PsPM: Psychophysiological Modelling

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by the PsPM team[1]:

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Part I

Background

1 What is psychophysiological modelling?

1.1 The psychophysiological inverse problem

Psychophysiology is concerned with the relationship between the mind (i.e. psychological processes) and the body (including the nervous system). This relationship is bidirectional: the mind influences the body, and the body is monitored by the mind via proprioception and interoception.

A very common application of psychophysiological knowledge is to evaluate processes in the mind by their influence on the body. For example, we may observe skin conductance responses in order to infer a person's fear memory. This is an inverse problem. We are not actually interested whether skin conductance is different between a CS+ and a CS- (the forward relation). We are interested, in this example, in whether a person successfully learned the association between a conditioned stimulus (CS) and an electric shock, and we use skin conductance to tap into this latent variable. To make this inverse inference, we "turn the forward model around" - we ask, what has happened in the mind, given what is measured in the body. There are several way of doing this, and all require good knowledge of the forward relation.

1.2 Operational analysis

Operational approaches leverage data features that closely follow a latent variable of interest. Operational data analysis algorithms extract these data features, to "index" latent variables. For example, to infer fear memory from skin conductance responses (SCR), one may filter the SCR data to reduce observation noise, define a response window after the CS, define some criteria to detect peaks within this window, and a scoring algorithm to deal with overlapping SCR. The amplitude of such peaks may then be taken as "index" of SA. The development of these indices is an important application of psychophysiology. Such indices are usually based on qualitative or semi-quantitative models of how the index relates to the latent variable. Model-based analysis has precisely the same goal as operational analysis - but seeks to make these implicit models explicit (i.e. testable) in mathematical form - see [1] and [2] for reviews.

1.3 Model-based analysis

Model-based approaches start with explicit, mathematical models that formulate how observed data are generated by psychological processes. For example, a model may formulate the relation between fear-conditioned sympathetic arousal (SA) and skin conductance responses (SCR), $SA \mapsto SCR$, in mathematical form. This kind of model is often termed a "forward model": it predicts a data time series (SCR) from a known psychological process (SA). Another term for this kind of model is "generative", because it describes how a latent variable generates the data. When we analyse experimental data, we are faced with the opposite situation: we know the observed data data but not the latent variable, and seek to infer the latent variable from the data. In order to do so, we have to turn the forward model backwards, to arrive at the relation $SA \leftarrow SCR$. In statistics, this process is often termed "model inversion". It provides the most likely estimate of the latent variable, given the observed data and the model.

2 Method comparison

2.1 General

How can we evaluate whether one method of inferring a latent variable is better than another, when the true values of the latent variable are unknown? Classical validity theory provides us with metrics such as reliability or convergent/discriminant validity, but these require stable between-person variance in the latent variable to be meaningful [3], a condition which is frequently not met for those latent variables that can be inferred from psychophysiological measurements (such as fear memory). Furthermore, convergent validity frequently does not tell us which of a set of somewhat related measurement methods is more or less valid (such as two slightly different SCR scoring methods).

The solution we propose is to experimentally induce known values of the latent variable, and evaluate how well a method recovers these known states [4]. We term this approach"experiment-based calibration", and the correlation between measured and intended scores "retrodictive validity" [5]. One can show that measurement methods with higher retrodictive validity have lower measurement error. Thus, retrodictive validity is the metric that we seek to maximise with PsPM.

In the example of fear conditioning, we could express retrodictive validity simply as effect size of the CS+/CS- difference in the estimates; the method with higher effect sizes will have lower measurement error. Since we are assessing this in finite samples, a frequent follow-up question is whether one method is "decisively" more valid than another. This can be assessed with a formal model comparison.

2.2 Implementation

In our example, we can try to predict CS identity (CS+/CS-) from the model estimates. This means we quantify evidence for a model in which individual participants' CS+ and CS- estimates are drawn from two distributions with different means, rather than the same mean. In other words, we are using a regression model that seeks to predict the known latent variable (i.e. the experimental conditions) as dependent variable from the estimated latent variable. Note that this is different from a more conventional regression or ANOVA model in which the data are the dependent variable and experimental conditions are the independent variable. This difference is important. In our approach, the dependent variable (the true state) will always be the same, and the independent variable (the estimate of the latent variable) will differ between methods. This means that the total sum of squares (TSS) in the model will be constant. Thus, we can use the residual sum of squares (RSS) to compute model evidence and compare models - i.e. compare evidence for the statement that the method's estimates of the psychological state predict the true psychological state.

To quantify model evidence, we often use the following approximation to Akaike Information Criterion (AIC) [6]:

$$AIC = n \log (RSS/n) + 2k = -2 \log (L) + 2k,$$

where n is the number of data points in the predictive model, L is the maximum of the likelihood function, and k the number of parameters in the predictive model. k is constant for all methods that are evaluated in a methods comparison. We only interpret AIC differences, so this complexity term disappears from methods comparison. AIC differences divided by 2 can be interpreted as approximate log Bayes Factors (LBF). In our case this quantifies the relative evidence that one method's estimates predict the true latent variable, relative to the other method. An absolute LBF of greater than 3 is usually regarded as decisive. This is because for a classical significance threshold of $\alpha = .05$, the probability of the data given the null hypothesis is $p < .05$. Similarly, for an LBF difference larger than 3, the relative probability that the inferior method predicts the true psychological state given the data is $p < \exp (-3) \approx 0.05$ [7].

All methods included in PsPM have empirically been shown to provide better or equal retrodictive validity than the best available corresponding conventional index. Although in most validation experiments only two conditions need to be distinguished (a discrimination problem), the goal of PsPM is to provide minimum-variance estimates of a latent variable also in situations in which the latent variable varies across more than just two levels. Of course, this approach to method comparison can also be used to improve operational indices, or event to create new indices in a blind classification approach based on large data sets.

Historical remark: Some papers from the PsPM team have used the formula: $NLL = n \log (RSS/n)$. If NLL is read as an arbitrary variable name, this formula is consistent with the previous paragraphs. However, note that NLL in this formula is not the negative log likelihood (as confusingly implied in the papers), but really the AIC without complexity correction. The numerical value of the negative log likelihood would in this terminology be $NLL/2$.

3 General model structure

3.1 General

All models in PsPM split the relation between mind and body into two models, a peripheral and a neural model. The peripheral model describes how a neural impulse is converted to a measurable signal. The neural model describes the relation between the latent variable and the neural input into the peripheral system. This distinction is historically based on SCR models. The neural signal that elicits SCR can be measured by intraneural recordings [8], and its properties are in principle known. Hence it appeared plausible for various research groups to create a peripheral model [9, 10, 11] that takes an arbitrary neural input, and several neural models were then combined with this peripheral model. This distinction has later been used for other modalities, too: first because it appeared simple from a practical standpoint, secondly because it is often plausible to assume that the peripheral process is not directly influenced by psychological states, but only via a neural input. Note, however, that the peripheral/neural distinction in the model implementation is not always consistent with biophysical reality and tends to follow a need for manageable inversion algorithms. Indeed, some models collapse peripheral and stereotypical neural processes into the peripheral model. Examples are the GLMs for fear-conditioned HPR, PSR, and RAR - this is unlike the non-linear SCR model in which parameters of the neural model are estimated explicitly.

3.2 Peripheral models

The peripheral models in PsPM collapse all physiological and biophysical processes involved in the generation of the measured signal. For most psychophysiological measures, these processes are not known at the level of detail required to build true biophysical models from theory. In fact, biophysical models for the best-investigated modality, SCR, tend to not fit the observed data very well [12, 9]. This is why PsPM uses purely phenomenological models, which treat the peripheral system as a black box. By applying controlled inputs into the system, and measuring the output, one

can then approximate the workings of this black box in mathematical form, without knowing its content.

LTI systems

Crucially, all models in PsPM assume that the peripheral system can be described by one (or several) linear time invariant (LTI) systems with the defining properties linearity and time invariance. A LTI system is unambiguously described by its response function (RF). By linearity, input and output are linearly mapped so the responses to several inputs can be simply obtained by summing the responses to individual inputs. Time invariance means that the output does not explicitly depend on the time, i.e. that the shape of the RF is constant over time while the amplitude can vary. It is usually also assumed that the RF is constant over individuals, although this assumption is not necessary in the PsPM framework.

In principle, linearity ensures pure summation of two overlapping inputs. This is not realistic if the system has limited dynamic range and saturates due to a quick succession of inputs (e. g. the heart rate cannot increase indefinitely). One can formulate limits, for each data modality, within which the model is a useful approximation to reality.

For some modalities, the two properties linearity and time invariance can be explicitly tested by neural recordings (e.g. for SCR). For other modalities, this is not possible.

Mathematically, the output $y(t)$ of a LTI system can be fully described by convolving input $u(t)$ with the system's response function $h(t)$ and can be written as

$$y(t) = u(t) * h(t) = \int_0^\infty u(t - \tau)h(\tau)d\tau.$$

This is the equation for a linear filter.

> *Note:* Convolution is more generally defined by integration over $\mathbb{R}$. Integrating over $\mathbb{R}^+$ (or alternatively, setting $h(t) = 0, \ t < 0$) ensures the causal structure of the model - only past inputs can have an effect only into the future, not future inputs into the past. It also reflects the implementation via Matlab's vector convolution function (`conv`) in PsPM.

In many cases, the peripheral system is not exactly LTI but can be approximated by the combination of several LTI systems. The common case is the inclusion of RF derivatives to account for between-subject variability in RF shape and latency, and a special case the combination of a dilation and a constriction RF in pupil size modelling. In our terminology, the RF then has k "components": $h(t) = h_{1..k}(t)$.

In such cases, the amplitude estimates for several response functions need to be combined. In PsPM, this is usually (unless indicated otherwise) done by multiplying each component of the RF with its amplitude estimate,

and adding them. The peak of highest absolute amplitude is then identified, and its signed amplitude extracted as estimate of neural input amplitude.

Signal frequencies in the data that are not present in the RF do not contribute to the model inversion and can be filtered out. If the true RF were known, the matched filter theorem provides a way of theoretically deriving a filter that maximises the signal-to-noise ratio for the model inversion. In most cases, the true RF is not precisely known, and also varies between individuals. This is why PsPM seeks to empirically determine the filter characteristics that maximise retrodictive validity of psychological state estimates.

3.3 Neural models

The neural model in PsPM describes the form of the neural input that the peripheral model can take, and thus, the relation between mind and neural system. In general, model inversion benefits from constraining the neural model, i.e. from reducing the number of parameters that have to be estimated. We have empirically shown for SCR models that in many cases, a strongly constrained neural model will result in higher retrodictive validity [13, 14, 15].

Most PsPM models assume an instantaneous (delta) neural input into the peripheral system at a known time point t_i:

$$u\left(t\right) = \delta\left(t_i\right).$$

Only the amplitude of the neural input is then estimated, and is taken as estimate of the psychological state. This renders the model suitable for GLM inversion (see below). Less constrained models require non-linear inversion methods and can also deal with variable onset, dispersion, or shape, of the neural input.

