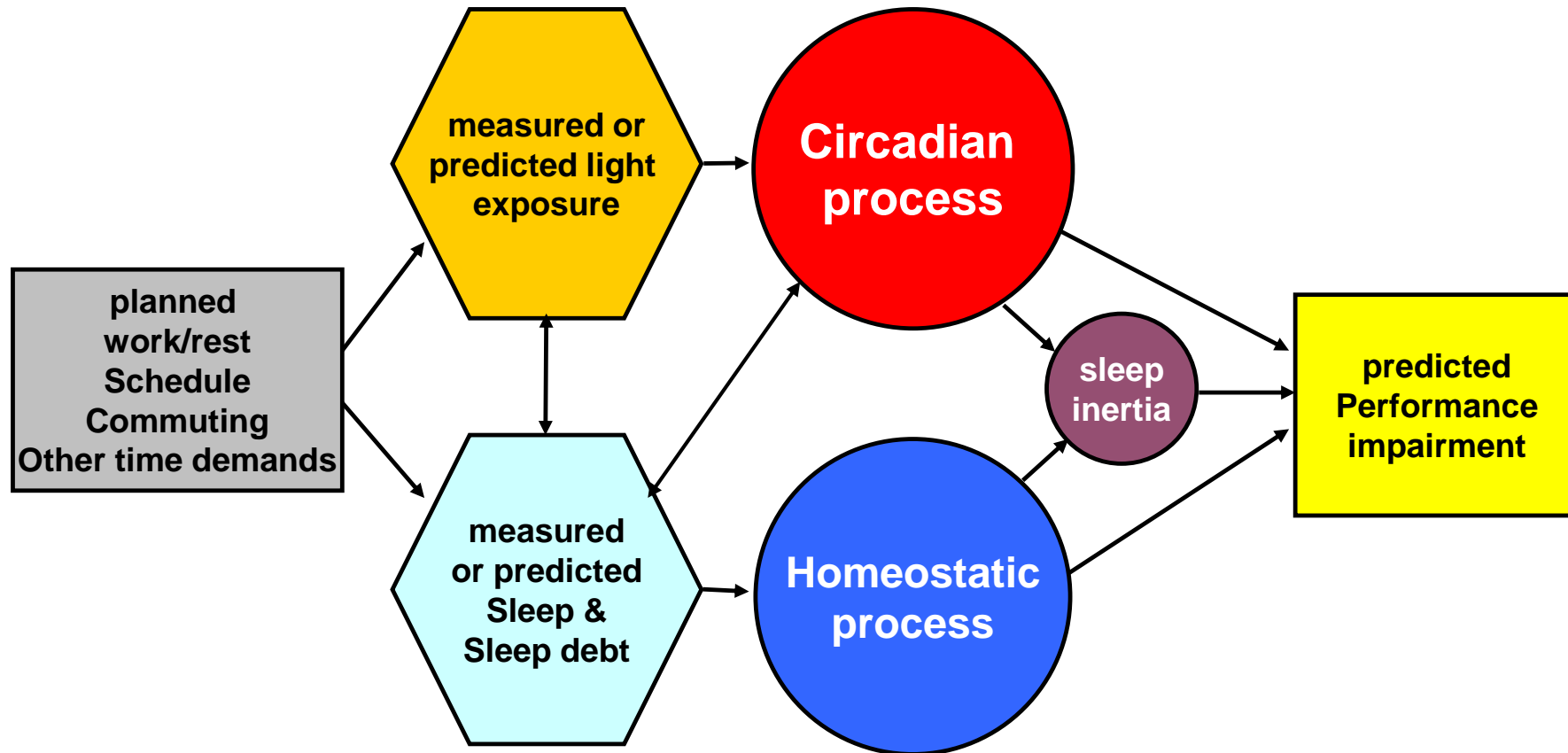


Borbély AA (1982). A two process model of sleep regulation. *Hum Neurobiol* 1: 195-204.

Van Dongen HPA, Belenky G (2009). Individual differences in vulnerability to sleep loss in the work environment. *Ind Health* 47: 518-526.



