

Supplementary Materials for **Neuronal noise as an origin of sleep arousals and its role in sudden infant death syndrome**

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Supplementary Materials

section S1. Sleep behavior of zebrafish larvae

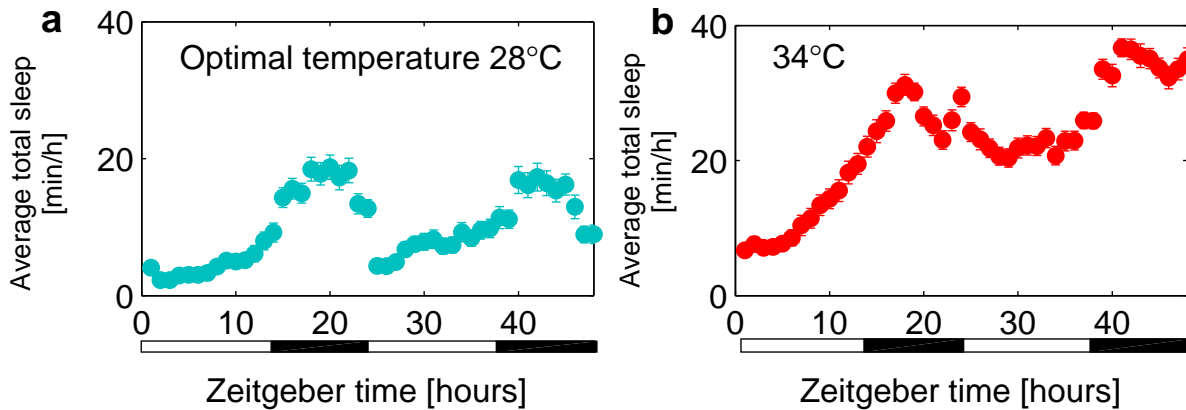


fig. S1. Sleep behavior of zebrafish larvae across 48 hours under 14 light/10-hour dark cycles at different temperatures. Group average duration of sleep for the zebrafish larvae ($n = 48$) are shown for each hour during the 48h experiment at water temperatures (a) 28°C and (b) 34°C. Note that during the dark periods the average sleep duration increases by about a factor of two when temperature changes from 28°C to 34°C.

section S2. Sleep behavior of healthy adult humans under different circadian temperatures

We performed additional empirical analysis to test the relationship between body temperature and arousability from sleep in young adults. We quantified arousability versus temperature by analyzing sleep/wake transitions from 20 healthy young adults during two nights, each containing in average 7h of sleep (55). Our empirical results show an inverse relationship between core body temperature and arousability from sleep: in the beginning of the sleep period (between the hours 12am and 2am) when core body temperature is higher, arousability is low, while in contrast at the end of the sleep period (between the hours 4am and 6am) when core body temperature reaches a minimum as a result of circadian variation (53, 54), arousability significantly increases (fig. S2). This empirical observation is also successfully reproduced by

our model (fig. S2), where we incorporate different levels of neuronal noise σ corresponding to different temperatures. Furthermore, this behavior in healthy adults is in agreement with our experimental results on temperature dependence of arousability in zebrafish larvae (Fig. 2).