3.4 Model inversion

3.4.1 Hierarchical summary statistic approach

It is common in psychophysiology (and psychology in general) to compute summary statistics for each cell of the design, and for each participant. These estimates of are then entered into a group-level model. To implement this approach, PsPM estimates parameters for each participant separately, either per experimental condition, or per trial. In line with fMRI terminology (and different from many branches of psychology), we use the terms "first-level" and "second-level" for the individual and group level.

3.4.2 Multi-level modelling

Multi-level models, also termed linear mixed effects model (LME) or random-effect models, are becoming increasingly popular in psychology [16]. The idea is to take variance between trials into account: a summary statistic that is computed from individual data points with high variance is less precise that a statistic from low-variance data, and such information is lost when averaging within each condition. PsPM offers the possibility to compute trial-by-trial estimates (by modelling each trial as a separate condition in GLM, or by default in DCM for SCR). This approach has been used for SCR, PSR and SEBR [17], see also [18] and [19]. For GLM, modelling trial-by-trial amplitudes and averaging within conditions yields the same result as modelling condition-by-condition amplitudes, if the design matrix is of full rank and if there is only one basis function. With more than one basis function, the results will deviate for the second and further basis functions in the basis set, because the orthogonalisation with the basis set is a nonlinear operation.

In theory it would also be possible to account for variability within the time series, i.e. between data points, not only between trials. Such approaches are implemented for fMRI, but they are not trivial. First, model inversion is much slower by the inclusion of many subjects. Secondly, in the time-series data analysed in PsPM, errors are usually not independent. This is usually not a problem for parameter estimation but impacts on the effective degrees of freedom and thus renders statistical tests in these models invalid, and this would apply to multi-level models, too. fMRI softwares solve this problem by estimating an auto-regression model on the first level but this is usually done on data from many data channels/voxels, and this is not possible for single-channel data in psychophysiology. This is why PsPM does not offer statistical tests on the time-series level. For the trial-wise or condition-wise summary statistic approach in PsPM, the dependencies between data points on the first level are unproblematic.

3.4.3 Probabilistic model inversion

All peripheral and neural models in PsPM are approximations to reality. It is hence assumed that there is measurement error (imprecision of the peripheral model) ε in the data, and that the neural input is not truthfully described by the neural model such that it contains latent error, ω. While this distinction between ε and ω is theoretically interesting and often physiologically plausible, the model inversion methods collapse these two sources of error:

$$y\left(t\right) = \varepsilon\left(t\right) + \left[u\left(t\right) + \omega\left(t\right)\right] * h\left(t\right)$$

$$= \varepsilon\left(t\right) + \omega\left(t\right) * h\left(t\right) + u\left(t\right) * h\left(t\right)$$

$$= \epsilon\left(t\right) + u\left(t\right) * h\left(t\right).$$

3.4.4   General linear convolution model (GLM)

Under the assumption of a delta neural model, we can harness GLM to estimate the neural input amplitude. A GLM can be written as

$$Y = X\beta + \epsilon.$$

Here, Y is the vector of observations (time series data), β is a vector of input amplitude parameters and ϵ is the error. X is design matrix in which each column is obtained by convolving impulse functions at known time points (e.g. event onsets for one condition) with each component of the RF. Each column takes the form:

$$X_{ij}\left(t\right) = u_i\left(t\right) * h_j\left(t\right),$$

where $u_i\left(t\right)$ is the neural input with unit amplitude for condition i, and j is the index of the RF component. Finally, X also contains a column for the intercept. It is possible to concatenate data from different experimental sessions, and an intercept is modelled for each session. The maximum-likelihood amplitude estimates are then computed using the Moore-Penrose pseudoinverse X^+, implemented in the Matlab function `pinv`:

$$\hat{\beta} = X^+ Y.$$

This allows to deal with situations in which X is not of full rank.

3.4.5   Non-linear model inversion

Models in which timing and/or dispersion of the neural input need to be estimated require non-linear model inversion. PsPM contains several efficient non-linear model inversion methods:

- a Variational Bayes (VB) algorithm [20] for dynamic systems. This can be applied either to an entire data set, or on a trial-by-trial basis, and requires the peripheral system to be written in the form of an ordinary differential equation (ODE).

- a Matching Pursuit algorithm that provides a fast approximation to the VB inversion for some models

4 Skin conductance (SCR) models

4.1 General

SCR arise from opening of sweat glands and are elicited via the sympathetic nervous system with negligible parasympathetic transmission (see [21] for the physiology of SCR). Nerve fibres carrying impulses to the sweat glands are termed "sudomotor nerve" (SN) fibres and can be measured by intraneural recordings. SN fibres are slow C-fibres. From their end terminal, the neurotransmitter Acetylcholine diffuses through the skin to reach sweat glands, a process on the time scale of up to a second.

The frequency and amplitude of SCR is mainly influenced by psychological arousal. Because not all forms of psychological arousal may influence SCR in the same way, we term the relevant psychological state "sympathetic arousal" (SA). Hence, the PsPM model is $SA \mapsto SN \mapsto SCR$.

4.2 Peripheral LTI model

4.2.1 Model evaluation

The peripheral LTI model can be evaluated explicitly (by intraneural recordings or stimulation) and implicitly (by assessing properties of the model $SA \mapsto SN \mapsto SCR$, an approach that collapses LTI violations with imprecision in the neural model).

Time invariance: the system's response does not explicitly depend on time, or in other words, a given input always produces the same output.

- Direct evidence: The amplitude of individual SN bursts is linearly related to the amplitude of ensuing SCR, with a considerable scatter [22]; to the maximal rate of sweat expulsion; and, somewhat more weakly, to the integrated sweat production during the skin response [23]. After initial dishabituation, constant SN stimulation leads to SCR, with constant amplitude and latency [24]. Repeated SN stimulation yields slightly different SCR shapes [25], although this could be due to variation in elicited neural responses that were not measured downstream. In summary, these findings are consistent with (but do not prove or disprove) the time invariance principle. [8] re-analysed data from an experiment in which brachial sudomotor neves were regularly stimulated under thoracic block and SCR recorded [24, 26]. They found that for stimulation rates below 0.6 s (1 stimulus every 1.7 s) around 95% of variance could be explained by an LTI model.

- Indirect evidence: We have shown that for short events (< 1 s duration) that are separated by at least 30 s, more than 60% of the variance in (high pass filtered) SCR can be explained under an LTI model, for aversive white noise bursts, aversive electric stimulation, aversive pictures, auditory oddballs, and a visual detection task [27]. Is this residual variance (40%) due to violations of the LTI assumptions? We have shown that in the absence of any event for 60 s, signal variance amounts to more than 60% of total variance during stimulus presentation. That is to say, by introducing events, residual baseline variance is reduced by 20%. This suggests that residual variance is not caused by violations of the time invariance assumption but variation of the neural input (for example, spontaneous fluctuations), and observation error.

Linearity: the system's response does not depend on previous inputs.

- Direct evidence: Latency of sweat expulsion is slightly shortened when sweat expulsion rate is very high (i. e. for very strong SN bursts) but not when SN firing is frequent [23]. SCR to individual SN stimulations depend linearly on skin conductance level, and are slightly suppressed upon repetition of the stimulation after 1 s [28]. This suggests that the linearity principle does not hold under all conditions. [8] re-analysed data from an experiment in which brachial sudomotor neves were regularly stimulated under thoracic block and SCR recorded [24, 26]. They found that for stimulation rates above 0.6 s (1 stimulus every 1.7 s), the response function looked very different from lower frequencies, suggesting non-linearities at that stimulation frequency. They did not quantitatively characterise these non-linearities.

- Indirect evidence: The linearity principle amounts to saying that SCR are not influenced by the (preceding) baseline signal. We tested this assumption by presenting two subsequent aversive white noise bursts with an inter stimulus interval (ISI) of either 2 s, 5.5 s, or 9 s, such that the baseline signal at these three time points differed markedly. Violations of the linearity principle in the peripheral system would imply that the amplitude of the subsequent response is dependent on the baseline signal, and thereby, upon the ISI. The second response was always smaller than the first. However, this was not dependent on the ISI, and hence not on the baseline signal. We interpret this effect as central repetition suppression (of the neural inputs into the peripheral system) and conclude that linearity is appropriate for the peripheral system. In other words, the peripheral response to one input is not modulated or affected by the response to another, even when they

overlap in time [27].

Model limits   Both properties appear good approximations to reality as long as the time interval between two SN firing bursts is not very short (< 2 s) or when the SN firing burst is not extremely strong. It would be possible to model non-linearities in a linear model, using Volterra kernels, as in the analysis of functional magnetic resonance images in the software SPM [29, 30]. Such possibility is however not implemented in PsPM.

4.2.2   Skin Conductance Response Function (SCRF)

The peripheral model in its general form does not specify a particular form of the SCRF. There are three principled ways of defining a SCRF in PsPM:

1. Individual response function. The most precise option is to measure the SCRF for each individual by providing brief inputs into the peripheral system and measuring the response. PsPM allows specifying individual response functions. The benefit of this approach has not been empirically tested.

2. Canonical response function. The most parsimonious method is to use a so-called canonical SCRF which is assumed to be constant across individuals. We have previously shown that a canonical SCRF can explain on average 50% of the variance in individual SCR elicited by various stimuli, while individual SCRFs explain about on average 75% of the variance [27]. Using a canonical SCRF, linear and non-linear models show a good retrodictive validity, superior to peak-scoring methods [13, 15].

3. Constrained response function. One can estimate an SCRF from the data of an actual experiment and use this for analysis. It is usually necessary to constrain the shape of the SCRF to make the model estimable. PsPM provides two options for this:

   • In GLM, one can estimate parameters of the (orthogonalised) time derivative of the SCRF. In order to combine this with the canonical SCRF, the response can afterwards be reconstructed for each experimental condition, and the peak amplitude taken as estimate of SA. This approach has higher retrodictive validity than using the canonical SCRF alone, or using a less constrained SCRF (canonical with time and dispersion derivative) [13].

   • In the non-linear model for event-related SCR, one can use the combined data from all evoked responses from one individual to estimate an SCRF. This approach only considers data within the inter-trial interval. In a validation experiments study with ITI of 7-11 s, this had lower

retrodictive validity than using the canonical SCRF, and we would not recommend it unless the ITI is longer than 20 s, so that the SCRF tail can be unambigouosly estimated [15].

Canonical Skin Conductance Response Function   The canonical SCRF that is currently implemented was derived from a large dataset of 1278 SCRs from 64 individuals subjected to different experimental manipulations (white noise 85 dB and 95 dB, painful electric stimulation, aversive IAPS pictures, detection of auditory oddballs, detection of a visual target in a stimulus stream). We extracted and mean-centred the 30 s following each stimulus onset and performed a principal component analysis. The first principal component served as empirical SCRF [27].