Simplified Schematic of Performance Prediction Models



Biomathematical modeling of sleep/wake homeostasis and allostasis

McCauley et al. (2009/2013) introduced a predictive model by applying a system of first-order ordinary differential equations (ODE's):

$$\frac{dp(t)}{dt} = \alpha_W [p(t) + \beta_W u(t)] + \kappa(t) [c(t) + \mu_W],$$

$$\frac{du(t)}{dt} = \eta_W u(t),$$

$$\frac{d\kappa(t)}{dt} = \lambda_W \kappa(t) \left(1 - \frac{\kappa(t)}{\xi} \right),$$

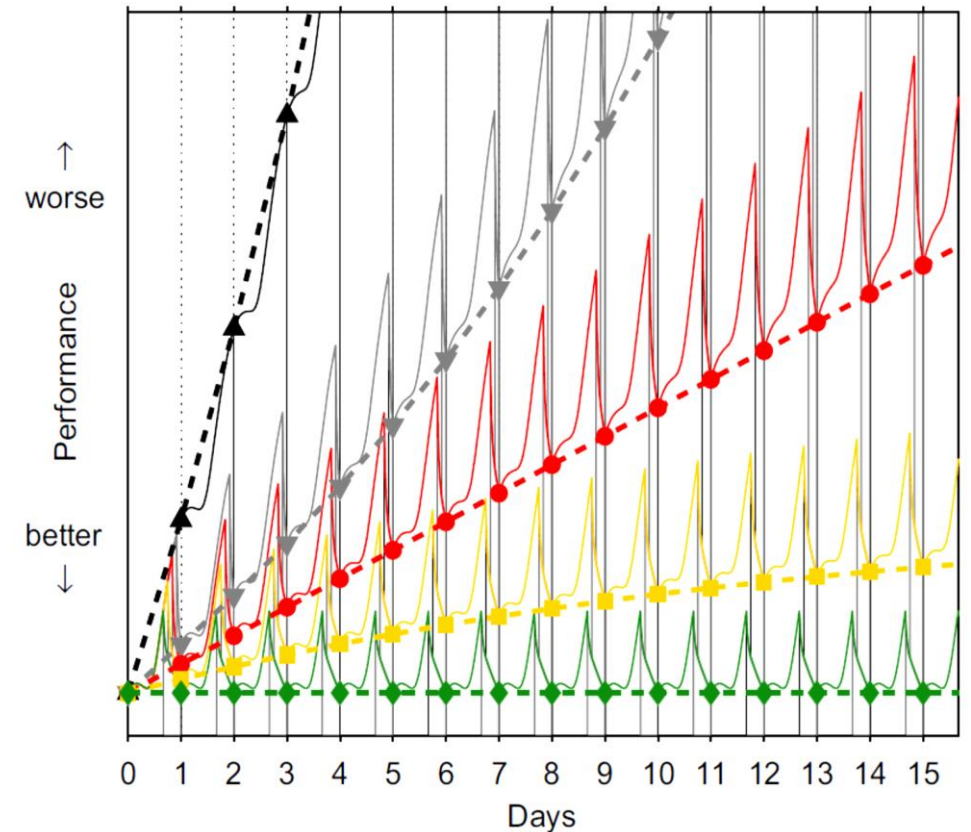
where:

$p(t)$ is the performance prediction in terms of lapses,

$u(t)$ represents the allostatic process,

$\kappa(t)$ represents dynamic changes in circadian amplitude

$c(t)$ represents 24-hour circadian rhythm oscillator.



McCauley P, Kalachev LV, Smith AD, Belenky G, Dinges DF, Van Dongen HPA (2009). *J Theor Biol* 256: 227-239.
 McCauley P, Kalachev LV, Mollicone DJ, Banks S, Dinges DF, Van Dongen HPA (2013). *Sleep* 36: 1987-1997.



