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From observed laterality to latent hemispheric differences: Revisiting the inference problem

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ABSTRACT
Researchers interested in hemispheric dominance frequently aim to infer latent functional differences between the hemispheres from observed lateral behavioural or brain-activation differences. To be valid, these inferences may not only rely on the observed laterality measures but also need to account for the antecedent probabilities of the studied latent classes. This fact is frequently ignored in the literature, leading to misclassifications especially when considering low probability classes as, for example, "atypical" right hemispheric language dominance. In the present paper, we revisit this inference problem (a) by outlining a general Bayesian framework for the inferential process and (b) by exemplarily applying this framework on the inference of hemispheric dominance for speech processing from dichotic-listening laterality scores. Utilizing large-scale empirical data sets as well as simulation studies, we show that valid inferences also regarding low probable latent classes can be drawn applying the present framework, although within certain boundaries. We further illustrate that repeated laterality measures of the same person may be used to improve the classification outcome. The article additionally provides R package and Shiny app implementations of the suggested Bayesian framework, which allow to explore the boundaries of valid inference for the present and other examples.

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KEYWORDS Bayesian classification; brain asymmetry; handedness; hemispheric differences; laterality

Introduction

Functional differences between the cerebral hemispheres represent a fundamental organizational principle of the human brain but differences in which hemisphere is dominant for a specific function exist (Ocklenburg & Güntürkün, 2018). For example, while in by far most individuals the left hemisphere

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is dominant for productive language abilities, "atypical" right hemispheric dominance can be found in a significant proportion of the population (Carey & Johnstone, 2014). Research on hemispheric differences thus often aims to determine which hemisphere is dominant for a given task, and measures of lateral difference in performance (e.g., in task measuring perceptual laterality) or in brain activation (e.g., in a task-based functional MRI task) are used to infer latent (unobserved) hemispheric differences.

Unfortunately, as first pointed out by Satz (1977), this inferential step from laterality measure to underlying hemispheric differences is far from straightforward. In particular when the antecedent probabilities of an individual being left- or right-dominant differ substantially, as for example is the case for language processing (Carey & Johnstone, 2014), the validity for inferring membership of the less likely class is severely threatened. Satz (1977) illustrated his point by applying Bayes' theorem on this inference problem using verbal dichotic listening as indicator of language dominance. Studies had established that individuals which are left-dominant for speech and language processing when tested with the sodium-amytal (Wada-) test, more likely show a right-ear advantage for verbal material in dichotic listening (i.e., reporting more stimuli from the right than the left ear), while right-dominant individuals usually show a left-ear advantage (e.g., Kimura, 1961). Based on this observation, Satz (1977) went on to determine the likelihood (conditional probability) that an individual is left or right dominant given an empirical right- or left-ear advantage, while considering the antecedent probabilities of being left/right dominant and having a left/right ear advantage, respectively. Satz (1977) referring to the then available data from Wada-examinations (Branch, Milner, & Rasmussen, 1964), that the antecedent probability of a right-handed individual being left vs. right dominant for language processing is .95 vs .05. Furthermore, based on own data, he estimated the proportion of individuals showing a right-ear advantage in dichotic-listening task to be .70. Applying Bayes' theorem using these prior probabilities, he showed that getting a right-ear advantage in dichotic listening slightly increased the likelihood of being left dominant from .95 to .97. However, getting a left-ear advantage does not increase the probability of being "atypical" right dominant to more than .10. Thus, even when showing a left-ear advantage, an individual is still far more likely left (.90) than right dominant for language. Faced with these sobering figures, Satz (1977) formulated his article as a warning to fellow laterality researchers to refrain from such inferences and concluded that any attempt of inductive inference based on laterality measures to be "both unwarranted and reckless" (p. 208).

In the present article, we revisit the inference problem (a) by offering a statistical framework for inferences from laterality measures to latent differences, and (b) by exploring the boundaries within which valid inferences can be drawn using dichotic listening as an example laterality paradigm. To this end, we extend Satz's Bayesian approach in the following two points. Firstly, Satz (1977) based his classification into left- and right-dominant on a binary classification of laterality into left and right preferences based on the sign of the obtained laterality index, while ignoring the actual value or magnitude of the laterality index. We here argue that the magnitude of the laterality index provides additional information about the confidence of the classification. Following the classical test theory, we assume that each individual tested has a true perceptual laterality index and that the sign of this true laterality index correctly indicates the hemisphere dominant for the tested function. As the paradigms assessing laterality are naturally not perfectly reliable (see Voyer, 1998 for behavioural paradigms), any empirical measure also contains measurement error resulting in a deviation of the empirical laterality index from the true laterality index. This error can only lead to an inductive misclassification when the observed laterality index deviates by sign from the true value. However, as the measurement error can be expected to be more or less normally distributed around the true laterality index, it can be argued that a sign deviation gets increasingly less likely the more the observed laterality is in magnitude from zero. Thus, we here extend Bayes' theorem to additionally consider the magnitude of the laterality index when calculating the conditional probabilities. Secondly, Satz calculated the probability considering a single empirical laterality measure. Contrasting this, we here extend the approach to utilize repeated assessments of empirical laterality indices in the same person. That is, the suggested procedure calculates the posterior probabilities of being left- or right-dominant, respectively, for a given series of empirical laterality indices, while considering the reliability of repeated measurements.

