Particle filter-based parameter estimation in a model of the human circadian rhythm

Particle Filter-based Parameter Estimation in a Model of the Human Circadian Rhythm

Jochem H. Bonarius[1] Jean-Paul M.G. Linnartz[1,2]
[1]Eindhoven University of Technology [2]Philips Lighting Research
Electrical Engineering, Signal Processing Systems
FLX 7.062, Postbox 513, 5600 MB, Eindhoven, The Netherlands
j.h.bonarius@tue.nl j.p.linnartz@lighting.com

Abstract

Recent insights into the effects of light on human health call for a more human-centric approach in automatic lighting control systems. We contribute to the provisioning of lighting settings tailored to the needs of individuals by addressing the challenge of predicting the response of an individual's circadian rhythm to light exposure. Existing models of the human circadian rhythm are not tailored to individual physiological characteristics such as intrinsic circadian period, light sensitivity and age. We propose to improve model accuracy by using Bayesian statistical inference to estimate the values of model parameters that reflect these physiological characteristics. We illustrate our generic method by applying to a combination of two popular models of the circadian rhythm. By processing individual light exposure- and actigraphy data recoded during a field trial with 20 human subjects with a Particle Filter, we estimate each subject's intrinsic circadian period. When correlating these to the subjects' Munich Chronotype Questionnaire Midsleep on Free Days time, a significant relationship was found: $r > 0.6$ and $p < 0.01$. This shows the proposed method has good potential for improving model accuracy.

1 Introduction

Humans have an internal circadian rhythm that regulates many of their biological processes such as temperature, hormone secretion, and the sleep-wake cycle. The timing of light exposure plays a major role in regulation of this circadian rhythm [1]. Determining the state of the circadian cycle has been a major subject in the field of Chronobiology. Within this field several mathematical models of the circadian rhythm have been proposed, often based on empirical observations gathered in clinical studies. Commonly, the human circadian rhythm is modeled as a deterministic system with certain inputs (light exposure, food intake, etc.) and outputs (body temperature, social markers, etc.). However, as these models were often created by fitting mathematical functions to the average of the collected data, their output will represent the average response, not that of an individual. This could lead to misprediction, for example were the model would indicate a circadian phase advance in response to certain light exposure, while actually the individual's circadian phase would be delayed.

We propose to improve model accuracy by using Bayesian statistical inference to estimate the value of model parameters that reflect physiological characteristics such as intrinsic circadian period, light sensitivity and age. Not only do these differ per individual, but they are also not always fully known. By observing an individual's

responses to inputs, we can iteratively update the estimation of the parameter values. This is schematically shown in figure 1.

Our target is to estimate parameter values that best correspond to an individual's characteristics, in order to reduce the modeling error for that individual. As we want to implement our models in automatic lighting control systems, we do not aim for a clinically accurate estimate, but we need an estimate that is adequate for choosing between different options for light settings.

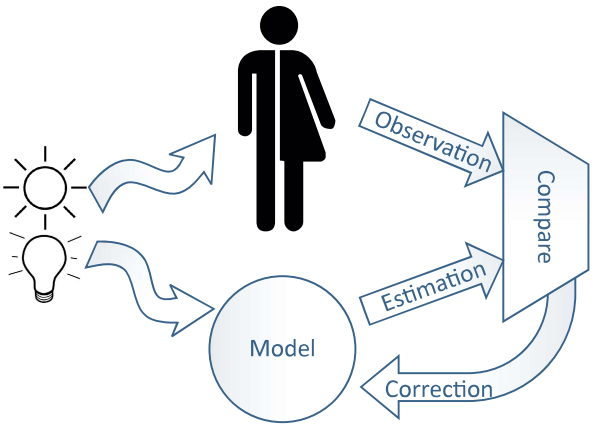

Figure 1: Schematic representation of the model parameter update loop. Unisex symbol ©Scott de Jonge

The use of Bayesian inference in this context has already been suggested by Mott, Dumont, Boivin, *et al.* [2]. They showed how a Particle Filter, a Sequential Monte Carlo method, can be used to approximate the system state (circadian phase) by observing light exposure and body temperature. We will extend on this method to estimate the models' parameter values using techniques developed by Liu and West [3].

