



Universität  
Zürich



**ZNZ** Zentrum für Neurosensibilität Zürich  
Neuroscience Center Zürich  
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# Comparative Physiology and Pharmacology of Sleep

## Sleep regulation (animals)

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Bio 333: HS 2012; 29.10.2011

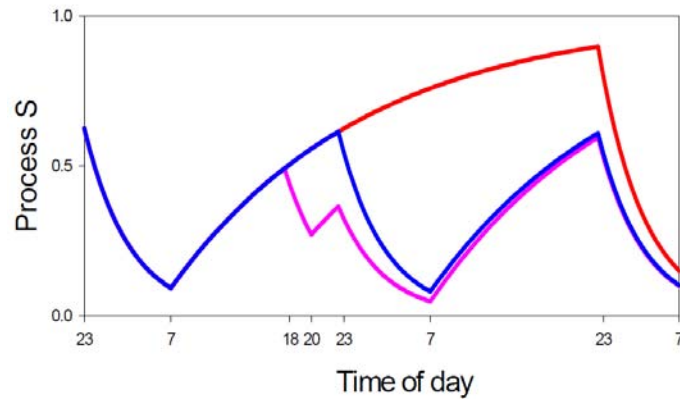
### Learning objectives

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At the end of the lecture you should be able to:

- Describe the homeostatic regulation of sleep in animals
- Understand mechanisms underlying sleep homeostasis