Following Satz, we illustrate the above for the example of using perceptual laterality assessed in a verbal dichotic-listening paradigm to infer underlying hemispheric dominance in speech and language processing. This choice was made mainly for practical reasons, as here the relevant probabilities are best documented in the literature. However, we would like to stretch that the same inference problem applies whenever researchers follow the aim to infer underlying hemispheric differences from observed measures of laterality, including laterality indices obtained from behavioural tasks, electrophysiological data, or any form of functional neuroimaging on an individual level. Also, Satz (1977) based his calculations on the then available antecedent probabilities. More than 40 years later, we have the opportunity to update probabilities of language dominance referring to meta-analytic evidence from both Wada test and functional imaging studies (Carey & Johnstone, 2014) promising a more reliable data basis. Finally, the article provides the classification algorithms in form of an R package (R Core Team, 2019) and a Shiny application (Chang, Cheng, Allaire, Xie, & McPherson, 2018) to allow for an easy implementation and adjustment of the here developed Bayesian framework for inference in laterality research.

A modified Bayesian model for the relation of observed laterality and latent hemispheric dominance

The goal of the following derivation is to provide a formula that allows estimating the probability that an individual has left or non-left hemispheric dominance in a cognitive function (e.g., speech and language processing) given one or more measurements of laterality in a given task (e.g., dichotic listening).

To this end, let the parameter $\alpha \in \{-1, 1\}$ denote underlying hemispheric dominance (brain asymmetry) as dichotomous class, where $\alpha = -1$ indicates dominance of one hemisphere and $\alpha = 1$ indicates dominance of the contralateral hemisphere. For simplicity of discussion, we hereafter will use "left dominance" vs. "non-left dominance" to refer to these two classes. For derivation of formulas for a trichotomous case (i.e., including a left, bilateral, and right dominant group) please refer to Appendix 2. We here focus on the dichotomous case as for the below outlined example relevant parameters were missing to utilize a three class model.

Regarding the observed laterality, we assume (for a given individual) that we have n observations of a continuous measure of laterality $x_i \in [a, b]$ $(i = 1, , n)$, e.g., as expressed by laterality index (cf. Bryden & Sprott, 1981; Marshall, Caplan, & Holmes, 1975; Seghier, 2008). We assume $a = -100$ and $b = 100$ as range for this measurement. A value of x_i close to a strongly suggests left preference, while x_i close to b strongly suggests non-left preference. Let $\mathbf{x} = (x_1, \ldots, x_n)'$ denote a vector of laterality measurements for an individual, obtained with a given experimental paradigm. An extension to multiple paradigms is outlined in Appendix 3. We are interested in the probability that this individual has hemispheric dominance α, given the laterality measures $\mathbf{x}$. Using Bayes' theorem this can be written as

$$p(\alpha \mid \mathbf{x}) = \frac{p(\mathbf{x} \mid \alpha)p(\alpha)}{p(\mathbf{x})}, \tag{1}$$

where $p(\alpha \mid \mathbf{x})$ is the probability of hemispheric dominance α for an individual in the population with laterality measures $\mathbf{x}$, $p(\mathbf{x} \mid \alpha)$ is the probability of obtaining laterality measures $\mathbf{x}$ for an individual in the population with hemispheric dominance α, $p(\alpha)$ is the prevalence of hemispheric dominance α in the population, and $p(\mathbf{x})$ is the marginal probability of having laterality measures $\mathbf{x}$ for an individual in the population.