2 Methods

2.1 Parameter search using a particle filter

We consider the circadian rhythm to be Markov process with transition density $p(\mathbf{x}_k|\mathbf{x}_{k-1}, \boldsymbol{\theta})$ and observation density $p(\mathbf{z}_k|\mathbf{x}_k, \boldsymbol{\theta})$. We want to determine the probability distribution of a (sub)set of fixed parameters in vector $\boldsymbol{\theta}$, given all observations $\mathbf{z}$ up to now: $p(\boldsymbol{\theta}|\mathbf{z}_{1:k})$. Using Bayes' theorem, the Chapman–Kolmogorov equation, and by including the state variable $\mathbf{x}$, the probability can be rewritten as an iterative algorithm, where the current state $\mathbf{x}_k$ and parameter estimation $\hat{\boldsymbol{\theta}}_k$ depend on the previous, according to

$$p(\hat{\boldsymbol{\theta}}_k, \mathbf{x}_k|\mathbf{z}_{1:k}) \propto \int p(\hat{\boldsymbol{\theta}}_k|\hat{\boldsymbol{\theta}}_{k-1}, \mathbf{x}_k, \mathbf{z}_k) p(\mathbf{z}_k|\hat{\boldsymbol{\theta}}_{k-1}, \mathbf{x}_k) \int p(\mathbf{x}_k|\hat{\boldsymbol{\theta}}_{k-1}, \mathbf{x}_{k-1}) p(\hat{\boldsymbol{\theta}}_{k-1}, \mathbf{x}_{k-1}|\mathbf{z}_{1:k-1}) \, \mathrm{d}\mathbf{x}_{k-1} \, \mathrm{d}\hat{\boldsymbol{\theta}}_{k-1}, \quad (1)$$

By defining the term $p(\hat{\boldsymbol{\theta}}_k|\hat{\boldsymbol{\theta}}_{k-1}, \mathbf{x}_k, \mathbf{z}_k)$, where the new estimation of $\boldsymbol{\theta}$ only depends on the previous -state, -observation, and parameter estimation and not on their entire history, it is implied that $\boldsymbol{\theta}$ has a simple, known distribution. Liu and West [3] suggest that this parameter density can be approximated using a weighted kernel

density constructed by adding N multivariate Gaussian densities*

$$p(\hat{\boldsymbol{\theta}}_k|\mathbf{x}_k, \mathbf{z}_k, \hat{\boldsymbol{\theta}}_{k-1}) \approx \sum_{i=1}^{N} w_k^{(i)} \mathcal{N}_{\dim(\boldsymbol{\theta})}(\hat{\boldsymbol{\theta}}_k|\mathbf{m}_k^{(i)}, (1-a^2)\mathbf{V}_k), \tag{2}$$

which was further reduced to

$$\hat{\boldsymbol{\theta}}_k^{(i)} \sim \mathcal{N}_{\dim(\boldsymbol{\theta})}(\mathbf{m}_k^{(i)}, (1-a^2)\mathbf{V}_k), \text{ for } i = 1, 2, \ldots, N. \tag{3}$$

'Smoothed' Gaussian mean vector $\mathbf{m}$ in the previous equations is determined using a mixture of the previous parameter estimate $\hat{\boldsymbol{\theta}}$ and the posterior parameter mean $\bar{\boldsymbol{\theta}}$

$$\mathbf{m}_k^{(i)} = a\hat{\boldsymbol{\theta}}_{k-1}^{(i)} + (1-a)\bar{\boldsymbol{\theta}}_k, \text{ for } i = 1, 2, \ldots, N, \tag{4}$$

where smoothing factor a (also in equation 2) is determined according to

$$a = \frac{3\delta - 1}{2\delta}, \tag{5}$$

for which we use a fixed discount factor $\delta = 0.98$. The posterior parameter mean $\bar{\boldsymbol{\theta}}$ is determined by

$$\bar{\boldsymbol{\theta}}_k = \sum_{i=1}^{N} w_k^{(i)} \hat{\boldsymbol{\theta}}_{k-1}^{(i)}. \tag{6}$$

The (normalized) particle weight $w^{(i)}$ is derived from the observation density, described by

$$w_k^{(i)} = \frac{p(\mathbf{z}_k|\boldsymbol{\mu}_k^{(i)}, \hat{\boldsymbol{\theta}}_{k-1}^{(i)})}{\sum_{i=1}^{N} p(\mathbf{z}_k|\boldsymbol{\mu}_k^{(j)}, \hat{\boldsymbol{\theta}}_{k-1}^{(j)})}, \text{ for } i = 1, 2, \ldots, N. \tag{7}$$

Here, the mean value $\boldsymbol{\mu}$ of the state $\mathbf{x}$ is determined by determining the expected value of the state equation (defined later-on in this paper) with

$$\boldsymbol{\mu}_k^{(i)} = \mathbb{E}\left[\mathbf{x}_k \middle| \mathbf{x}_{k-1}^{(i)}, \hat{\boldsymbol{\theta}}_{k-1}^{(i)}\right], \text{ for } i = 1, 2, \ldots, N. \tag{8}$$