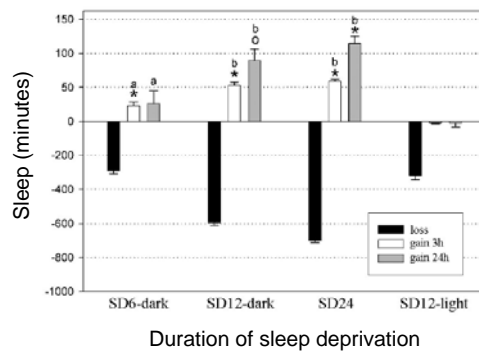
## sleep homeostasis



Achermann & Borbély 2003

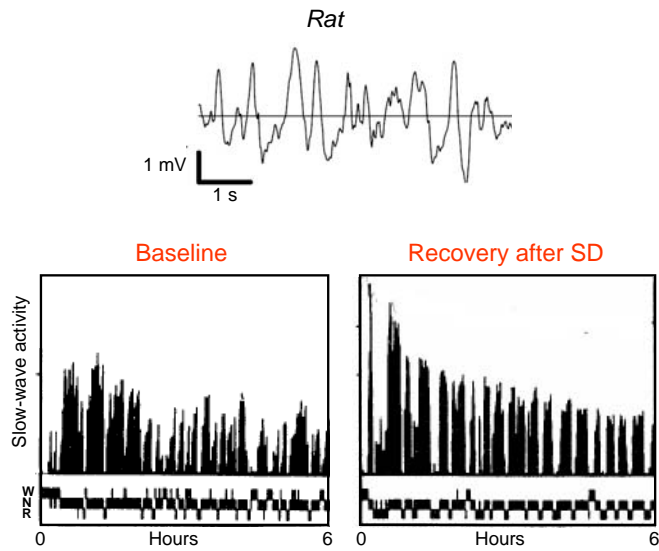
## Dose-dependent relationship

*Fruit fly*



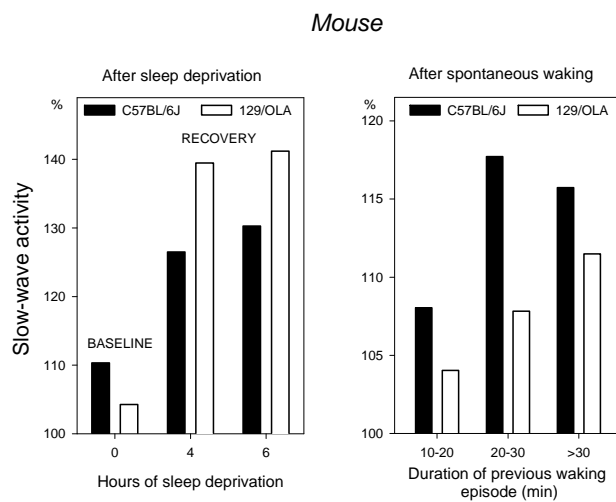
Huber et al., 2004

## Slow wave activity increase



*Franken et al., 1991*

## Dose-dependent relationship



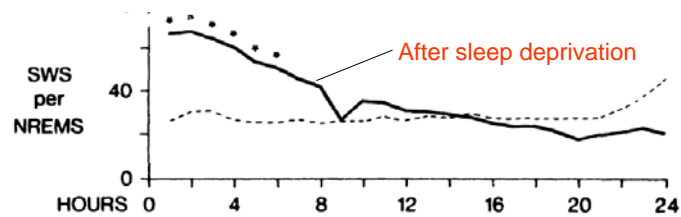
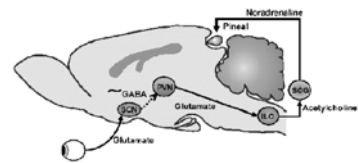
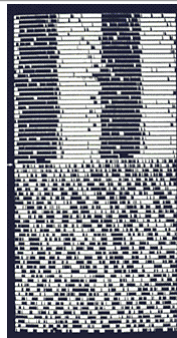
*Huber et al., 2000*

## Independence from circadian effects

Suprachiasmatic nuclei



rest-activity plot

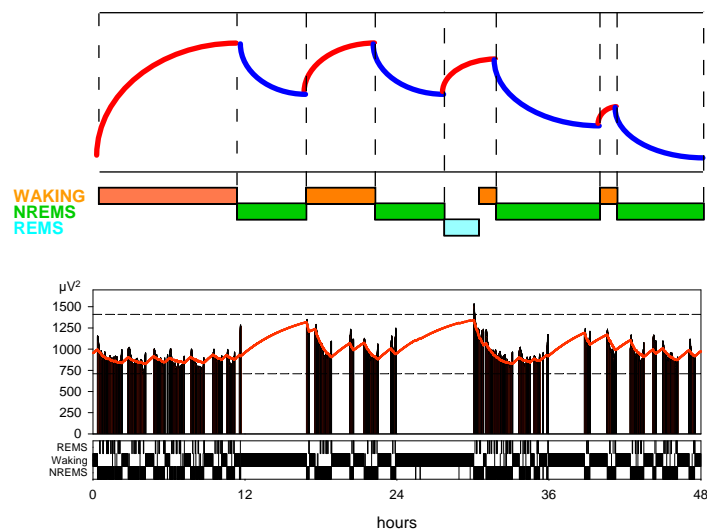


Tobler et al., 1983

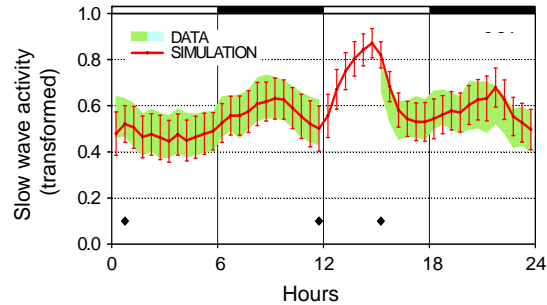
## Simulation of process S

increasing process:  $S_{t+1} = 1 - (1 - S_t) * e^{-dt/TI}$

decreasing process:  $S_{t+1} = S_t * e^{-dt/Td}$



## Simulation of process S

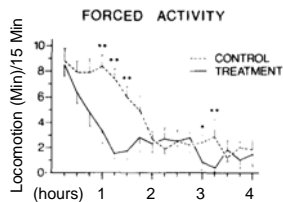


Huber et al., 2000

The dynamics of sleep homeostasis can be quantified.

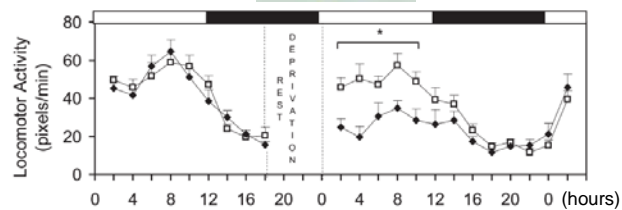
## Sleep homeostasis in the animal kingdom