The term $p(\mathbf{x})$ in Equation (1) is not a function of α. It thus only contributes to the normalizing constant of this distribution. This means we can neglect it, and obtain the unnormalized posterior (Gelman, Carlin, Stern, & Rubin, 2004, Sec. 1.3)

$$p(\alpha \mid \mathbf{x}) \propto p(\mathbf{x} \mid \alpha) p(\alpha), \tag{2}$$

where ∝ means "is proportional to." Normalization ensures that the sum over all probabilities equals one, and requires dividing the term on the right-hand side of Equation (2) by the sum over all possible values of α, obtaining the normalized posterior

$$p(\alpha \mid \mathbf{x}) = \frac{p(\mathbf{x} \mid \alpha) p(\alpha)}{p(\mathbf{x} \mid \alpha = -1) p(\alpha = -1) + p(\mathbf{x} \mid \alpha = 1) p(\alpha = 1)} = k p(\mathbf{x} \mid \alpha) p(\alpha),$$

where

$$k = \frac{1}{p(\mathbf{x} \mid \alpha = -1) p(\alpha = -1) + p(\mathbf{x} \mid \alpha = 1) p(\alpha = 1))}$$

is the normalizing constant. However, we here follow convention and work with unnormalized distributions, assuming proper normalization is performed in the computational implementation.

Hemispheric dominance α is our target, and by defining the distributions $p(\mathbf{x} \mid \alpha)$ and $p(\alpha)$, we can use (2) to obtain the posterior probability distribution of a. If we, based on prior knowledge, are able to create models for the probability $p(\mathbf{x} \mid \alpha)$ of obtaining laterality measures $\mathbf{x}$ given hemispheric dominance, and the probability $p(\alpha)$ of having a given hemispheric dominance, Equation (2) gives us a way of estimating hemispheric dominance α conditional on $\mathbf{x}$.

Models for observed laterality and hemispheric dominance

Given that a single laterality measurement is a number in $[a, b]$, we model it with a truncated normal distribution with parameters depending on hemispheric dominance. For a vector $\mathbf{x}$ of n observations of a given individual, we hence use the model

$$p(\mathbf{x} \mid \alpha; \mu_{-1}, \mu_1, \Sigma, a, b) = \begin{cases} N_n(\mu_{-1}, \Sigma, a, b) & \text{if } \alpha = -1 \\ N_n(\mu_1, \Sigma, a, b) & \text{if } \alpha = 1, \end{cases} \tag{3}$$

where $N_n(\mu_i, \Sigma, a, b)$ denotes an n-dimensional multivariate normal distribution with mean μ_i in all n dimensions and covariance matrix Σ, truncated at lower limit a, and upper limit b. The parameters of this model are the mean observed laterality for subjects with left hemispheric dominance (μ_{-1}) and right hemispheric dominance (μ_1), which are assumed equal across repeated measurements on the same individual, and the covariance matrix Σ. In the single measurement case ($n = 1$), Σ is a single number σ^2, equal to the variance between single measurements on subjects with a given hemispheric dominance. In the multiple measurements case, assuming that repeated measurements on the same individual have correlation coefficient r, we have

$$\Sigma = \sigma^2 \begin{pmatrix} 1 & r & \cdots & r \\ r & 1 & r & \vdots \\ \vdots & r & \ddots & r \\ r & \cdots & r & 1 \end{pmatrix}. \quad (4)$$

The probability of hemispheric dominance is modelled with a binomial distribution with probability π_{-1} of left hemispheric dominance and $\pi_1 = 1 - \pi_{-1}$ of non-left hemispheric dominance, $p(\alpha) = \pi_\alpha$.

Numerical illustrations for laterality measures obtained with dichotic listening

Parameter estimates

As derived above, the inference from observed laterality to latent hemispheric dominance requires information about the distribution of observed laterality in the hemispheric dominance groups. We here refer to the article by Van der Haegen, Westerhausen, Hugdahl, and Brysbaert (2013) which provides dichotic listening laterality measures and standard deviations for participants which were grouped as left and right dominant based on measured brain activation in an fMRI picture-naming task. For the group of right-handed individuals with left-hemispheric dominance, the reported estimate of mean observed laterality was $\mu_{-1} = 12$. As the study does not include a group of right-handed individuals with right dominance, we here use $\mu_1 = -24$ which was reported for right dominant left-handed participants as approximation of the mean. In both cases we used the standard deviation was $\sigma = 17$ which was reported for left hemispheric dominant right-handers.[1]

The correlation r used in the covariance matrix in Equation (4) for the multiple measurements setting can be estimated for any given dataset by computing the within-subject standard deviation σ_W and then let $r = \sigma^2/(\sigma_W^2 + \sigma^2)$, where σ is the standard deviation between single measurements on individuals with a given hemispheric dominance, defined in the previous paragraph. We also require the antecedent probabilities of being left and non-left dominant. Regarding left dominance, these were taken from a recent meta-analysis of studies using the Sodium Amytal (Wada) procedure to classify hemispheric dominance (Carey & Johnstone, 2014). Based on

[1]Of note, we here use observed laterality (in brain activation) as "ground truth" for the classification although the same inference problem would apply if the classification was based on fMRI data. However, the study only included participants with strong activation asymmetry, which should lead to valid classifications. In any case, for the present example, the reported data provides the best available estimate of the here required distribution.