The posterior covariance matrix of the parameter distribution $\mathbf{V}$ is described by

$$\mathbf{V}_k = \sum_{i=1}^{N} w_k^{(i)} (\hat{\boldsymbol{\theta}}_{k-1}^{(i)} - \bar{\boldsymbol{\theta}}_k)(\hat{\boldsymbol{\theta}}_{k-1}^{(i)} - \bar{\boldsymbol{\theta}}_k)^{\mathrm{T}}. \tag{9}$$

Equation 2 implies a point-mass representation can be used to approximate the parameter density, which we realize using a particle filter [4]. Hence, in the equations above, subscript (i) indicates the particle index and N represents the total number of particles. As the total number of particles is limited, it is important that the majority of particles provides an effective contribution to the point-mass representation. If the weight of most particles is close to zero, then the accuracy of the estimated probability distribution will be low. To prevent this from happening, a *resampling* step is used after each iteration: particles with low weight are dropped and particles with high weight are replicated [4]. The new indexes for resampling are sampled from a multinomial distribution with parameters $p_i = w^{(i)}$, for $i = 1, 2, \ldots, N$. This will be shown in pseudocode at the end of this paper.

*We use $\mathcal{N}_D(\mathbf{x}|\boldsymbol{\mu}, \boldsymbol{\Sigma}) = (2\pi)^{-D/2}|\boldsymbol{\Sigma}|^{-1/2} \exp\left(-\frac{1}{2}(\mathbf{x}-\boldsymbol{\mu})^{\mathrm{T}}\boldsymbol{\Sigma}^{-1}(\mathbf{x}-\boldsymbol{\mu})\right)$ to denote the probability density function of a D-variate Gaussian distribution with mean vector $\boldsymbol{\mu}$ and covariance matrix $\boldsymbol{\Sigma}$. $D = 1$ when omitted.

2.2 Mathematical model of the circadian rhythm

We consider the Kronauer limit cycle oscillator model, a popular mathematical model of the circadian pacemaker that estimates the response of the circadian pacemaker to ambient light input, as a base for our work [5]. However, the output markers that can be related to the state of that model, such as the time-of-minimum core body temperature ($\mathrm{CBT}_{\mathrm{min}}$) [5] or dim light melatonin onset (DLMO) [6], are impractical to measure in daily situations: a subjects either need to wear an internal thermometer, or lab analysis of saliva samples is required. Therefore, we combine the model with the mathematical model of the homeostatic sleep drive by Phillips and Robinson [7] that relates the circadian clock to the sleep-wake cycle, as its relatively easy to use actigraphy to determine the sleep-wake state of an individual. In [8] and [9], it was already suggested to combine these models. Furthermore, the model combination also fits into the concept of the two-process model of sleep regulation [10].

We connect the models in a way that the system has an input vector $\mathbf{u}$ and an output vector $\mathbf{z}$, as shown schematically in figure 2.

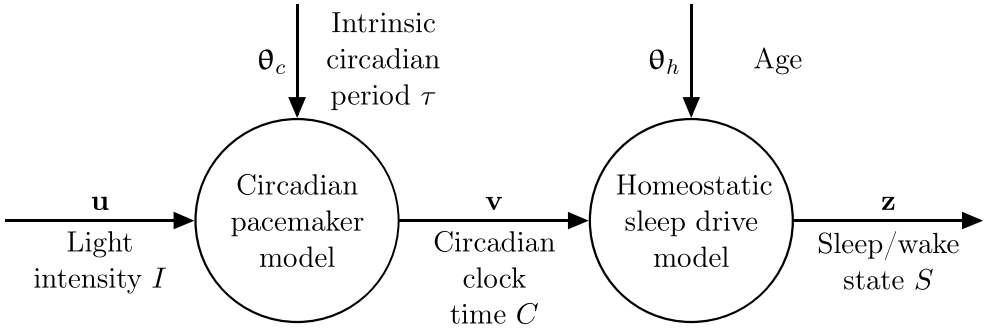

Figure 2: Block diagram of the interconnected models.