Formulation for linear models   The first PCA component of the empirical SCRF was approximated was fitted by a Gaussian smoothed bi-exponential function (also named bi-exponentially modified Gaussian function), and this provided better fit than other function categories, in particular Gaussian smoothed monoexponential function, exponential-Gaussian hybrid function, or smoothed sigmoid-exponential function. The function is thus defined as

$$h\left(t\right) \propto \int_0^t N\left(t-\tau\right)\left(E_1\left(\tau\right)+E_2\left(\tau\right)\right)d\tau \, , \, t \geqslant 0, \tag{4.1}$$

$$N\left(t\right) = \frac{1}{\sqrt{2\pi}\sigma}e^{-(t-t_0)^2/2\sigma^2},$$

$$E_i\left(t\right) = e^{-\lambda_i t},$$

with estimated parameters: $\hat{t}_0 = 3.0745$ seconds for peak latency; $\hat{\sigma} = 0.7013$ for definition of the rise time; $\hat{\lambda}_1 = 0.3176$ and $\hat{\lambda}_2 = 0.0708$ to define the two decay components. This function is normalised to its maximum such that an infinitely short SN impulse with unit amplitude elicits an SCR with unit amplitude. This renders parameter estimates from linear models easily interpretable in relation to conventional (peak-scoring) analysis.

Historical remarks:

(a) The appendix of [13] contains a typographic error in the definition of the canonical response function, in particular in the integration limits of eq. (4.1). However, in all versions of the software (PsPM 1.0-now) the canonical SCRF was constructed using the Matlab function `conv()` which defines vector convolution analogous to the integral defined above. This implementation has not changed since the initial formulation of the model.

(b) The initial formulation of the SCRF [10] used a Gaussian-smoothed Gamma distribution, based on a smaller dataset. In the extended data set published in [13], the polynomial part of the Gamma distribution was estimated to be one, resulting in a Gaussian smoothed exponential function.

Formulation for non-linear models   An alternative formulation is provided for non-linear models which require a definition of the SCRF in the form of an inhomogeneous ordinary differential equation (ODE). We use an third-order linear ODE to describe the data $y(t)$:

$$\dddot{y} + \vartheta_1 \ddot{y} + \vartheta_2 \dot{y} + \vartheta_3 y - u(t - \vartheta_4) = 0; \tag{4.2}$$

where dot notation is used for time derivatives, and this formulation embeds convolution of the SCRF with the SN time series. Parameters were estimated from the empirical SCRF by using a Gaussian bump as canonical SN input (see section on SN below) as $\hat{\vartheta}_1 = 1.342052$, $\hat{\vartheta}_2 = 1.411425$, $\hat{\vartheta}_3 = 0.122505$, $\hat{\vartheta}_4 = 1.533879$. Amplitude of the response function is rescaled such that a canonical Gaussian bump SN impulse with unit amplitude elicits an SCR with unit amplitude.

Formulation for spontaneous fluctuations   For modelling spontaneous fluctuations (SF), a different database was used that contained 1153 semi-automatically detected SF from 40 male participants [31] The first PCA component was taken as empirical SCRF which has slightly different shape than the empirical SCRF for evoked responses. A number of reasons may account for this difference, from participant selection over data pre-conditioning to differences in the canonical SN input. In the absence of further knowledge about the reason for this difference, we propose to use this empirical response function for SF. We estimated the ODE parameters (eq. 4.2): $\hat{\vartheta}_1 = 2.1594$, $\hat{\vartheta}_2 = 3.9210$, $\hat{\vartheta}_3 = 0.9235$, $\hat{\vartheta}_4 = 1.533879$ seconds. Amplitude of the response function is rescaled such that a canonical Gaussian bump SN impulse with unit amplitude elicits an SF with unit amplitude.

Note: In the Matlab implementation, the third order ODE is converted to a 3-dimensional system of first-order ODEs. In that process, the order of the parameters $\vartheta_{1..3}$ is reversed, and they are renamed. With substitutions $y_1 = y$, $y_2 = \dot{y}$, $y_3 = \ddot{y}$, the ODE becomes:

$$\begin{aligned}
\dot{y}_1 &= y_2 \\
\dot{y}_2 &= y_3 \\
\dot{y}_3 &= -\vartheta_1 y_3 - \vartheta_2 y_2 - \vartheta_3 y_1 + u(t - \vartheta_4)
\end{aligned}.$$

4.3   Neural model and model inversion

4.3.1   Physiological evidence

[8] recorded from C-fibres in the superficial branch of the common peroneal nerve proximal to the ankle, while participants heard loud sounds, or

responsed to oddball sounds. They found that the average SN response was well described by a Gaussian bump with 0.25 - 0.30 s standard deviation. PsPM models SN bursts as a Gaussian bump with 0.30 s standard deviation.

4.3.2 General Linear Model (GLM) for evoked SA

This model was developed for experiments in which short experimental events with evoke SA with amplitude a. For each experimental condition i with onset vector t_{o_i}, we assume $u_i(t) = a_i \delta(t_{o_i})$. See 3.4.4 for details on the model inversion.

4.3.3 Non-linear model (DCM) for event-related SA

This model [32] assumes that event-related SA with amplitude a causes a Gaussian bump-like SN firing burst after some delay and with a specified dispersion. For each experimental event:

$$u_{exp}(t) = a \exp \frac{-(t - \mu)^2}{2\sigma^2} + \omega, \ 0 < \mu < \mu_{max}, \ \sigma_{min} < \sigma < \sigma_{max}.$$

For situations in which short external stimuli elicit SA, this model uses a canonical central burst latency of zero and dispersion of $\sigma_e = 0.3$ seconds ("fixed response"). For situations in which central processes translate SA into SN with unknown parameters, latency and dispersion are estimated from the data, alongside the SA amplitude, using the following constraints: $\sigma_{min} = 0.1$, $\sigma_{max} = 0.5\mu_{max}$ where μ_{max} is the maximally allowed response latency ("flexible response").

The full model also accounts for spontaneous fluctuations (next subsection) and baseline changes between trials and can be written as:

$$y(t) = y_{exp}(t) + y_{SF}(t) + y_{SCL}(t) + \epsilon$$

The SCR components are defined by eq. (4.2) with respective parameters and a respective input function $u(t)$. Specifically, the experimental SCR component models evoked and event-related responses, and the SF component models spontaneous fluctuations between trials (part of the latent error). The SCL term is an explicitly modelled error term that absorbs baseline fluctuations and is defined as

$$u_{SCL}(t) = a \exp \frac{-(t - \mu)^2}{2\sigma^2}, \ \sigma = \sigma_0$$

where dispersion is set to $\sigma_0 = 1.0$ seconds, and μ is estimated from the data. By default, PsPM automatically mdoels SN bursts that occur more than 5 s after the previous trial, and more than 2 s before the next trial. These limits ensure that the modelled SCL and SF do not absorb variance

caused by the experiment. The use of different limits has not empirically been tested.

In this model, the parameter space is too large to invert it at once. Inversion is done in a trial-by-trial approach: a number of trials, $T_{1..n}$ is inverted. The ensuing parameter estimates for T_1 are extracted, and the parameter estimates for $T_{2..n}$ are used as prior values for the next inversion for trials $T_{2..n+1}$ where the estimated hidden state values at the start of trial 2 are taken as starting values of the hidden states x. This is continued until all trials have been estimated. This scheme ensures that inversion is kept tractable, and at the same time overlapping responses are taken into account. It also means that estimation errors accumulate over trials which is why part of the latent error is explicitly modelled as SF and SCL. At an inter trial interval of around 10 seconds, inverting 2 or 3 trials at the same time yields comparable retrodictive validity [15].

4.3.4   Non-linear model for tonic SA (spontaneous fluctuations, SF)

Spontaneous SN bursts cause spontaneous fluctuations (SF) in skin conductance. The number of spontaneous SN bursts is thought to depend on SA. Each spontaneous SN burst is modelled as a Gaussian bump with unknown timing and amplitude and fixed dispersion. For each spontaneous SF burst:

$$u_{SF} = a \exp \frac{-\left(t - \mu\right)^2}{2\sigma^2} + \omega, \ \sigma = \sigma_0, \ a > 0$$

The dispersion is set to $\sigma_0 = 0.3$ seconds. This model is inverted using a Variational Bayes algorithm [33, 20]. Because the number of SN bursts is difficult to estimate directly, the SF model inversion uses a fixed rate of SN bursts (set to $f = 0.5$ Hertz by default) the amplitude of which is estimated from the data. An amplitude threshold is defined to separate "true" SN bursts from noise. An amplitude threshold of 0.1 µS rendered the predictive highest validity in a validation paper [34]. The results from this paper have been replicated in an unpublished re-analysis using AIC as objective function in a manner similar to [13]. Re-analysing the second data set described in [34], the optimal threshold was between 0.15 - 0.20 µS. Further systematic research is needed to fine tune the optimal threshold.

Furthermore, PsPM uses a Matching Pursuit (MP) algorithm as fast (< 1 s per minute of data) approximation to the DCM inversion (ca. 1 min. per minute of data). Using simulated data, this method was less precise, but empirically it was comparable to DCM results in three different data sets [35].

4.4 Data conditioning

4.4.1 Filtering

Skin conductance signals return to a baseline after an SCR, but this baseline can change over time within a large dynamic range. Such fluctuations of the skin conductance level need to be filtered out to make the data accessible to an LTI model. A unidirectional 1st order Butterworth high pass filter with cut off frequency 0.05 Hz was optimal for GLM [13]. The design matrix of the GLM is filtered with the same frequency to account for distortions of response shape. For the non-linear model (DCM) for event-related responses, an optimal filter frequency was found at 0.0159 Hz when using a canonical SCRF and inversion of 2 trials at the same time [15]. Filter characteristics of SF models have not been investigated. In order to reduce computation load, data are resampled to 10 Hz sampling rate for all data analyses which requires a low-pass filter cut off frequency of 5 Hz.

Historical remark: The SCRF was developed using a high pass filter with cut off frequency of 0.0159 Hz as commonly employed in conventional analysis (bidirectional for phasic responses, unidirectional for spontaneous fluctuations). However, this turned out to not be the optimal filter for GLM in follow-up analyses of optimal data conditioning. Note that the canonical SCRF was developed from data filtered with the original settings, and this has not changed since.

4.4.2 Normalisation

For within-subjects analysis, we propose data normalisation after filtering to remove SCR scaling differences due to peripheral factors such as skin property. This increases retrodictive validity (unpublished analyses). For methods that yield trial-by-trial estimates, post-hoc normalisation of amplitude estimates across trials, before averaging within conditions, yields even better retrodictive validity [15]. For between-subjects analysis, this is not an option as it removes between-subjects variance.

4.5 Implicit estimates of tonic sympathetic arousal

Our model for SF implies that

$$\int_I \left[y\left(t\right) - y_0\right] dt \propto \sum_{i=1}^{n} a_i$$

where I is a time interval, and $a_{1..n}$ are the amplitudes of the n sudomotor bursts in this interval and y_0 is the skin conductance level at rest. That is, by simply taking the time integral, or area under the curve (AUC), of the

baseline-corrected data, we get a measure of the number x amplitude of spontaneous SN bursts [31]. This measure is implemented in the software as well. However, we have subsequently shown that the number of spontaneous SN bursts is a better predictor of tonic SA than AUC, and hence we recommend to use the non-linear model for tonic SA.