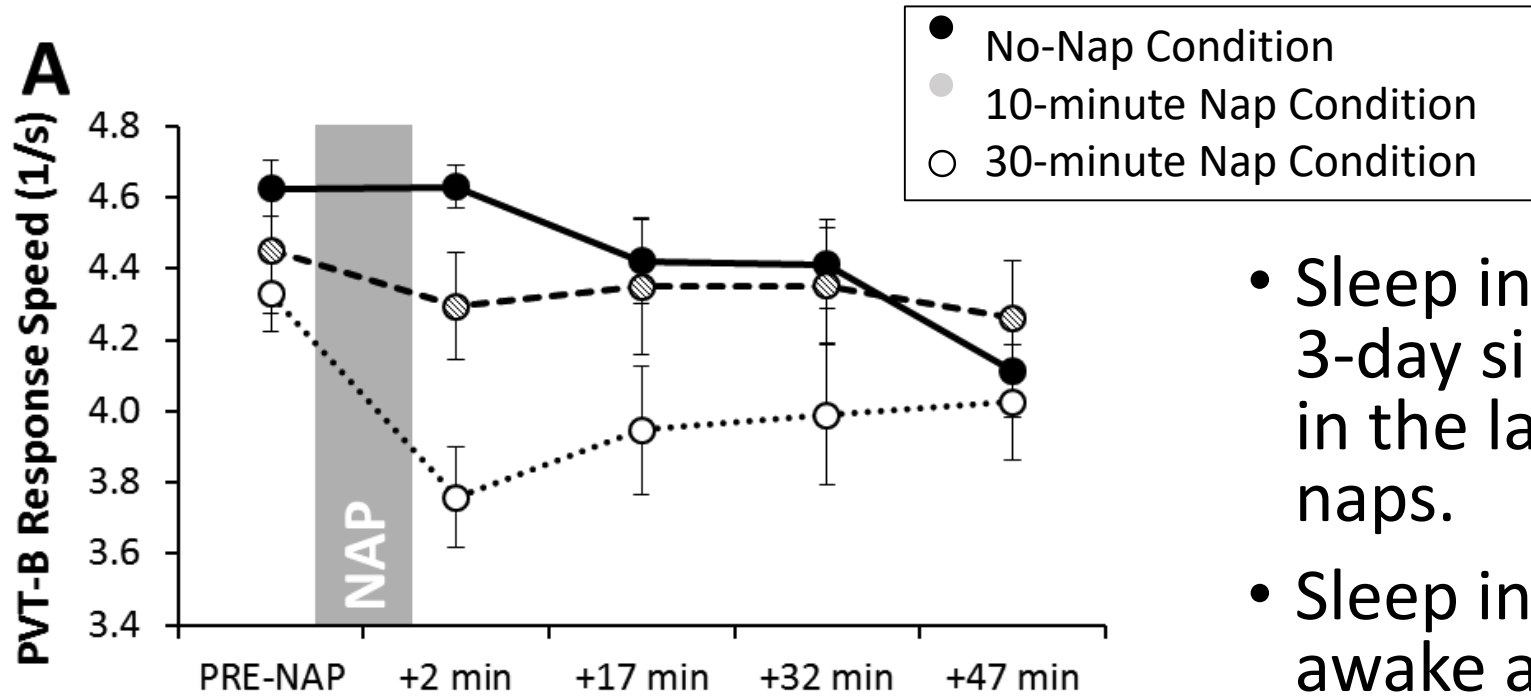
Sleep Inertia

- *Sleep inertia*: refers to a period of reduced alertness, grogginess and impaired cognitive performance experienced immediately upon awakening
- Magnitude of effects dependent on multiple factors such as: sleep duration, sleep stage prior to awakening, prior sleep deprivation, time of day of awakening, etc.
- Sleep inertia effect declines upon awakening exponentially over time awake.

Tassi, P, Muzet, A (2000). Sleep Inertia. Sleep Medicine Reviews 4(4): 341-353.



Sleep Inertia and Performance



- Sleep inertia effects captured in a 3-day simulated night shift study in the laboratory using scheduled naps.
- Sleep inertia, in addition to time awake and time of day, impacts the magnitude and rate of change of performance upon awakening.

Hilditch, CJ, Centofanti, SA, Dorrian J, Banks, S (2016). A 30-minute, but not a 10-minute nighttime nap is associated with sleep inertia. *Sleep* 39(3): 675-685.



Enhanced Model with Sleep Inertia

1. To include sleep inertia, an additional differential equation was formulated:

$$\frac{dx(t)}{dt} = \rho x(t),$$

where:

$x(t)$ represents magnitude of sleep inertia,

ρ is the constant rate of decline over time awake.

2. To preserve original model dynamics, a new prediction outcome variable was designated:

$$\frac{df(t)}{dt} = [v_1 + 2v_2 + \gamma x(t)] \frac{dp(t)}{dt} + \gamma p(t) \frac{dx(t)}{dt},$$

where: v_1 and v_2 are coefficients for relating lapses to effectiveness,

γ scalar for sleep inertia,

$x(t)$ magnitude of the sleep inertia effect (proportional to $p(t)$),

$p(t)$ performance impairment at time t .