We combine all the models' system state variables in state vector $\mathbf{x} \triangleq \begin{bmatrix} n & x & y & V_v & V_m & H \end{bmatrix}^{\mathrm{T}}$. In this work only the parameter τ, representing the period of the circadian pacemaker, is considered for estimation, as there are strong indications that this parameter is the dominant source behind individual variation in circadian phase [6]. We consider all other parameters fixed at their suggested value. The dynamics of the system are then described by

$$\dot{\mathbf{x}} = \begin{bmatrix} \dot{n} \\ \dot{x} \\ \dot{y} \\ \dot{V}_v \\ \dot{V}_m \\ \dot{H} \end{bmatrix} = \begin{bmatrix} 60(\alpha(1-n) - 0.007n) \\ \frac{\pi}{12}\left(y + 0.13\left(\frac{1}{3}x + \frac{4}{3}x^3 - \frac{256}{105}x^7\right) + B\right) \\ \frac{\pi}{12}\left(\frac{1}{3}By - x\left(\left(\frac{24}{0.99729\tau}\right)^2 + 0.55B\right)\right) \\ 360\left(D_v - V_v - 2.1Q_m\right) \\ 360\left(1.3 - V_m - 1.8Q_v\right) \\ \frac{1}{45}\left(\mu_H Q_m - H\right) \end{bmatrix} \triangleq \mathbf{f}(\mathbf{x}, I; \tau), \tag{10}$$

describing dynamics of the ratio of activated photoreceptors n, the circadian pacemaker oscillator pair x and y, the mean cell body potential of the sleep-active ventrolateral preoptic (VLPO) area of the hypothalamus V_v, the mean cell body potential of the wake-active ascending arousal system's monoaminergic nuclei (MA) V_m, and the

homeostatic sleep drive H. Supporting equations are

$$\alpha = 0.1\sqrt{\frac{I}{9500}}\frac{I}{I+100}, \tag{11}$$

$$B = 37\alpha(1-n)(1-0.4x)(1-0.4y), \tag{12}$$

$$C = 0.5(1+0.8x-0.55y), \tag{13}$$

$$Q_i = \frac{100}{1+\exp\left(\frac{10-V_i}{3}\right)}, \text{ with } i \in \{v,m\}, \text{ and} \tag{14}$$

$$D_v = H - \nu_{vc}C - 10.2, \tag{15}$$

describing the photoreceptor activation rate α following light exposure I, the resulting photic drive B, the circadian clock time C (modified from [8] to fit the model from [5]), the mean firing rate of the VLPO Q_v and MA Q_m and the drive on the VLPO mean cell body potential D_v. In the equations, homeostatic dampening factor μ_H and circadian clock sensitivity ν_{vc} are related to the age of the modeled person [8]. We will suggest values for these variables based on our data set in the Results section.

As output, only the sleep-wake state S_{sw} is considered, because it is relatively easy to measure in ambulatory conditions as was explained at the beginning of this subsection. It is derived from [7] as[†]

$$S_{sw} \triangleq \mathcal{H}(Q_m - 1) = \begin{cases} 1(\text{awake}), & \text{if } Q_m \geq 1 \\ 0(\text{sleeping}), & \text{otherwise} \end{cases}. \tag{16}$$

However, the above equation is constant most of the time: every circadian cycle ($\sim 24\,\text{h}$) only one 0-to-1 transition (wake up) and one 1-to-0 transition (sleep onset) occurs[‡]. The times in-between transitions do not give us much information. Therefore, only the transitions are considered interesting for our parameter estimation. Thus, we introduce observation set Z which contains all the times t at which a 0-to-1 or 1-to-0 transition occurs in S_{sw} - that is, the transition times from sleep to wake or vice versa. We then evaluate the system output $z_k \in Z$, for $k = 1, 2, \ldots, 2 \times \#\text{days}$, i.e. two events per day. Effectively, we evaluate the model until a $Q_m = 1$ event occurs, indicating either a sleep onset or a wake up time. We will then compare this estimated time (denoted as $\hat{z}$) with the actual sleep onset or wake up time z observed with the human subject. To support this, we define output function $\mathbf{h}$ which maps state $\mathbf{x}$ to observation z by evaluating equations 14 and 16 and determining the time a transition occurs.

As the above equations show, the models of the circadian pacemaker and the homeostatic sleep drive are described to be deterministic. However, real-life biological processes are stochastic in nature. We introduce stochasticity into the existing model by adding white Gaussian process noise and -measurement noise to the state respectively

[†]We use $\mathcal{H}(x) = \begin{cases} 0, & x < 0, \\ 1, & x \geq 0 \end{cases}$ to denote the unit-/Heaviside step function.