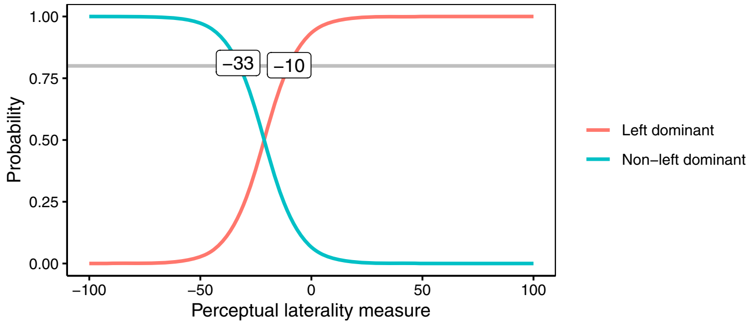

Figure 1. Probability of being left or non-left hemispheric dominant given a single measurement of perceptual laterality. [To view this figure in color, please see the online version of this journal.]

their findings, for right-handed individuals we here estimate the probability to be $\pi_{-1} = .87$. Correspondingly, the probability of not being left dominant was assumed to be $\pi_1 = 1 - \pi_{-1} = .13$.

Probability of left or non-left dominance as a function of single measure of perceptual laterality

Figure 1 shows the probability of being left or non-left hemispheric dominant for language as a function of the magnitude of a single measure of perceptual laterality for right-handers. The horisontal gray line shows an 80% confidence threshold which can be used for classification. Given the parameter estimates assumed here, the following statistical statements can be read out of the numbers underlying Figure 1:

- The probability of being left dominant exceeds 80% if laterality index is above -10.
- The probability of being non-left dominant exceeds 80% if the laterality index is below -33.

These thresholds illustrate again that inferences about the underlying hemispheric dominance depend strongly on the antecedent probabilities of being left or non-left dominant. Remarkably, a laterality index of larger than -10 is sufficient for a classification as left dominant. That is, even yielding a small left-ear advantage does result in a classification as left dominant, as the left dominance has a high antecedent probability. Of note, the above thresholds deviate from "0," suggesting that even when it is the aim to confirm left hemispheric dominance (e.g., as inclusion criterion for participants in a study), using only the direction (sign) of the ear preference is associated with some uncertainty for laterality scores below these thresholds. That also means, in basing

Table 1. Comparison between classifical classification with a cut-off at zero and classification based on the Bayesian model developed in this paper.

	Classical classification		
Bayesian classification	Left	Unclassified	Right
Left	2,075	196	246
Unclassified	0	0	233
Right	0	0	105

his calculations on binary classification into left- and right-ear advantage groups at 0, Satz's sobering probability estimates were actually too lenient.

Empirical data example

Finally, to evaluate the practicality of the above threshold, we classified a sample of $N = 2,855$ right-handed individuals based on the above thresholds. The sample contains dichotic-listening data collected with the same paradigm as used by Van der Haegen et al. (2013) and included data either acquired in laboratory conditions or using the iDichotic iPhone app (Bless et al., 2015; Hugdahl et al., 2009). Of the total sample, 2,517 (88.2%) individuals were classified as left dominant using the Bayesian thresholds, 105 (3.7%) were classified as non-left dominant, when requiring 80% or higher probability for classification. The remaining 233 (8.2%) individuals could not be conclusively classified. Thus, the percentage classified as left dominant matched the 87% expected from the Wada test (e.g., Carey & Johnstone, 2014). In this respect, the present approach promises better classification results than just using "0" as cut-off, which only would suggest 72.7% left dominant individuals in the sample. Table 1 compares the classifications based on a Bayesian model with 80% confidence threshold to those based on a cut-off at zero. Of note, all subjects either classified as left dominant or unclassified by the classical model, are classified as left dominant by the Bayesian model. We also emphasize that an 80% classification threshold implies that among classified individuals, the probability of belonging to the given class varies between 80% and 100%. The average probability of left dominance among individual classified as left dominant was 97.4%, implying an expected proportion of classification errors equal to $(100 - 97.4)\% = 2.6\%$. For right dominance the average probability was 93.1%, with an expected proportion of classification errors equal to $(100 - 93.1)\% = 6.9\%$. Figure 2 shows boxplots of the distribution of dichotic listening scores among subjects classified to each group.