4.6   Comparison with other model-based methods for SCR

Several further approaches to model-based analysis of SCR have been introduced in the literature [36, 9, 11, 12, 37] - for one of them, the implementation is publicly available in the software package Ledalab. In this method, SN is calculated from SCR using a deterministic inverse filter. Peaks in the SN time series are then identified and used as operational index of SA. In a head-to-head comparison, retrodictive validity to identify states with known SA was compared for experiments involving short stimuli and evoked SA. PsPM had better retrodictive validity than Ledalab in 4 out of 5 tested contrasts, and equal validity in the fifth. Ledalab did not consistently perform superior to classical peak scoring analysis [14].

4.7   Recommendations

- Experimental design:

    – SOA > 2 s between events eliciting SCR. SCR amplitudes appear to be linear with an SOA of 3.5 s between subsequent stimuli [27] and non-linear with SOA < 1 s [28].

- Model set up:

    – Use GLM wherever possible. GLM is more sensitive than non-linear models in evoked SCR paradigms [13].

    – Use default filter frequencies (0.05 - 5 Hz unidirectional filter for GLM [13]; 0.0159 - 5 Hz bidirectional filter for non-linear model [15]). In case of sparse SCR (e.g. in paradigms with long ITIs), the bidirectional filter can distort the signal to an extent that it becomes difficult to model. In such cases, it might be preferable to use a unidirectional filter (see e.g. [38])

    – GLM: include all experimental events that evoke SCR (including block starts, break messages, etc.).

    – GLM: canonical SCRF with time derivative and reconstruction of amplitudes is more sensitive than just canonical SCRF, or SCRF plus time and dispersion derivative [13]. The benefit of subject-specific SCRFs has not been tested.

- **non-linear model:** canonical SCRF is more sensitive than using subject-specific SCRFs based on short ($\sim$ 10 s) ITIs [15]. The use of individual SCRFs based on long ITI paradigms has not been tested.

- **non-linear model:** for fear conditioning paradigms, the best way of modelling anticipatory SCR is currently under investigation. It is possibly suboptimal to model one anticipatory "flexible" response, in particular at longer CS/US SOAs when this flexible response may absorb SCR elicited by US or US omission. See e.g. [38, 39]

- **GLM and non-linear model:** z-normalisation of data is recommended for within-subjects designs, and should not be used for between-subjects designs.

- Model inversion:

  - **SF model:** the VB inversion is theoretically better suited than the MP inversion when the expected number of SF is > 10/minute [40].

- Post-processing

  - **non-linear model:** trial-by-trial normalisation of amplitude estimates before averaging within conditions can increase sensitivity in within-subjects designs [15] but should not be used in between-subjects designs.

5 Heart Period Response (HPR) Models

contributed by Philipp C. Paulus and Giuseppe Castegnetti, and edited by Dominik R. Bach

5.1 General

Cardiac rhythm is generated locally in the sinoatrial node, but is modulated by central neural input. Therefore, heart rhythm can be used to infer psychological states. To quantify phasic changes in cardiac chronotropy, two measures are common: heart rate (beats per minute) or heart period (milliseconds). Heart period appears to relate to autonomic input linearly, as revealed in experiments in which autonomic nerves in rodents were electrically stimulated with varying frequencies to elicit heart period changes [41]. This is why PsPM models heart period. Heart period information is

only available at discrete time points. To facilitate analysis within the existing algorithms, PsPM assigns each heart period to its following heartbeat and linearly interpolates this time series at 10 Hz resolution.

For the analysis of event-related, i.e. phasic cardiac responses, PsPM includes two models: A model for event-related HPR [42] and a model for fear-conditioned bradycardia [43]. As in previous models for SCR, both models are optimised with regard to *retrodictive validity*, i.e. the ability to separate experimental conditions (e.g., CS+ vs. CS-).

Operational analysis has shown that event-related HPR pattern strongly depends upon properties of the input - i.e. modality, intensity and presentation duration of the stimulus material. It follows that both models can only be applied in experiments with similar conditions, including stimulus presentation times (i.e. ≤ 1 s for event-related HPR). Pharmacological studies have suggested a differential time course of sympathetic and parasympathetic nervous input, but it is not yet known how this maps onto the response components modelled here.

5.2   Peripheral and neural model

In the absence of information on the time course of cardiac information, it is difficult to separate a neural and a peripheral model. Hence, these two are collapsed for the purpose of quick and simple inversion with GLM (see 3.4.4). This means that the implemented models - for evoked HPR and fear-conditioned or reward-conditioned HPR - use a different RF, although of course the peripheral system is the same in both cases. Castegnetti et al. [43] relate the two models to each other, and derived the neural input producing fear-conditioned bradycardia (see figure 1 of [43]).

5.3   Model for event-related HPR

The model for event-related HPR [42] was developed on data from 84 participants that underwent three different experiments: An experiment using loud white noise sounds ($\sim 85dB$), an experiment using an auditory oddball task, and an experiment using emotional pictures from the International Affective Picture System (IAPS; [44]). All stimuli were presented with long ITIs (> 30 s) to allow the cardiac system to return to baseline after stimulus presentation and avoid overlapping responses. The first three principal response components were extracted, and individual peaks fitted with Gaussian Functions as RF:

$$h\left(y\right) = \frac{1}{\sigma\sqrt{2\pi}}e^{\frac{-(t-\mu)^2}{2\sigma^2}} \tag{5.1}$$

To test whether a modeled peak qualified as a RF, we tested whether it explained interesting variance in the data. We started with a single RF and included further RFs. Specifically, we created a first-level GLM for each

participant by convolving the event onsets with the specific subset of RFs, and extracted estimates of the response amplitudes for each RF and condition from the continuous heart period data. In order to qualify as RF, parameter estimates for this RF were either required to depict a stable response (i.e., acceleration or deceleration) across all experiments, tested by a one-sample t-test, or to add to the *retrodictive validity* of the model. This second criterion was evaluated by subjecting the parameter estimates to a between-subject analysis of variance (ANOVA) testing for a main effect of experimental condition.

Hence, the following steps were taken:

Step 1. Test all potential RFs modeled from PCs individually and retain each single RF if it depicts a stable acceleration or deceleration across all experiments or if it allows separation of at least two of the three experiments. All potential RFs fulfilled one of these criteria.

Step 2. Take the chronologically first RF from Step 1 and combine it with the chronologically second RF from Step 1, or with any other RF that overlaps with this second RF. Orthogonalize each set in temporal order, using a Gram-Schmidt algorithm. Retain the best set if additional RFs allow the separation of the three experiments.

Step 3-5. Take the current set, and add the chronologically next untested RF from Step 1, or any other RF that overlaps in time with this second RF. Repeat the strategy of Step 2, and retain the best set if additional RFs allow the separation of the three experiments.

This testing procedure yielded a basis set of six RFs. Model constants are depicted in Table 1.

In an independent model-validation experiment with short ISI (10 s) that used white-noise sounds of varying intensities ($\sim$85 vs. $\sim$65 dB) and both negative and positive pictures from the International Affective Picture System (IAPS; [44]), the following RFs allowed separation of the different experimental conditions:

RF1 allowed the discrimination of 85 dB white-noise sounds and IAPS pictures as well as Positive and Negative IAPS pictures. RF2 allowed the discrimination of 85 dB and 65 dB white-noise sounds, as well as Positive and Negative IAPS pictures. RF3 allowed the discrimination of Negative and Positive IAPS pictures. RF4 did not allow discrimination of any experimental conditions in the validation experiment, but showed a trend to significance for the discrimination of 85 dB white-noise sounds and IAPS pictures ($p = .051$) and a trend for discrimination of Positive and Negative IAPS pictures ($p = .068$).

Because the data are interpolated, apparent responses to stimuli can start before stimulus presentation. This is evident in these RFs some of which overlap time point 0 and therefore start before the actual stimulus.

Table 1: Model constants for evoked HPR

Response Function (RF)	Parameters of Gaussian Function	
	μ	σ
1	1.0	1.9
2	5.2	1.9
3	7.2	1.5
4	7.2	4.0
5	12.6	2.0
6	18.85	1.8

Note. μ =mean; σ = standard deviation

In PsPM this phenomenon is automatically accounted for.

5.4 Model for fear-conditioned HPR

For the analysis of fear-conditioned HPR, we sought to build a data-driven RF for discriminating between HPR to CS+ and CS- [43]. This model-based analysis was developed on the basis of four independent data sets, acquired during diverse implementations of a fear conditioning protocol. The shape of the response was determined by visually identifying a gamma distribution as the function that qualitatively best resembled the difference between grand means. This function

$$y = \frac{A}{\theta^k \Gamma(k)}(x - x_0)^{k-1} e^{-\frac{x-x_0}{\Theta}} \tag{5.2}$$

was fitted it by finding the values of the shape parameter k, the scale parameter θ, the time onset x_0 and the amplitude A that minimised the residual sum of squares (RSS). The resulting parameters were $k = 1373$, $\theta = 0.0311$, $x_0 = -38$, with A left free to vary during the model inversion. Shifts in the response are modelled by its first time derivative. The ensuing model-based analysis reliably distinguishes HPR to CS+ and CS-, and does so significantly better than model-free analogues (e.g., peak scoring, area under the curve).

5.4.1 Adaptation to different SOAs

By considering fear conditioning sessions with different SOAs between CS and US, we investigated how this changes the anticipatory response. Our analysis suggested that for different SOAs the anticipatory HPR is time-locked to the US, with no changes in shape. This can be modelled by time-locking the RF (developed for 3.5 s) to the US. In PsPM, the default SOA

is 3.5 s, and it can be modified to assume any positive value. However, we recommend not using SOAs shorter than 2 s. This procedure has been successfully tested with SOAs of 4 [43] and 6 s [45].

5.5   Model for reward-conditioned HPR

For analysis of reward-conditioned HPR with an SOA of 5 s, we built a response function on an exploration data set and validated it on a confirmation data set [46]. The RF caputured responses observed during acqusition, as well as during retention 7 days later. The RF implemented in PsPM was updated on the combined data set. Parameters for eq. (5.2) were estimated as $k = 171.6$, $\theta = 0.1400$, $x_0 = -17.60$, with A left free to vary during the model inversion.

5.6   Data Conditioning

5.6.1   Heart beat detection

PsPM uses a modified offline version of the Pan & Tompkins [47] QRS detection algorithm. The algorithm analyses slope, amplitude, and width of QRS complexes. It uses digital band-pass filters to reduce noise and its thresholds are periodically adjusted to low values. The algorithm works best on data with a time-resolution of 200 Hz. Data with higher sampling rate will automatically be downsampled to the optimal time-resolution. The QRS complex is marked at the rising edge of the integrated waveform signal that usually corresponds well with the position of the R-spike of the ECG.
For the offline version of the Pan & Tompkins QRS detection algorithm some adjustments were made:

- The originally used cascaded integer filters were replaced by a second order Butterworth filter that approximates the desired passband from 5 to 15 Hz better than the original filters.