Cockroach



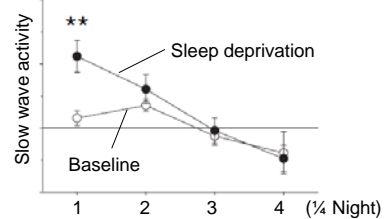
Tobler et al., 1983

Zebra fish



Zhdanova et al., 2006

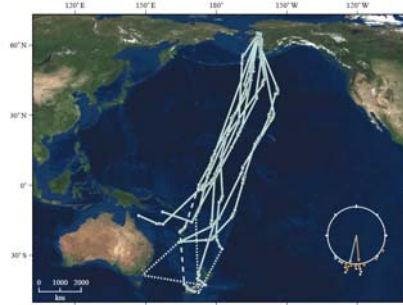
Pigeon



Martinez et al., 2008

## Exceptions?

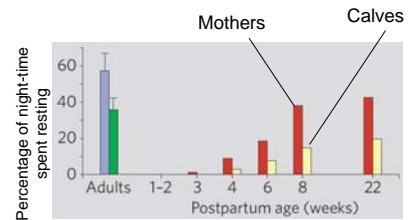
### *Godwits (limosa)*



non-stop flight 8117–11 680 km

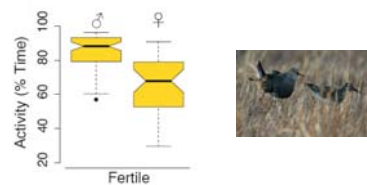
*Gill et al., 2009*

### *Killer wale*



*Lyamin et al., 2005*

### *Sandpiper*



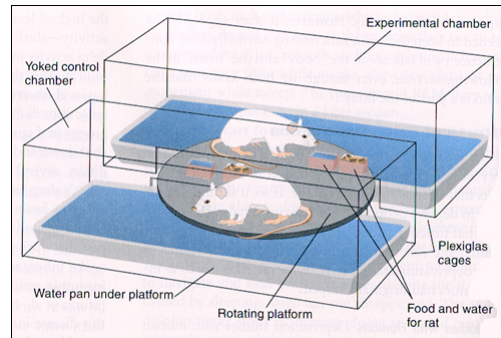
*Lesku et al., 2012*

Sleep need is homeostatically regulated.

All investigated species show sleep homeostasis.

What is responsible for the increased sleep need?

## Sleep deprivation may lead to death (?)



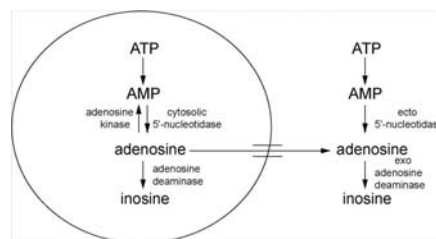
*Rechtschaffen et al., 1993*

## „Sleep substance“

- Hypothesis: Hypnotoxin accumulates during waking and is metabolized during sleep (Piéron, 1913).
- Experiment: Injection of cerebrospinal fluid of sleep deprived sheep leads to increase of NREM sleep in rats (Pappenheimer et al., 1967).
- Factor S: Muramyldipeptide was identified from such cerebrospinal fluid (Pappenheimer et al., 1975; Krueger et al., 1982).

## Energy conservation

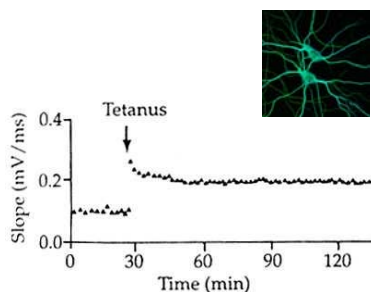
- Hypothesis: Replenishment of energy stores which were depleted during waking (Benington and Heller, 1995).
- It was postulated that Adenosine increases and Glycogen decreases during wakefulness.
- The increase of Adenosine leads to increased sleep need.



## Synaptic strength

*Waking: Strengthening*

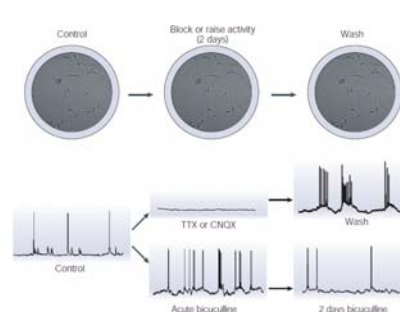
Long term potentiation (LTP)



Bliss & Lomo 1973

*Sleep: Weakening*

Synaptic scaling (downscaling)