Enhanced System of ODE's

- Taken together, the system of ODE's are as follows:

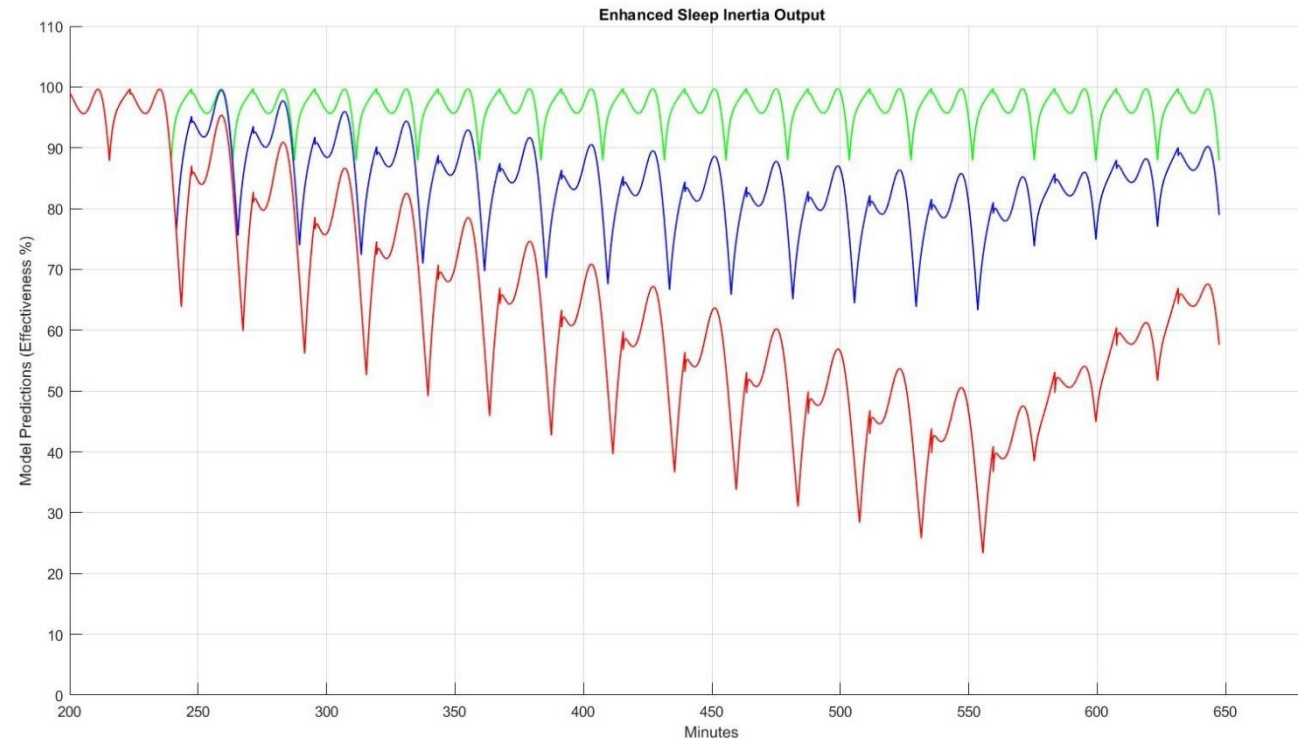
$$\frac{dp(t)}{dt} = \alpha_w [p(t) + \beta_w u(t)] + \kappa(t) [c(t) + \mu_w],$$

$$\frac{du(t)}{dt} = \eta_w u(t),$$

$$\frac{d\kappa(t)}{dt} = \lambda_w \kappa(t) \left(1 - \frac{\kappa(t)}{\xi} \right),$$

$$\frac{dx(t)}{dt} = \gamma x(t),$$

$$\frac{df(t)}{dt} = [v_1 + 2v_2 + \gamma x(t)] \frac{dp(t)}{dt} + \gamma p(t) \frac{dx(t)}{dt}.$$



Conclusion

- ODE framework allows for additional mediators impacting the dynamics of sleep/wake regulation to be incorporated.
- Flexibility of ODE approach allows for additions both mediating fundamental dynamics, as well as, moderators causing transient changes.
- Enhanced model is conceptual and must be calibrated using actual data from investigations of sleep inertia.
- Further measurements of sleep inertia under a variety of homeostatic, circadian and allostatic states is needed for this estimation and validation of parameters.





Questions?

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