- To increase detection accuracy heart rate values were restricted to the interval of 20 bpm (IBI of 3000 ms) to 300 bpm (IBI of 300 ms).

- To allow for a manual inspection and possible correction of detection failures, the ECG editor allows visually inspecting the results of QRS detection.

Depending on the quality of the recordings, QRS detection can achieve a very high accuracy in detecting QRS complexes of up to 99.66% [42].

PsPM also contains a QRS detection algorithm for ECG data acquired in MRI environments. The algorithm is described in [48]. The implementation is obtained from the software link given in the paper. To process pulse oxymetry data, PsPM contains a template matching algorithm [43] and an interface to the HeartPy toolbox [49].

5.6.2 Interpolation and Filtering

To transform the discontinuous heart-beat information into a continuous signal of heart-period, the heart-beat events are interpolated at a fixed sampling rate of 10 Hz using the built-in function `pspm_hb2hp`. The interpolation shifts some early evoked responses such that they appear to start before an event - this is automatically being taken care of by a response function that starts slightly before an event definition.

Before obtaining parameter estimates for the individual response functions the interpolated heart beat time-series is filtered with a second-order Butterworth band-pass filter. For evoked HPR, PsPM uses a pass band of 0.01-2 Hz [42]. For fear-conditioned HPR, PsPM uses a 0.015-0.5 Hz bidirectional 4th order Butterworth filter (cf. [43]).

5.7 Recommendations

- Experimental design:

    - evoked HPR model: use only those RFs that peak within the SOA between subsequent events that elicit an HPR. A formal test of the linearity assumption has not been done yet. Therefore, the number of RFs that can be applied depends upon the SOA.

    - fear-conditioned HPR: use default model for CS/US-SOAs between approximately 2-8 s. The model is tested for 3.5 - 6 s.

    - reward-conditioned HPR: use default model for CS-US-SOA of around 5 s. The model is tested for 5 s.

- Model set up:

    - Use default filter frequencies (0.01 - 2 Hz unidirectional 2nd order Butterworth filter for evoked HPR [42]; 0.015 - 0.5 Hz bidirectional 6th order Butterworth filter for fear- and reward-conditioned HPR [43, 46], although there is apparently no strong impact of filter frequency.

    - Fear-conditioned HPR: using first derivative and reconstructing response amplitude is more sensitive that using just the canonical RF [43].

6 Pupil size response (PSR) models

contributed by Christoph W. Korn

6.1 General

Pupil size is under control of two antagonistic muscles [50]: Dilation (mydriasis) results from sympathetic inputs on the M. dilatator pupillae. Constriction (miosis) results from parasympathetic inputs on the M. sphincter pupillae. Pupil size reacts to changes in illuminance (light falling onto the eye, directly related to the luminance of screen presentations). It also responds to many cognitive processes including attention, perception, memory, and emotion (see [51] for references). Such cognitive processes are supposed to be relayed via the Edinger-Westphal nucleus and noradrenergic inputs into the locus coeruleus, among others [50]. On the basis of two experiments that elicited (il)luminance changes, we have developed a model for steady state pupil size and, more importantly, an model for changes of pupil size that is based on two LTI systems. These LTI systems can be harnessed to infer the neural input into the pupillary system that is elicited by cognitive processes (under the assumption of a common final pathway of (il)luminance-mediated inputs and cognitive inputs). We have also developed and validated a specific LTI system that allows distinguishing responses to CS+US- and CS- in fear-conditioning setups employing different sensory modalities and timings [52]. In this latter model, neural and peripheral system are collapsed for the purpose of quick and simple inversion with GLM (see 3.4.4).

6.2 Model for pupil size changes elicited by (il)luminance changes

The system controlling pupil size is non-linear. To be able and use linear methods for analysis, PsPM splits the model into several parts.

6.2.1 Model for steady-state pupil size

An exponential function is used to relate illuminance (in$[lx]$) or luminance (in$\frac{cd}{m^2}$) to steady-state pupil size (in arbitrary units as determined by the Eyelink system or in mm). These functions were specified on the basis of the first experiment described in [51] (see **??**). The functional relationship should cover the (il)luminance range employed in most cognitive experiments.

$$d(E_v) = C + A \exp(BE_v).$$

Here, d is the z-scored steady-state pupil diameter and E_v is the respective illuminance level in (in $[lx]$). We obtained the following parameter values: $A = 49.79$; $B = -0.50[\frac{1}{lx}]$; $C = -1.05$. Whether the non-linearity occurs in the peripheral or neural system is currently not known. An extension that is similar to our model within the (il)luminance range specified in our experiments, but extends across a wider range, can be found in [53].

6.2.2 Model for pupil dilation/constriction

Dilations and constrictions differ in shape, and can thus not be modeled by a single LTI system (which would assume that positive and negative changes do not differ in shape but just in sign). Hence, we identified a combination of two LTI systems that provide a good approximation of pupil size changes elicited by (il)luminance changes (see first two experiments in [51]). The first LTI-system describes changes to continuous (il)luminace inputs and the second LTI-system models the difference between constriction and dilation. The second system thus receives a brief input for any increase in (il)luminance. Both systems are specified by canonical response functions that take the form of gamma probability density functions.

$$d(t) = c\frac{(t - t0)^{k-1}\exp(-(t + t0)/\theta)}{\theta^k\Gamma(k)}$$

where d is the z-scored steady-state pupil diameter, t is time, Γ is the gamma function, and k, θ, c and $t0$ are free parameters. The fitted parameter values were: System 1: $k = 2.40$, $\theta = 0.29s^{-1}$, $c = 0.77$; System 2: $k = 3.24$, $\theta = 0.18s^{-1}$, $c = 0.43$. Since the latency of the empirical responses was around 200 ms, $t0$ was set to 200 ms prior to fitting. (We also modelled the first system with a Gaussian smoothed biexponential function; $d(t) = aN(t)*(E_1(t)+E_2(t))$; where $*$ is the convolution operator; $N(t)$ is a centered Gaussian function $N(t) = (2\pi\sigma)^{-0.5}\exp(-t^2/2\sigma^2)$ and $E_1(t)$ and $E_2(t)$ are exponential functions of the form $E(t) = \exp(-\lambda t)$; parameter values: $\sigma = 0.27$, $\lambda_1 = 2.04s^{-1}$, $\lambda_2 = 1.48s^{-1}$, $a = 0.004$).

In GLM-based analyses, these systems explain considerable variance in pupil size time series in two experiments with (il)luminance inputs of long and short duration (with the second LTI system being particularly relevant for brief, i.e., sub-second, inputs). The modeled pupil size time series can be easily specified given a time series of (il)luminance values (see **??**). These time series can be used as nuisance regressors in GLMs. Because the end stage of the pupil system does not depend on where the neural input comes from, the specified canonical response functions can also be used to estimate the shape (i.e., the temporal characteristics) of likely inputs into the pupillary systems for cognitive tasks. We provide examples for this for auditory oddball tasks with three different timings, for an emotional words task, and for a visual detection task (see [51]).

6.3 Model for pupil size changes elicited by fear conditioning

This model collapses peripheral and neural processes into one RF, in order to use GLM for the inversion. On the basis of four experiments employing simple and complex auditory, visual, and somatosensory CS, we have

determined a canonical response function that reliably distinguishes pupil responses to CS+US- and CS- [52]. retrodictive validity exceeds (or is at least equal to) peak scoring and calculating the area-under-the-curve. The response function was initially based on a CS to US SOA of 3.5 s but the same function can be used for an SOA of 6 s. The overall best performing model did not include the temporal derivative but this is still accessible in PsPM. The gamma probability density function followed the same form specified above with the parameter values $k = 6.03$, $\theta = 0.73s^{-1}$, $c = 1.6$, $t0 = 0.029$ ($t0$ was fitted for this model).

6.4   Data preconditioning

We provide procedures to import pupil data from Eyelink, SMI and View-Point files, but they can also be imported from other sources via matlab or text files. All PsPM models specify pupil diameter. Eyelink import automatically converts input into diameter in absolute units (mm). SMI diameter values are returned in pixel values. ViewPoint diameter values are returned in ratio units as they are given in the data file. For other sources it may be necessary to convert the data using the respective conversion function. Missing data due to blinks, saccades, or slight head movements can be linearly interpolated before z-scoring. These missing data can then be retained, or not, for the GLM.

Pupil area appears smaller to the eyetracking camera when the participant does not maintain fixation. Whether this "Pupil foreshortening error" (PFE) influences recordings depends on the eyetracker. Geometrically, it would be possible to fit the visible pupil shape with an ellipse and retain the long axis as pupil diameter, which is invariant to eye movements. However, apparently many eyetrackers simply report the number of pupil pixels, ie. an area measure. For example, although the Eyelink 1000 eyetracker has the possibility to choose an ellipsoid model, this is according to the manual (User Manual. v.1.4.0, p. 23) only used to determine pupil position, but not pupil area or diameter ("Measure of Area or Diameter are always based on the Centroid Model").

To account for loss of fixation, PsPM includes two options: exclude these time intervals, or correct pupil size with a geometric model. (1) To detect loss of fixation there is a specific function . The user has to specify the distance between screen and eye, the screen size, the position of the fixation point (by default the middle of the screen is assumed but additionally a time series of fixation points can be specified), and the threshold for exclusion set in degrees of visual angle. (2) PsPM also includes a method to perform pupil foreshortening error (PFE) correction as described in [54]. The implementation itself is eyetracker or measurement method independent; however, we use Eyelink in its name because the method was proposed specifically

for Eyelink 1000 eyetracker. To perform PFE correction, PsPM requires extra information about the recording setup. Specifically, screen resolution, screen size and the screen-camera-eye geometry setup must be known.

Pupil size obtained using eyetrackers may be contaminated with high noise. Before using this data in various statistical models, it might be beneficial to preprocess it in order to increase signal-to-noise ratio. PsPM offers a pupil size preprocessing utility that is independent of the eyetracker used. The method is described in [55]. We use a modified version of the software published in this paper. All the modifications are documented and the changelog is part of PsPM. The preprocessing method can be used without any additional information about the recording setup. PsPM exposes all the preprocessing parameters used by the underlying software to the user for finetuning.

Finally, we found that filtering provided equal or worse proportions of explained variance and therefore there is no default filtering although this may be beneficial for other experimental designs.

6.5   Recommendations

- Experimental design:

    - fear-conditioned PSR: use default model for CS/US-SOAs between approximately 2-8 s. The model is tested for 3.5 - 6 s.