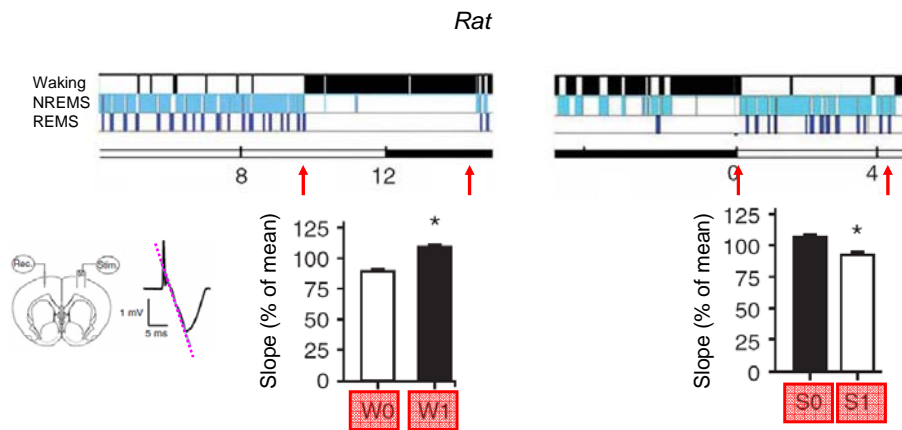


Turrigiano & Nelson 2004



## Synaptic Homeostasis

By Tononi and Cirelli, 2006



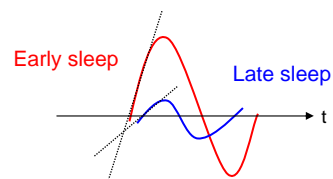
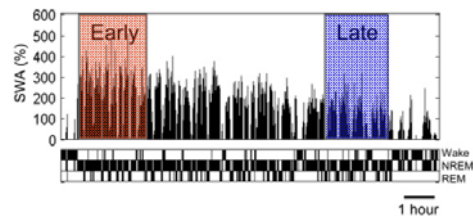
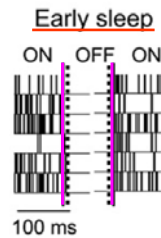
Vyazovskiy et al., 2008

The synaptic homeostasis hypothesis unifies existing hypotheses about the function of sleep (sleep substance, energy).

The hypothesis provides direct explanation for the increase in slow wave activity.

## Synchronization of activity

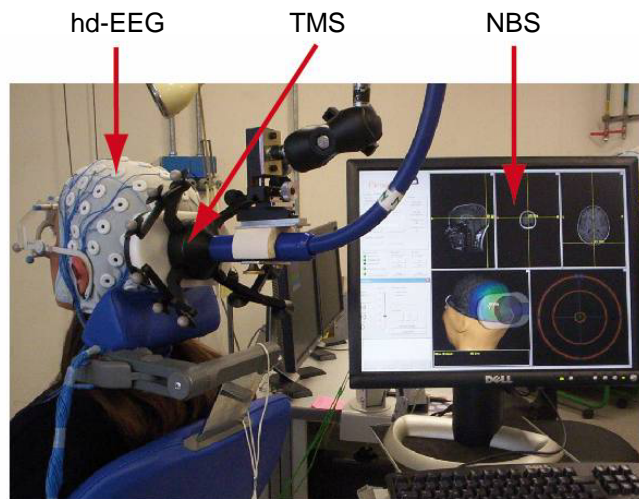
Ratte: Multiunit Recording



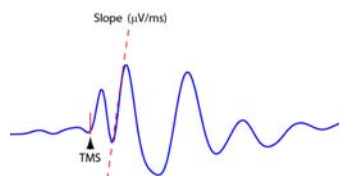
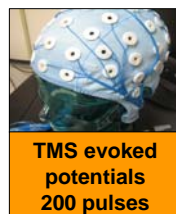
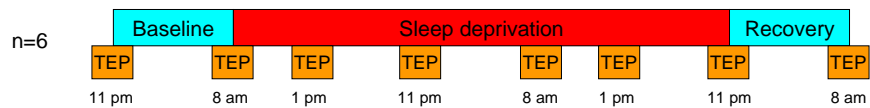
Vyazovskiy et al., 2009

Evidence for changes in excitability  
also exist for humans.

## Design



## Study protocol



## Time course of cortical excitability