[‡]In reality the sleep cycle is much more complex and a person can actually wake up multiple times during that cycle. But our simplified model only considers the initial sleep onset and the final wake up time.

the output. Following this, the state transition density and observation density are described by

$$p\left(\mathbf{x}_k|\mathbf{x}_{k-1},\boldsymbol{\theta}\right) = \mathcal{N}_6\left(\mathbf{x}_k|\mathbf{F}_k(\mathbf{x}_{k-1},I;\tau),\boldsymbol{\Sigma}_\mathbf{x}\right) \text{ and} \tag{17}$$

$$p\left(\mathbf{z}_k|\mathbf{x}_k,\boldsymbol{\theta}\right) = \mathcal{N}\left(z_k|\mathbf{h}(\mathbf{x}_k),\Sigma_z\right), \tag{18}$$

with $\mathbf{F}_k$ being the discrete-time approximation of the state equation 10. Since the mean of additive white Gaussian noise is 0, only the covariance matrix of the process noise $\boldsymbol{\Sigma}_\mathbf{x}$ and the variance of the measurement noise Σ_z appear in the equations. Determining the process noise in covariance matrix $\boldsymbol{\Sigma}_\mathbf{x}$ is out of the scope of this work. For now we assume a value of $\boldsymbol{\Sigma}_\mathbf{x} = (0.01)^2\mathbf{I}_6$. Next, we assume that the variance of the observation noise Σ_z is related to the variance in sleep-onset and wake-up times. Therefore, we set Σ_z equal to the variance of the sleep onset- and wake up times observed with the human subject under evaluation.

With the state transition density and observation density defined, the particle filter described in subsection 2.1 can be constructed [4]. Determining the optimal number of particles is out of the scope of this research. Instead, $N = 240$ particles, suggested by Mott, Dumont, Boivin, *et al.* [2], is used as it shows consistent results.

The particle filter was implemented in MATLAB. We approach $\mathbf{F}_k$ numerically using MATLAB's ordinary differential equation solver "ode23s". A pseudo-code description of the particle filter implementation can be found in Algorithm 1 at end of this paper.

3 Results

To illustrate our method, the particle filter algorithm was applied to data obtained in a field study with 20 human subjects. However, 4 data sets had to be dropped because of hardware issues and user errors. For the 16 data sets left, the average age of the subjects was $70.9 \pm 4.0\,\mathrm{yr}$.

Each subject wore a Philips Actiwatch Spectrum Pro, measuring actigraphy, and a Martin light-logger, measuring ambient light intensity, for a minimum of 168 h (7 days). In parallel, each subject was asked to maintain a sleep dairy, indicating their "to bed"- and "out of bed" times. As described by the Munich Chronotype Questionaire (MCTQ) [11], this information can be used to determine the subjects' sleep preference (Chronotype). As the subjects are retired and don't use alarm clocks, their sleep preference (Chronotype) can be directly derived from their Midsleep on Free Days time (MSF), as described by

$$\mathrm{MSF} \triangleq 0.5\left(t_{\text{sleep onset}} + t_{\text{wake up}} - 24\,\mathrm{h}\right). \tag{19}$$

By combining the sleep diary data with actigraphy data recorded by the Actiwatches, each subject's sleep onset and wake up times were estimated by hand to form observation set Z. For example, for subject 17, the (partially shown) set is

$$Z = \left\{01{:}15,\quad 08{:}05,\quad 26{:}05,\quad 32{:}50,\quad 49{:}40,\quad \ldots,\quad 152{:}00\right\}. \tag{20}$$

In [8], the values for age-related parameters ν_{vc} and μ_H are suggested to be $\nu_{vc} \approx 2.35\,\mathrm{mV}$ and $\mu_H \approx 3.95\,\mathrm{nM\,s}$ for old age. However, analysis of the data showed that