- Model set up:

    - fear-conditioned PSR: use no filter [52]

    - fear-conditioned PSR: use no derivative, If possible, model the US response separately (requires a command-line function call to `pspm_glm`) [52]

7   Respiratory response models

contributed by Giuseppe Castegnetti and Dominik R Bach

7.1   General

Brain stem centres regulate respiration via autonomic nervous efferents, and these centres are influenced by higher cognitive processes [56, 57]. This may allow inferring psychological states from measured respiration, although it is not very well know which psychological variables or events elicit phasic respiratory responses. PsPM implements four models for respiratory responses, derived from a single chest belt system. In principle,

this system only allows assessing respiration period, while for precise quantification of respiratory amplitude, a double-belt system would be required to measure both thoracic and abdominal compartments [58]. However, if the ratio between thoracic and abdominal contribution is relatively constant within any individual, it may still be possible to approximate respiratory amplitude up to a linear constant from the single-belt system. We confirmed in [59] that respiration amplitude from a single chest belt system can be usefully analysed. PsPM considers the following measures:

- Respiration period (RP) is the duration of a breathing cycle. PsPM models RP rather than the more common respiration rate, its inverse, in analogy to analysis of event-related cardiac responses where heart period has been shown to linearly relate to autonomic nervous system input [41]

- Respiration amplitude (RA) is the amplitude in rib cage excursion on that cycle, which linearly relates to current tidal volume (VT) [58].

- Respiration flowrate (RFR), RA/RP, which is linearly related to tidal volumetric flow rate, i.e. tidal volume per time unit. RFR is computed per cycle with variable duration. Otherwise it is similar to minute volume, or RLL (respiration line length), which are computed over fixed intervals rather than respiratory cycles.

In these measures, we identified the following pattern of phasic responses [59]:

- Respiratory period responses (RPR) are elicited by various external events (aversive sounds, electric shocks, picture viewing, visual detection) and reliably distinguish events from non-events

- Respiratory amplitude responses (RAR) are elicited by aversive sounds and shocks, and by picture viewing. Response amplitudes are smaller for picture viewing (including aversive pictures) than aversive sounds. RAR are also elicited by fear-conditioned stimuli.

- Respiratory flow-rate responses (RFRR) are elicited by aversive sounds and shocks, and by picture viewing. Response amplitudes are smaller for picture viewing (including aversive pictures).

7.2   Peripheral and neural model

In the absence of information on the timecourse of input into breathing control, it is difficult to separate a neural and a peripheral model. Hence, these two are collapsed for the purpose of quick and simple inversion with GLM (see 3.4.4). This means that the two implemented models for RAR - evoked RAR and fear-conditioned RAR - use a different RF, although of course the peripheral system is the same in both cases.

Table 2: Model constants for evoked respiratory responses

Response Function (RF)	Parameters of Gaussian Function	
	μ	σ
RPR	4.20	1.65
RAR	8.07	3.74
RFRR	6.00	3.23

Note. μ = mean; σ = standard deviation

7.3   Models for evoked respiratory responses

These models are based on responses from 46 participants and on the following task conditions: visual detection, aversive electric shocks, IAPS picture viewing. The model was validated on an independent sample of 20 participants and the following task conditions: aversive and less aversive white noise sounds, positive and negative IAPS picture viewing.

We modelled responses with Gaussian functions:

$$h\left(y\right) = \frac{1}{\sigma\sqrt{2\pi}} e^{\frac{-(t-\mu)^2}{2\sigma^2}} .$$

Model constants after filter optimisation are summarised in table 2. Later response components that were visually identified in the development data set did not contribute to detecting overall responses or separating experimental conditions. Modelling the time derivative of the RF improved the RA and RFR models, but not the RP model [59].

7.4   Model for fear-conditioned RAR

After showing that RAR may be better suited to distinguish cognitive processes than respiration period [59], we investigated whether RAR allow assessment of fear memory in cued fear conditioning. Following the same procedure as in [43], we built the RF from data collected during six experiments, involving diverse stimuli and two types of breathing belts (bellows and cushion systems). The ensuing winning model was the combination of an early and a late response components, modelled by gamma distributions

$$y = \frac{A}{\Theta^k \Gamma(k)} (x - x_0)^{k-1} e^{-\frac{x-x_0}{\Theta}}$$

with parameters $k_e = 2.570 * 10^7$, $\Theta_e = 3.124 * 10^{-4}$, $x_{o,e} = -8.024 * 10^3$ and $k_l = 3.413$, $\Theta_l = 1.107$, $x_{0,l} = 7.583$, respectively. This method distinguishes RAR to CS+ and CS- better than model-free scoring of RAR (e.g., peak scoring). Compared to other measures of fear learning, RAR turn out to perform

similar to SCR, but are less sensitive than HPR. By comparing CS/US SOAs of 3.5, 4, and 6 s, it is evident that the RAR are most likely time locked to the US. In the model, both components of the RF are shifted in time as a function of the SOA. To avoid deformation of the early RF due to violations of the linearity assumptions, however, we recommend to use this method only with experiments involving SOAs longer than 2.5 s.

7.5   Data Conditioning

7.5.1   Breathing cycle detection

Bellows system   Transducer output is filtered offline with an anti-aliasing bidirectional first-order Butterworth low-pass filter and a cut-offfrequency of 5 Hz. Data are then downsampled to 10 Hz resolution. Respiration traces are mean-centred, filtered with a bidirectional Butterworth band pass filter and cut-off frequencies of 0.01 Hz and 0.6 Hz, and median filtered over 1 s. A negative zero-crossing is taken as start of inspiration. After each detected cycle, PsPM imposes a 1 s refractory period, to account for residual signal noise with might cause several zero-crossings on the same cycle. In the validation data set, we compared this method to visual detection as gold standard and found, for the automated method, a sensitivity of 99.3%, and a positive predictive value of 99.5%. For the time difference between visual and automated detection, we found a median delay of 0.1 s and a standard deviation of 0.1 s [59].

Cushion system   For data obtained from the cushion/belt system, the above algorithm must be adapted to account for the different response of cushion/-belt system to ventilator activity. Specifically, we defined the onsets of the inspirations as the minima of the respiratory trace. Hence, the algorithm was adapted to extract zero crossings of the derivative of the time series (i.e., the extrema), from which the positive ones (i.e., the minima) were set as the start of the inspiration.

7.5.2   Interpolation and Filtering

To transform the discontinuous RP, RA and RFR information into a continous signal, they are assigned to the start of the following inspiration cycle and linearly interpolated with 10 Hz sampling frequency. PsPM also allows writing out the respiration time stamps for quality control. The interpolation shifts some early evoked responses such that they appear to start before an event - this is automatically being taken care of by a response function that starts slightly before an event definition. The best filter frequencies in [59] were: 0.01-1 Hz for RP, 0.001-1 Hz for evoked RA and RFR. For

fear-conditioned RA a 0.01-2 Hz bidirectional 6th order Butterworth filter provided the best results (cf. [45]).

7.6   Recommendations

- Experimental design:

    - evoked respiratory response models: make sure the SOA between subsequent events that elicit an respiratory response is longer than the peak of the respective RF. A formal test of the linearity assumption has not been done yet.

    - fear-conditioned RAR: To avoid deformation of the early RF due to violations of the linearity assumptions, we recommend to use this method only with experiments involving SOAs longer than 2.5 s.

- Model set up:

    - Use default filter frequencies (0.01-1 Hz for RP, 0.001-1 Hz for evoked RA and RFR. 0.001-2 Hz for fear-conditioned RA.)

8   Startle eye blink response models

8.1   General

The startle response is a fast defensive reflex to an unexpected intense auditory, visual, or haptic stimulus. Functionally, it appears to protect an organism from an imminent blow to the head [60]. The human startle response encompasses a postural change and an eyeblink response which is easy to measure [61]. While the startle response itself is very stereotypical, its amplitude is susceptible to various physiological and psychological manipulations, many of which can be summarised in a decision-theoretic model in terms of optimising the cost of the startle response, and of a putative predator attack [62]. In this context, the most important phenomenon is fear-potentiated startle, a stronger startle response during a CS+ than CS- in fear conditioning [63].

8.2   Peripheral and neural model

In the absence of information on the millesecond-time course of neural response in the centres controlling startle, it is difficult to separate a neural and a peripheral model. Hence, these two are collapsed for the purpose of quick and simple inversion with GLM (see 3.4.4). Because the startle response is so stereotypical, the same RF is used for all applications, and the amplitude estimated. There appears to be some variability in the latency

of the startle response between trials and participants, such that the neural model contains a (constrained) latency parameter that is estimated from the data. The startle eye blink response function (SEBRF) is based on data from 19 participants that heard startle sounds with no other manipulation. Pre-processing parameters were optimised to distinguish CS+/CS- in a fear retention task with 20 participants in which startle onsets were recorded for enhanced temporal precision. They were then validated on two independent samples of 15 and 14 participants in a fear retention, and fear acquisition task, respectively. The SEBRF is described as a gamma distribution

$$y = \frac{A}{\Theta^k \Gamma(k)} (x - x_0)^{k-1} e^{-\frac{x-x_0}{\Theta}}$$

with parameters $k = 3.5114$, $\Theta = 0.0108$, $x_o = 0.0345$ [64].

8.3   Data preconditioning

The algorithm expects raw data from orbicularis oculi EMG. Data filtering and preprocessing is taken care of by a separate PsPM function (see **??**) and includes a 4th order Butterworth band-pass filter with cutoff frequency of 50 Hz and 470 Hz, removal of mains noise with a 50 Hz notch filter. Filtered continuous EMG signals are rectified and smoothed using a 4th order Butterworth low-pass filter with a time constant of 3 ms corresponding to a cutoff frequency of 53.05 Hz. No more data pre-conditioning is applied during GLM inversion, which allows to visually inspect the filtered EMG data in advance to the inversion. To specify startle sound onsets with high precision, you can use the function **??** to detect these onsets from recorded audio signals.

8.4   Recommendations

- Experimental design:

  – record audio output from your startle equipment and use PsPM to detect sound onsets

- Preprocessing:

  – use default pre-processing

- Model setup:

  – model each trial as separate event type such that the response latency can be estimated per trial, rather than per condition

9   Scanpath speed (SPS) model

9.1   General

Various salient stimuli, e.g. threat-conditioned cues, capture overt attention in a bottom-up process [65], as shown in multiple stimulus competition paradigms using aversive cues. This yields a possibility to assess threat memory by overt attention. In cue competition paradigms, overt attention is usually measured as gaze patterns; for example, fixation duration, saccade initiation latency, and number of erroneous saccades. Here, we implement a model that captures gaze patterns during exclusive presentation of a single cue, by assessing scanpath speed, the length of scanpath per time unit, quantified as degree visual angle per second [66]. In our publication, we refer to scanpath length, which is the integral of scanpath speed over time. Since we used constant cue presentation times in our publication, average scanpath speed and scanpath length were identical up to a multiplicative constant.

9.2   Model for fear-conditioned SPS

Scanpath speed/length allow differentiating CS+ and CS- in fear-conditioning paradigms with visual cues, and without fixation instructions or fixation cross. PsPM implements two simple models that build on the GLM inversion algorithm (see 3.4.4). The first model is to compute average scanpath speed during a 2-s time window before US (shock) delivery. This was validated on three independent samples in [66]. The model is implemented with a simple boxcar response function without mean-centering and is the default option. Parameter estimates can be interpreted as average scan path speed per second, and if they are multiplied with 2 then the resulting values can be interpreted as scan path length during the 2 s preceding the US. We also implement a gamma RF that describes the shape of the scanpath speed during the CS-US interval better than the boxcar function, but did not yield higher retrodictive validity in inferring the CS-/+ difference. This RF was fitted to the data of 21 participants and validated in an independent sample; it is described by a gamma probability density function:

$$y = \frac{A}{\mu^k \Gamma(k)} (t - t_0)^{k-1} e^{-\frac{t-t_0}{\mu}}$$

with parameters $k = 10.0913, \mu = 0.4213, t0 = -1.9020 + (SOA{-}3)$ [66], where SOA is the duration of the interval between CS onset and US onset in seconds.