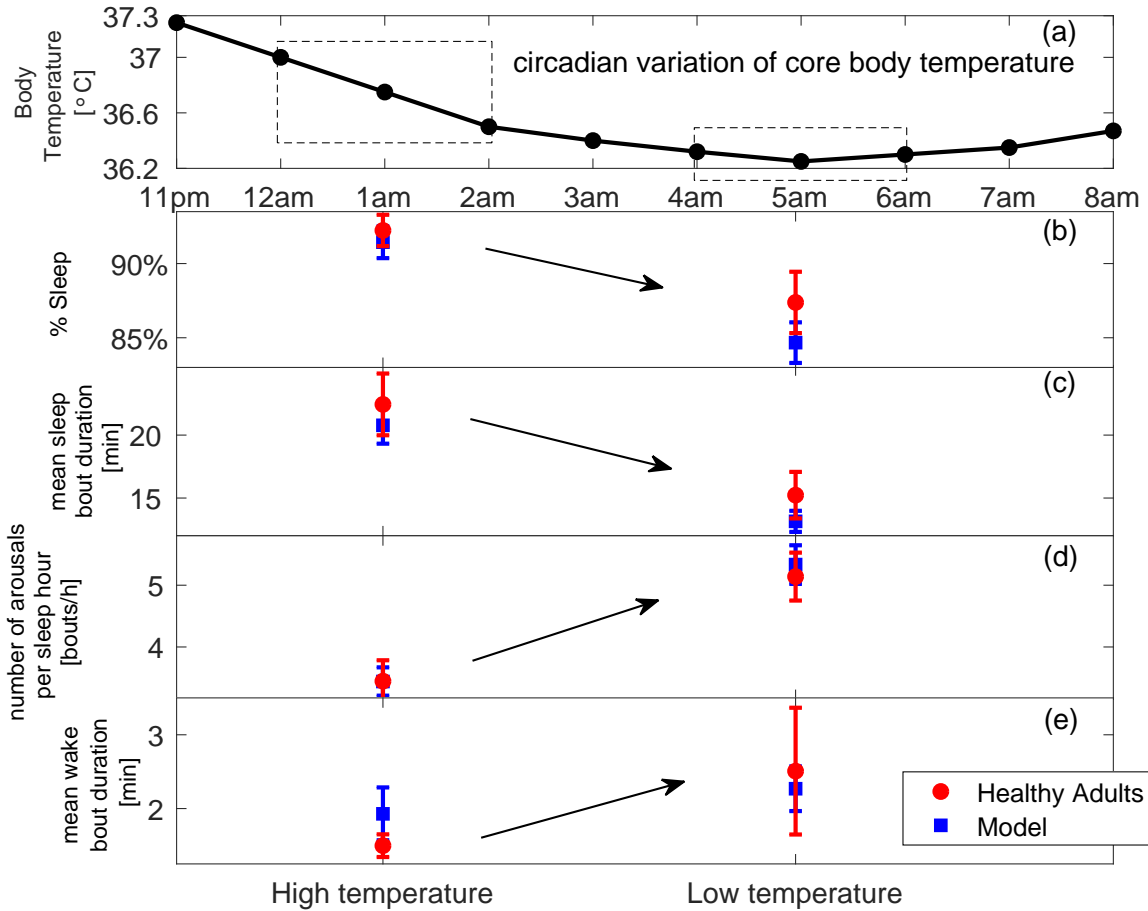


fig. S2. Experimentally obtained sleep and wake characteristics for adult subjects as a function of core body temperature during the night (red circles) compared to our model simulations (blue squares). Percent of total sleep time and mean sleep bout duration significantly decrease due to decreasing core body temperature (Tukey's test yields $p < 0.05$). In contrast, the number of arousals and mean arousal/wake bout duration significantly increase with lowering the core body temperature (Tukey's test: $p < 0.05$). The good agreement between our experimental measurements obtained for adult subjects and our model results for different noise levels strongly supports our hypothesis that arousals/brief awakenings from sleep originate from neuronal noise. These observations are also supported by our findings from the zebrafish experiments and modeling shown in Fig. 2. In all panels, we present group average and standard error of 20 adult subjects during two nights of sleep with 7h duration each as well as the model results for each neuronal noise level σ obtained from 20 7h independent model simulations matching the duration of the experimental measurements. The circadian variation in core body temperature in panel (a) is adopted from (53).