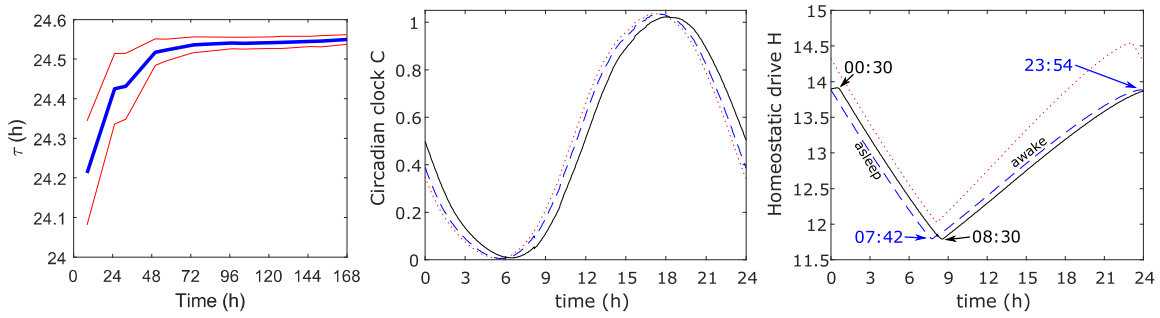

Figure 3: Particle filter output for subject 17 (male, 73 yr). The first graph shows the estimated intrinsic circadian period τ as a function of simulation time. The blue middle line shows the posterior mean and the red lines show the posterior standard deviation. The graph shows that τ converges to 24.55 h with an exponential curve. The second and third graphs show the circadian clock time C and homeostatic sleep drive H at day 7 of the collected data. Red dotted line: the original models with their original parameters. Blue dashed line: a particle filter(PF) with proposed parameters $\nu_{vc} = 2.9\,\mathrm{mV}$ and $\mu_H = 4.0\,\mathrm{nM\,s}$, only estimating the state. Black solid line: the proposed PF, estimating state and τ. The state-only PF estimates a small circadian phase delay of ~ 20 min, while the proposed PF estimates a more significant delay of ~ 60 min. This is reflected in the homeostatic sleep drive output: the estimated sleep onset/wake up times of the proposed PF are closer to the actual times observed with this subject: sleep onset at 01:29 and wake up at 08:12.

$\nu_{vc} = 2.9\,\mathrm{mV}$ and $\mu_H = 4.0\,\mathrm{nM\,s}$ best fit our data set, which we will use in our experiments. Further analysis of the data showed that the average initial state $\bar{\mathbf{x}}_0 = [\ 0.25\ -0.9\ -0.5\ 2.5\ -12\ 13.8\ ]^{\mathrm{T}}$.

The light data of each subject was individually processed by the particle filter, using the sleep-wake times as observation input. To illustrate the results, the proposed Particle Filter's output for subject 17 is shown and compared to prior methods in figure 3.

In [12], the MCTQ MSF has been associated with the intrinsic period of the circadian pacemaker τ. Therefore, we correlate the resulting posterior mean of the intrinsic period for each subject to that subject's MSF time using linear regression analysis. The results of two successive runs can be seen in figure 4. The Pearson correlation coefficient shows significant correlation with strength $r > 0.6$ and significance $p < 0.01$, which indicates that our proposed method can estimate the intrinsic period of the circadian pacemaker.

4 Discussion and Future Work

Our proposed method utilizes both input- (light exposure) and output (observation) data, which both contain information about the circadian rhythm of an individual. In our study we specifically use the observation set Z that contains natural sleep onset and wake up times of an individual from which we extract information indicating the actual circadian phase for this individual. At the same time, we also use this data to determine the subject's MCTQ MSF. This works well for our situation. However, the natural sleep-wake rhythm is disrupted in the case an individual uses an alarm clock: in that case we lose an important observation channel. In a test with a second dataset where the subjects were using alarm clocks, we did not find a significant correlation,

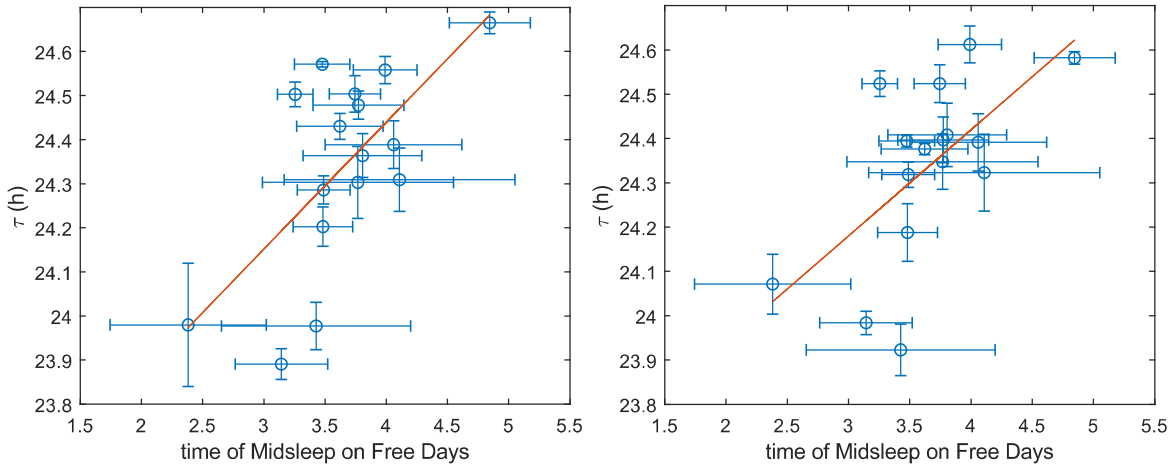

Figure 4: Two scatter plots showing the output of two sequential runs of the particle filter with the data from the study. The estimated intrinsic circadian period τ on the vertical axis is plotted against the MCTQ MSF time on the horizontal axis. For each of the estimated values, the standard deviation is shown as an error bar. The linear regression line is shown in red. The output of the sequential runs show that the particle filter will give a different result every run. This is caused by the stochasticity the underlying model. However, both runs show the correlation is significant: Pearson's $r = 0.66$ with $p = 0.005$ for the left plot and $r = 0.62$ with $p = 0.0099$ for the right plot.

which is intuitively appealing. It is a subject of our future research to find a suitable alternative input or output parameter that provides information on the circadian phase.