9.3 Data preconditioning

PsPM provides procedures to import scan path speed directly. More commonly, it is convenient to import gaze coordinates in pixels, distance units, or visual angle, and convert them to scanpath speed. This requires interpolation of missing values which is done automatically. Conversion from pixels to mm or visual angle in degree is also possible. No filtering or smoothing is required for both RF during model inversion with GLM.

9.4 Recommendations

- Experimental design:

    - use visual cues during fear conditioning and avoid fixation guides.
    - use a SOA longer than 2 s. Tested SOAs are 3.0 s and 3.5 s.

- Model setup:

    - use the default boxcar function and specify custom SOA.

Part II
User Guide

10 File types

PsPM knows two file types:

- Data files - the original file name is prepended with 'pspm_' during import. Various pre-processing steps prepend additonal letters to the name. These files are loaded and saved with the function `pspm_load_data`.

- First-level model files - all models use a similar data structure. The name can be freely specified by the user. These files can also contain reconstructed responses in GLM. These files are loaded and saved with the function `pspm_load1`.

11 Functions that create new data files

All functions in the Matlabbatch menu item "Data preparation" create new data files. These functions ask whether an existing file with the same name should be overwritten - unless you specify 'overwrite' in the options.

- Import - prepended with 'pspm_'

- Trim - prepended with 't'

- Split sessions - appended with '_sn<nr>'

- Rename - user-defined file name

- Interpolation - prepended with 'i' (only if run on all channels of the file)

12   Functions that create or modify data channels in an existing file

All functions in the Matlabbatch menu item "Data preprocessing" create new channels. These functions allow you to select where to store a modified data channel. The following options exist:

- add: A new channel is created with the new data

- replace: If one or several channels of the output type exists, the last of these will be overwritten. For some functions, this can overwrite the original data, i. e. if a conversion function produces an output of the same type as the input. If no channel of the output channel type is found, a channel will be added.

13   Import details

Here, we list some additional information regarding the import of various data types.

CED Spike

Text   Text files can only contain numbers (i.e. no header lines with channel names) and one data column per channel. Make sure you use the decimal point (i.e. not decimal comma). At the moment, no import of event time stamps is possible, but continuous event marker channels are supported.

Matlab   Each input file must contain a variable called data that is either a cell array of column vectors, or a data points $\times$ channels matrix. The import of event markers is supported. Marker channels are assumed to be continuous if the input data is a matrix or if the input data is a cell and the given samplerate is larger than 1 Hz. A sample rate has to be specified for any type of data.

Biopac AcqKnowledge (up to v. 3.9)   Imports original files.

exported Biopac AcqKnowledge   Converted with manufacturer's export function.

bioread-converted Biopac AcqKnowledge (any version)   Loads mat files which have been converted using the bioread tool acq2mat. Bioread can be installed using pip (installed by python) or can be downloaded and installed manually from here `https://github.com/njvack/bioread`. It requires python and the python libraries numpy and scipy.

Labchart (any Version, Windows only)   Supports the import of any original Labchart (.adicht) file. Since it uses an external library, this import is restricted to Windows systems only and does not work on any other operating system.

Labchart exported (up to v. 7.1)   Export data to matlab format (plugin for the LabChart software, available from www.adinstruments.com)

Labchart exported (v. 7.2 and higher)

VarioPort

Biograph Infiniti exported   Export data to text format, both "Export Channel Data" and "Export Interval Data" are supported; a header is required

Mindmedia Biotrace exported

BrainVision

Windaq (Manufacturer's version)   Requires an ActiveX Plugin provided by the manufacturer and contained in the subfolder Import/wdq for your convenience. This plugin only runs under 32 bit Matlab on Windows.

Windaq (PsPM Version)   Windaq import written by the PsPM team. Is platform independent, thus has no requirements for ActiveX Plugins, Windows or 32bit Matlab. Imports the *.wdq files. Up to now the import has been tested with files of the following type: Unpacked, no Hi-Res data, no Multiplexer files. A warning will be produced if the imported data-type fits one of the yet untested cases. If this is the case try to use the import provided by the manufacturer (see above).

Observer XT compatible

NeuroScan

BioSemi

Eyelink Eyelink output files (with extension *.edf) must first be converted to ASCII format (extension *.asc). This is done with the utility edf2asc.exe (normally included in the Eyelink software in <Path to Program Files>\SR Research\EyeLink\EDF_Access_API\). Otherwise there is a Data viewer, available at `http://www.sr-research.com/dv.html` (registration needed), which installs a utility called 'Visual EDF2ASC'. This also allows the conversion and does not require a license. The composition of channels depends on the acquisition settings. Available channels are Pupil L, Pupil R, x L, y L, x R, y R, Blink L, Blink R, Saccade L, Saccade R. The channels will be imported according to a known data structure, therefore channel ids passed to the import function or set in the Batch will be ignored. If the import function defines PsPM file channels that are not available in the data file, these channels will be filled with NaN values. Periods of blinks and saccades will be set to NaN in the gaze and pupil channels. To reduce the impact of loss of fixation on recorded pupil size, we recommend setting ELCL_PROC to ELLIPSE during acquisition.

Pupil Channels and Eyetracker distance Distance between eyetracker camera and recorded eyes in length units. If the given eyetracker distance is given as a positive numeric value, it enables the pupil data to be converted from arbitrary area or diameter units to diameter (mm) and then to the length unit of the eyetracker distance. If eyetracker distance is not given, or if it is not a positive numeric value, then the conversion to mm is disabled. In this case, pupil data will be imported in arbitrary (Eyelink) units. (Use only if you are interested in relative values)

The relation between arbitrary units (a.u.) and diameter is assumed to be linear such that for diameter data

$$d = m_{diameter} \cdot \frac{dist}{dist_{ref}} \cdot d_{a.u.}$$

and for area data [54]

$$d = m_{area} \cdot \frac{dist}{dist_{ref}} \cdot \sqrt{d_{a.u.}}$$

for data d in mm, data $d_{a.u.}$ in arbitrary units, reference camera-eye distance $dist_{ref}$ in mm, used camera-eye distance $dist$ in mm and a proportionality factor m in mm. In our equations, $m_{area}/dist_{ref}$ ratio corresponds to

Table 3: Coefficients Used for Eyelink Data Conversion

Coefficient	Variable in `pspm_get_eyelink.m`	Value	Unit
$dist_{ref}$	`reference_distance`	700	mm
$m_{diameter}$	`diameter_multiplicator`	0.00087743	mm
m_{area}	`area_multiplicator`	0.119	mm

tab:eyelink_coefficients

the scaling factor in [54]. For area-based conversion, we use the scaling factor $\alpha = 1.70 \times 10^{-4}$ as given in [54]. For a reference distance of 700 mm this translates to $m_{area} = 0.119$ mm. For diameter-based conversion, we determined reference distance and the proportionality factor in a simpler calibration with three different artificial pupil sizes setting using linear regression. We note that for a different Eyelink eye-tracker setup, conversion with these values yielded results with slight deviance from the expected value, such that they are either not entirely precise, or there may be small differences between different eyetrackers. The table below summarises all coefficients:

For custom setups reference distance (field `reference_distance`) and proportionality factor (`diameter_multiplicator` or `area_multiplicator`) can be set at the top of `pspm_get_eyelink.m` file.

Gaze Channels Gaze channels are reported exactly as given in the datafile without any conversion. Gaze channel units are pixels.

Distance unit The length unit in which the eyetracker distance is given. It can be mm, cm, m or inches.

Blink/Saccade Edge Discard Samples surrounding a blink or saccade period may be noisy. For this reason, Eyelink import provides a parameter that allows users to specify the amount of samples they want to discard on each side of every blink and saccade period. This value is multiplied by the sampling rate of the recording to determine the number of samples to discard from one end. Therefore, for each blink/saccade period, $2 \cdot factor \cdot F_{sampling}$ many samples are discarded in total, and effectively blink/saccade period is extended.

This value also corresponds to the duration of samples to discard on one end in seconds. For example, when it is 0.01, we discard 10 ms worth of data on each end of every blink/saccade period.

The default value has been changed to 0 in PsPM revision r803 to reduce the amount of discarded data. Note that this might result in noisy

samples around blink/saccade points. Therefore, it is highly recommended to perform pupil size data preprocessing **??** and gaze data filtering **??**.

SMI (SensoMotoric Instruments)   SMI output files (with extension *.idf) must first be converted to ASCII format (extension *.txt) using IDF converter.

SMI iView X EyeTracker sample and optionally also event files can be imported. The SMI sample file contains pupil, gaze and position related information. The SMI event file contains information about blink/saccade events. Available channels to import are Pupil L, Pupil R, Gaze x L, Gaze x R, Gaze y L, Gaze y R, Blink L, Blink R, Saccade L, Saccade R, Marker, Custom. All channels except custom are imported according to a known data structure. Therefore, there is no need to specify the column indices of channels. If specified channels are not available, they will be filled with NaN values. If an event file is given so that blinks/saccades are available, blink and saccade periods will be set to NaN.

There are multiple ways to specify pupil information in SMI sample files. Instead of importing all the channels for a given eye, PsPM selects only one of the available ones according to the following precedence order:

1. Mapped Diameter (mm)

2. Dia X (mm)

3. Dia (squared mm)

4. Dia X (px)

5. Dia (squared px)

If the chosen pupil channel is in squared px or squared mm, then it is converted to diameter by assuming the shape is a circle. However, no conversion from pixels to milimeters is performed for pupil channels. Therefore, if a pixel or squared pixel channel is chosen, it is returned in pixel units.

Returned gaze coordinates assume that (0, 0) point of the calibration area is the top left corner. x coordinates increase towards right and y coordinates increase downwards. If the resolution of the whole stimulus window is given, the gaze values are returned in the desired target unit. Otherwise, they are returned in pixels. It is important to note that the values can be negative or larger than the sides of the screen, if gaze is outside the calibration area.

Gaze values are reported in pixels by SMI. The conversion from pixels to milimeters is performed by using the size and the resolution of the stimulus window to calculate px/mm ratio, and then using this ratio for scaling.

Viewpoint (Arrington Research)   Arrington Research ViewPoint EyeTracker files can be imported into PsPM. Available channels to import are Pupil L, Pupil R, Gaze x L, Gaze x R, Gaze y L, Gaze y R, Blink L, Blink R, Saccade L, Saccade R, Marker, Custom. Currently, blink and saccade events can only be imported if they are stored as asynchronous messages in the datafile. This is enabled by "Include Events in Datafile" option in ViewPoint EyeTracker software. All channels except custom are imported according to a known data structure; therefore, there is no need to specify the column indices of channels. If specified channels are not available, they will be filled with NaN values.