section S3. Occurrence of SIDS and heat loss versus infant age

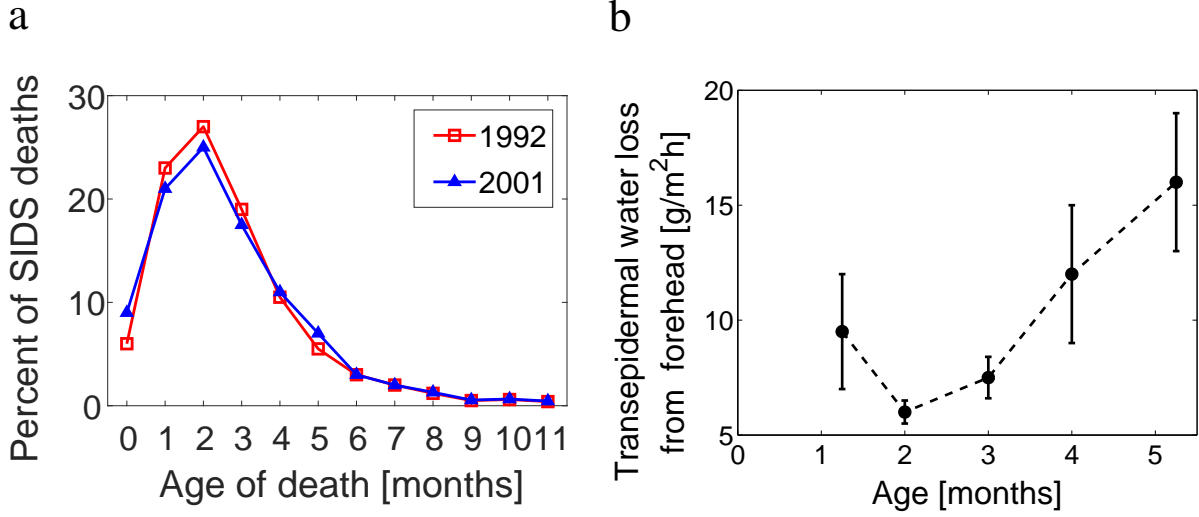


fig. S3. Occurrence of SIDS and heat loss versus infant age. (a) Percent of SIDS deaths per age of the affected infants as confirmed by two independent epidemiological studies from 1992 and 2001 (adopted from (19)). (b) The water lost by diffusion and by active secretion (sweating) is measured by transepidermal water loss (TEWL) which is a good estimation of overall heat loss. Inadequate TEWL may result in overheating and hyperthermia (56). The measurements in panel (b) show TEWL as measured from infants' foreheads (adopted from (56)), which is the most intense sweating site in infants (57, 58) and an important source of body heat loss (52). Note that both of the curves in panels (a) and (b) reach extreme values at around age 2 months.

section S4. Model parameters to simulate the sleep/wake statistics of zebrafish larvae

In our model we simulate the statistics of sleep/wake bout durations of zebrafish larvae using $b = 20 \text{ mV}^2/\Delta t$ and $\Delta = 10 \text{ mV}$. In order to simulate the sleep/wake behavior at different water temperatures, we change the neuronal noise level σ : for 25°C we use $\sigma = 7.6 \text{ mV}/\sqrt{\Delta t}$, for 28°C $\sigma = 7.3 \text{ mV}/\sqrt{\Delta t}$, for 31°C $\sigma = 6.1 \text{ mV}/\sqrt{\Delta t}$ and for 34°C $\sigma = 5.5 \text{ mV}/\sqrt{\Delta t}$, where $\Delta t = 0.08 \text{ s}$ is the time resolution of each simulation. The results are shown in Figs. 2 and 3 (main text). In our model, Δ is a function of the difference between the Nernst potential of potassium ions, V_K , and the voltage threshold V_{Th} (Fig. 1b main text), both of which do not change much with temperature if the temperature is within a physiological range (50).

For our model simulations, we choose a temporal resolution for sleep/wake epochs of $\Delta t = 0.08$ s. This is in agreement with the experimental setup where a sampling rate of 12.5 frames per second is used for the video camera to track the motion of the zebrafish larvae and to decide whether larvae are awake or asleep (39). To match experimental measurements, in our model simulations consecutive 0.08 s epochs are grouped into $\Delta t = 1$ min bins, and bins are labeled as wake, if in at least one of the 750 epochs ($= 12.5$ frames per second \times 60 seconds) the voltage exceeds the excitability threshold V_{Th} . For each temperature, we perform 48 simulations (matching the total number of zebrafish larvae for each temperature). The total duration for each simulation is chosen to be 20h in order to match the total duration of the dark periods in the zebrafish experiments.