Our study shows that one can get a good estimation of model parameters even with a very limited number of particles. Adding more particles does not improve the results. This is surprising because we consider relatively many variables: In Mott, Dumont, Boivin, *et al.* [2] only the Kronauer model with 3 state variables is used. By including the Phillips and Robinson model and searching for τ, we add 4 more variables. This would suggest $(240)^{7/3} \approx 360000$ particles are needed. We believe that we can work with fewer particles because our initial state is very close to the actual state, because the homeostat model closely follows the circadian clock, and because the process noise (in $\mathbf{\Sigma_x}$) is chosen quite small. Hence, our particle filter barely has to put effort in finding the state. Most effort goes into finding τ, which is feasible with only a small number of particles. In further studies, we want to explore to what extent increased process noise degrades the particle filter results, or could even cause divergence. In such case more particles would be required.

Our tests revealed a statistical deviation of the parameters ν_{vc} and μ_H from the age-dependent model suggested by [8]. In fact, we saw difference between individuals of the same age. This can explain the mismatch between estimated- and actual sleep-wake times for instance shown in figure 3. Our results suggest that these parameters should preferably also be estimated for each individual and therefore should be included in $\boldsymbol{\theta}$.

The average estimated intrinsic circadian period τ for all participants in our population is around 24.4 h. This is notably higher then the mean of 24.18 h determined by Czeisler, Duffy, Shanahan, *et al.* [13] and comparable research. This can be coincidently related to the selection of our participants.

The time interval $\Delta t = z_k - z_{k-1}$ is not constant. As a result the process- and observation noise covariance matrices $\mathbf{\Sigma_x}$ and Σ_z depend on k. However, because under

normal conditions the expected time between two sleep onset or wake up times is 24 hours ($\mathbb{E}[z_k - z_{k-2}] = 24\,\mathrm{h}$), it is reasonable to assume the modeled noise is sufficiently accurate.

5 Conclusion

Existing mathematical models of the circadian rhythm often model the average response of physiological processes that control the human circadian rhythm, which does not represent the response for an individual. This can result in a misprediction of an individual's circadian phase. We have shown how a Particle Filter can estimate values for the model's parameters to fit an individual's physiological characteristics. We have illustrated this by applying a Particle Filter to a combination of two existing models: the Jewett, Forger, and Kronauer circadian pacemaker model and the Phillips and Robinson homeostatic sleep drive model. By processing individual light exposure- and actigraphy data from 16 human subjects with the proposed Particle Filter, we estimate the parameter τ representing the subject's intrinsic circadian period. When correlating the estimated parameter values to the subjects' MCTQ MSF time, a significant relationship was found: $r > 0.6$ and $p < 0.01$. This demonstrates that a Particle Filter can estimate the intrinsic circadian period of an individual with reasonable accuracy, which will allow us to make a more accurate prediction of the effect that a specific lighting setting will have on the circadian rhythm of that individual.

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References

[1] T. A. Bedrosian and R. J. Nelson, "Timing of light exposure affects mood and brain circuits", *Transl. Psychiatry*, vol. 7, no. 1, 2017.

[2] C. Mott, G. Dumont, D. B. Boivin, and D. Mollicone, "Model-based human circadian phase estimation using a particle filter", *IEEE Trans. Biomed. Eng.*, vol. 58, no. 5, pp. 1325–1336, 2011.

[3] J. Liu and M. West, "Combined Parameter and State Estimation in Simulation-Based Filtering", in *Seq. Monte Carlo Methods Pract.* A. Doucet, Ed., Springer Science+Business Media New York, 2001, pp. 197–223.

[4] M. S. Arulampalam, S. Maskell, N. Gordon, and T. Clapp, "A tutorial on particle filters for online nonlinear/nongaussian bayesian tracking", *IEEE Trans. Signal Process.*, vol. 50, no. 2, pp. 174–188, 2002.

[5] M. E. Jewett, D. B. Forger, and R. E. Kronauer, "Revised limit cycle oscillator model of human circadian pacemaker", *J. Biol. Rhythms*, vol. 14, no. 6, pp. 493–499, 1999.

[6] T. Woelders, D. G. M. Beersma, M. C. M. Gordijn, R. A. Hut, E. J. Wams, and A. Kota Gopalakrishna, "Daily Light Exposure Patterns Reveal Phase and Period of the Human Circadian Clock", *J. Biol. Rhythms*, vol. 32, no. 3, pp. 274–286, Jun. 2017.