ViewPoint reports data for eye A in monocular mode and for eyes A and B in binocular mode. PsPM performs the following mapping from A/B to L/R:

1. If only one eye is specified by user (only L or only R) and there is only eye A in data, then data for eye A is returned as the eye specified by user

2. In all other cases, eye A is mapped to eye R and eye B is mapped to eye L.

All gaze and diameter values are reported as ratios by ViewPoint:

1. Gaze value for a given axis is the ratio of the gaze coordinate to the length of that axis.

2. Pupil diameter is the ratio of pupil width to the EyeCamera window width.

Since ViewPoint data files contain the size of the stimulus window in milimeters, PsPM converts normalized gaze values to values in milimeter. This is performed by multiplying the ratio with the length of the corresponding stimulus window axis. Returned gaze coordinates assume that (0, 0) point of the stimulus window is the top left corner. x coordinates increase towards right and y coordinates increase downwards. The gaze values are returned in the desired target unit. It is important to note that the values can be negative or larger than side of the screen which correspond to looking outside the stimulus window.

Pupil diameter is returned as ratio without any conversion.

European Data Format (EDF)

Philips Scanphyslog   This functions imports psychophysiology files from Philips MRI scanners. The physlog ascii file contains 6 channels with physiological measurements:

Channel id	Event type
1	ECG1
2	ECG2
3	ECG3
4	ECG4
5	Pulse oxymeter
6	Respiration

Depending on your scanner settings, there are 10 trigger channels (see complete list below) of which channel 6 marks time t of the last slice recording. After importing, a time window from t minus $(\#volumes)*(repetition time)$ seconds until t should be used for trimming or splitting of sessions to constrain data in the imported file to the EPI recording window and easier matching with experimental events from a separate source.

Available trigger channels are:

Channel id	Event type
1	Trigger ECG
2	Trigger PPG
3	Trigger Respiration
4	Measurement ('slice onset')
5	Start of scan sequence
6	End of scan sequence
7	Trigger external
8	Calibration
9	Manual start
10	Reference ECG Trigger

SCR Transfer Function [for SCR data only]   The transfer function supports two recording systems, which are either a conductance based system (default) or a resistance based system. Depending on the recording system the relation between measured conductance G in μS to recorded voltage U in V is either

$$G = \frac{1}{\frac{c}{U-offset} - R_s * 10^{-6}},\tag{13.1}$$

or

$$G = \frac{1}{\frac{U-offset}{c} - R_s * 10^{-6}}.\tag{13.2}$$

For a transfer constant c in $V/\mu S$ (for 13.1) or in $V/M\Omega$ (for 13.2), series resistor R_s in Ohm, and a fixed offset in V which was added to the initially

measured voltage. If there is no offset and series resistor, this is equivalent to

$$G = \frac{U}{c}, \, U = cG$$

or

$$G = \frac{c}{U}, \, U = cR = \frac{c}{G},$$

There are three options how to enter this information:

- File: Enter the name of the .mat file that contains the variables: 'c', 'Rs' (in Ohm) and 'offset', 'recsys' (possible values: 'conductance' or 'resistance').

- Input: Enter the transfer constants manually.

- None: No transfer function. Use this only if you are not interested in absolute values, and if the recording settings were the same for all subjects.

Part III
Tutorial data sets

Contributed by Christoph Korn & Matthias Staib.

14   GLM for SCR: Appraisal data

To analyse this data set, follow tutorials 1-2 on the PsPM website. Tutorial 6 shows how to adapt your scripts for multiple participants. In this tutorial, we analyze SCR data using a general linear model (GLM). The example data set comprises SCR data from 15 participants and can be downloaded from https://bachlab.github.io/PsPM/courses/. Results from this data set have been previously published [13, 14]. Each participant saw 45 neutral and 45 aversive pictures within one session that included two short breaks. SCR data were recorded using a 0.5 V coupler, optical (wave to pulse) transducer, and CED Spike, with a minimum sampling rate of 100 Hz.

15 Non-linear SCR analysis: Delay fear conditioning data

To analyse this data set, follow tutorial 3 on the PsPM website. Tutorial 6 shows how to adapt your scripts for multiple participants. In this tutorial, the non-linear model is estimated. The estimated parameters can then be used to test the within-subject hypothesis that the sympathetic arousal between CS+ and CS- are different on a group level. The example data set comprises SCR data from 20 participants, with 40 trials each, which can be downloaded from https://bachlab.github.io/PsPM/courses/ together with the result files of the model inversion. Participants underwent a differential delay fear conditioning paradigm where coloured circles were presented for 4 seconds each. Either the blue or orange coloured circles (balanced over participants) were probabilistically paired with an electric stimulation (unconditioned stimulus, US) that coterminated with the stimulus (conditioned stimulus, CS+) while the CS- were always presented alone.

Presenting the CS+ causes phasic sympathetic arousal in anticipation of an electric shock. This anticipatory reaction typically occurs with an unknown and variable latency after stimulus onset. For such cases, a GLM should not be used because it assumes that sympathetic arousal follows the stimulus with a fixed latency. In contrast, the non-linear model allows estimating (i) a variable onset within a user-specified time window and (ii) a variable duration of a sympathetic response. Additionally, the non-linear model includes estimation of spontaneous fluctuations that occur between trials.

Part IV
How to reference PsPM

To justify our development and maintenance effort, we ask you acknowledge PsPM when you use it: "Data were analysed using PsPM [version number], available at `http://bachlab.github.io/pspm`."

We ask you reference our papers to justify your analysis steps and models in the following way:

- General PsPM reference:

    - Bach DR, & Friston KJ (2013). Model-based analysis of skin conductance responses: Towards causal models in psychophysiology. Psychophysiology, 50, 15-22.

    - Bach DR, Castegnetti G, Korn CW, Gerster S, Melinscak F, Moser

T (2018). Psychophysiological modelling - current state and future directions. Psychophysiology, 55, e13214.

- General PsPM reference for fear conditioning experiments:

  - Bach DR, & Melinščak F (2020). Psychophysiological modelling and the measurement of fear conditioning. Behaviour Research and Therapy, 127, 103576.

- GLM for SCR

  - general reference: Bach DR, Flandin G, Friston KJ, & Dolan RJ (2009). Time-series analysis for rapid event-related skin conductance responses. Journal of Neuroscience Methods, 184, 224-234.

  - canonical SCRF: Bach DR, Flandin G, Friston KJ, & Dolan RJ (2010). Modelling event-related skin conductance responses. International Journal of Psychophysiology, 75, 349-356.

  - assumptions of the model: Gerster S, Namer B, Elam M, Bach DR (2018). Testing a linear time invariant model for skin conductance responses by intraneural recording and stimulation. Psychophysiology, 55, e12986.

  - optimised filter settings: Bach DR, Friston KJ, Dolan RJ (2013). An improved algorithm for model-based analysis of evoked skin conductance responses. Biological Psychology, 94, 490-497.

  - comparison with Ledalab and peak-scoring methods: Bach DR (2014). A head-to-head comparison of SCRalyze and Ledalab, two model-based methods for skin conductance analysis. Biological Psychology, 103, 63-88.

- non-linear model for event-related SCR:

  - general reference: Bach DR, Daunizeau J, Friston KJ, & Dolan RJ (2010). Dynamic causal modelling of anticipatory skin conductance responses. Biological Psychology, 85, 163-70.

  - optimised filter settings: Staib M, Castegnetti G, Bach DR (2015). Optimising a model-based approach to inferring fear learning from skin conductance responses. Journal of Neuroscience Methods, 255, 131-138.

  - optimised forward model for short SOA paradigms (see supplementary material): Tzovara A, Korn CW & Bach DR (2018). Human Pavlovian fear conditioning conforms to probabilistic learning. PLOS Computational Biology, 14, e1006243.

- non-linear model for SF:

- **general reference:** Bach DR, Daunizeau J, Kuelzow N, Friston KJ, & Dolan RJ (2011). Dynamic causal modelling of spontaneous fluctuations in skin conductance. Psychophysiology, 48, 252-57.

- **canonical SCRF:** Bach DR, Friston KJ, & Dolan RJ (2010). Analytic measures for quantification of arousal from spontaneous skin conductance fluctuations. International Journal of Psychophysiology, 76, 52-55.

- **MP algorithm:** Bach DR, Staib M (2015). A matching pursuit algorithm for inferring tonic sympathetic arousal from spontaneous skin conductance fluctuations. Psychophysiology, 52, 1106-12.

- GLM for evoked HPR: Paulus PC, Castegnetti G, & Bach DR (2016). Modeling event-related heart period responses. Psychophysiology, 53, 837-846.

- GLM for fear-conditioned HPR: Castegnetti G, Tzovara A, Staib M, Paulus PC, Hofer N, & Bach DR (2016). Modeling fear-conditioned bradycardia in humans. Psychophysiology, 53, 930-939.

- GLM for evoked respiratory responses: Bach DR, Gerster S, Tzovara A, Castegnetti G (2016). A linear model for event-related respiration responses. Journal of Neuroscience Methods, 270, 147-155.

- GLM for fear-conditioned RAR: Castegnetti C, Tzovara A, Staib M, Gerster S, Bach DR (2017). Assessing fear memory via conditioned respiratory amplitude responses. Psychophysiology, 54, 215-223.

- GLM for illuminance-elicited PSR: Korn CW & Bach DR (2016). A solid frame for the window on cognition: Modeling event-related pupil responses. Journal of Vision, 16, 28.

- GLM for fear-conditioned PSR: Korn CW, Staib M, Tzovara A, Castegnetti G, Bach DR (2017). A pupil size response model to quantify fear conditioning. Psychophysiology, 54, 330-343.

- GLM for SEBR: Khemka S, Tzovara A, Gerster S, Quednow BB, Bach DR (2017). Modeling startle eyeblink electromyogram to assess fear learning. Psychophysiology, 54, 204-214.

- GLM for scanpath speed: Xia Y, Melinščak F, Bach DR (2020). Saccadic scanpath length: an index for human threat conditioning. Behavior Research Methods, 53, 1426-1439.

- Integration of different measures: Mancinelli F*, Sporrer JK*, Myrov V, Melinscak F, Zimmermann J, Huaiyu L, Bach DR (2024). Dimensionality and optimal combination of autonomic fear-conditioning measures in humans. Behavior Research Methods, 56, 6119–6129.

Part V

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- Model development and model inversion: Jean Daunizeau, Guillaume Flandin, Karl Friston.

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- SPM physiology toolbox for CED spike *.smr import (Eric Featherstone, Chloe Hutton)

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PsPM incorporates the following published toolboxes and/or methods:

- SCR quality control [67]

- pupil preprocessing [55]

- pupil foreshortening error correction [54]

- QRS detection for fMRI enviornments [48]

- HeartPy toolbox for pulse oxymetry [49]

- VBA toolbox [33]

Part VI

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