[7] A. J. Phillips and P. A. Robinson, "A quantitative model of sleep-wake dynamics based on the physiology of the brainstem ascending arousal system", *J. Biol. Rhythms*, vol. 22, no. 2, pp. 167–179, 2007.

[8] A. C. Skeldon, A. J. K. Phillips, and D.-J. Dijk, "The effects of self-selected light-dark cycles and social constraints on human sleep and circadian timing: a modeling approach", *Sci. Rep.*, vol. 7, no. 45158, pp. 1–14, 2017.

[9] A. J. K. Phillips, C. A. Czeisler, and E. B. Klerman, "Revisiting Spontaneous Internal Desynchrony Using a Quantitative Model of Sleep Physiology", *J. Biol. Rhythms*, vol. 26, no. 5, pp. 441–453, 2011.

[10] A. A. Borbély, S. Daan, A. Wirz-Justice, and T. Deboer, "The two-process model of sleep regulation: A reappraisal", *J. Sleep Res.*, vol. 25, no. 2, pp. 131–143, 2016.

[11] T. Roenneberg, A. Wirz-Justice, and M. Merrow, "Life between Clocks: Daily Temporal Patterns of Human Chronotypes", *J. Biol. Rhythms*, vol. 18, no. 1, pp. 80–90, Feb. 2003.

[12] A. Hida, S. Kitamura, Y. Ohsawa, M. Enomoto, Y. Katayose, Y. Motomura, Y. Moriguchi, K. Nozaki, M. Watanabe, S. Aritake, S. Higuchi, M. Kato, Y. Kamei, S. Yamazaki, Y. I. Goto, M. Ikeda, and K. Mishima, "In vitro circadian period is associated with circadian/sleep preference", *Sci. Rep.*, vol. 3, pp. 1–7, 2013.

[13] C. A. Czeisler, J. F. Duffy, T. L. Shanahan, E. N. Brown, J. F. Mitchell, D. W. Rimmer, J. M. Ronda, E. J. Silva, J. S. Allan, J. S. Emens, D.-J. Dijk, and R. E. Kronauer, "Stability, Precision, and Near-24-Hour Period of the Human Circadian Pacemaker", *Science*, vol. 284, no. 5423, pp. 2177–2181, 1999.

Algorithm 1 Particle Filter for Intrinsic Circadian Period Estimation

Input: Light history I and sleep-wake times Z
Output: Posterior parameter mean: $\bar{\tau} = \sum_{i=1}^{N} w_k^{(i)} \hat{\tau}^{(i)}$

procedure ParticleFilter:
  for particle $i = 1, \ldots, N$ **do**
    Draw initial state: $\mathbf{x}_0^{(i)} \sim \mathcal{N}_6(\bar{\mathbf{x}}_0, \mathbf{\Sigma_x})$
    Draw initial theta: $\hat{\tau}_0^{(i)} \sim \mathcal{N}(24.18, (0.13)^2)$ (values from [13])
  end for
  foreach successive observation $z_k \in Z$ **do**
    for particle $i = 1, \ldots, N$ **do**
      Estimate mean state progression: $\boldsymbol{\mu}_k^{(i)} \leftarrow \mathbf{F}_k(\mathbf{x}_{k-1}^{(i)}, I; \hat{\tau}_{k-1}^{(i)})$
      Estimate observation: $\hat{z}_k^{(i)} \leftarrow \mathbf{h}(\boldsymbol{\mu}_k^{(i)})$
      Determine weight: $w_k^{(i)} \leftarrow \mathcal{N}(z_k | \hat{z}_k^{(i)}, \Sigma_z)$
    end for
    Normalize the weights: $w_k^i \leftarrow w_k^i / \sum_{j=1}^{N} w_k^j$
    Estimate posterior parameter mean: $\bar{\tau}_k = \sum_{i=1}^{N} w_k^{(i)} \hat{\tau}_{k-1}^{(i)}$
    Estimate posterior parameter covariance matrix: $V_k = \sum_{i=1}^{N} w_k^{(i)} (\hat{\tau}_{k-1}^{(i)} - \bar{\tau}_k)^2$
    for particle $i = 1, \ldots, N$ **do**
      Sample new index j from $\text{Multi}_N\left(w_k^{(1)}, w_k^{(2)}, \ldots, w_k^{(N)}\right)$
      Resample state: $\mathbf{x}_k^{(i)} \sim \mathcal{N}_6(\boldsymbol{\mu}_k^{(j)}, \mathbf{\Sigma_x})$
      Resample theta: $\hat{\tau}_k^{(i)} \sim \mathcal{N}(a\hat{\tau}_{k-1}^{(j)} + (1-a)\bar{\tau}_k, (1-a^2)V_k)$
    end for
  end for
end procedure