Effect of multiple measurements

In this section, we aim to demonstrate the effect of utilizing multiple laterality measurements obtained with the same paradigm for classification in three

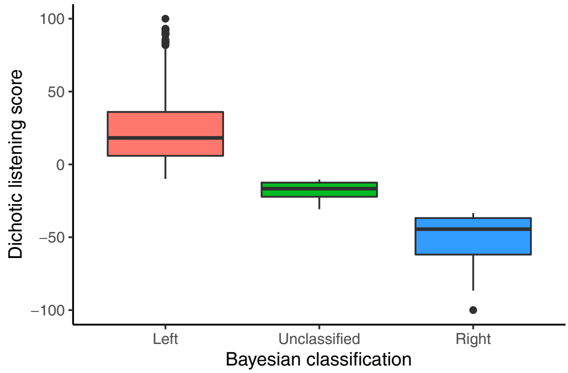

Figure 2. The boxplots show the distribution of dichotic listening scores for left dominant, unclassified, and right dominant subjects, according to the Bayesian classification, for the example in Section "Empirical data example". [To view this figure in color, please see the online version of this journal.]

steps. Firstly, we illustrate the impact of multiple testing on the classification for a single individual. Secondly, we apply the classification to available multiple-testing datasets. Finally, we conduct a simulation experiment to evaluate how many measures of laterality are required for an optimal classification outcome given the present parameters.

The impact of multiple laterality measures

Figure 3 illustrates the impact of a second measurement on the probability curve shown in Figure 1. That is, we assume after the first laterality measure, a second measurement has been obtained, with value −60, −20, 0, 20, or 60, given by the colour legend. The coloured curves show the final probabilities of left dominance as a function of this second measurement, while the dashed black line shows the corresponding curve in the case of a single measurement (between −100 and 100; i.e., it is equivalent to the curve in Figure 1). The graph illustrates that a second measurements shifts the original probability along the y-axis. A positive value in the second measurement increases the probability of left hemispheric dominance (blue and purple curves). Similarly, a negative value in the second measurement decreases the probability of left hemispheric dominance (red and yellow curves). That also means that if the values of the two obtained measurements are close, this typically leads to higher statistical confidence compared to a single measurement. For example, if the first measurement of a right-handed subject is 10, and the second measurement is 20, the probability of left dominance is closer to 1.0 than if only a single measurement of value 10 had been obtained, as can be seen by the blue curve being above the dashed black curve.

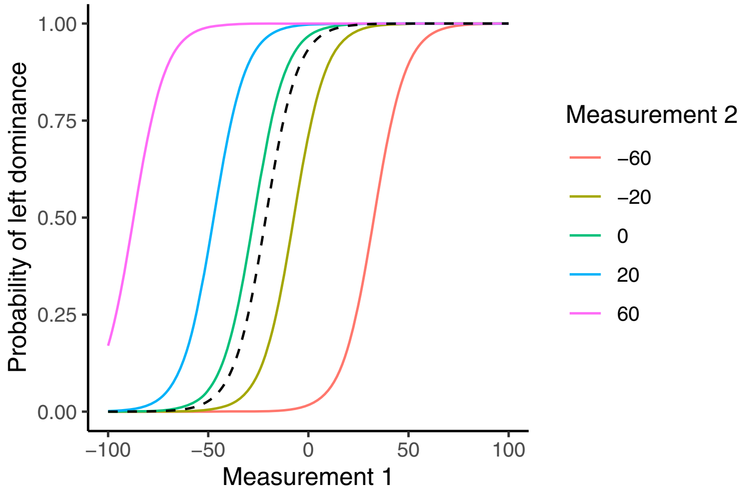

Figure 3. If a first measurement with value given by the *x*-axis has been obtained for a right-handed subject, the curves show the value of the final probability of left hemispheric dominance after a second measurement has been obtained with value given by the colour legend. The dashed black line shows the same probabilities in the case where only a single measurement has been obtained. [To view this figure in color, please see the online version of this journal.]

To further illustrate the beneficial effect, Table 2 illustrates the impact of obtaining multiple times the same laterality measurement. In the table, the probability of left dominance after obtaining one, two, three, or four measurements of identical magnitude is shown. For laterality indices well below zero, a repetition of the same value decreases the probability of being left dominant. For positive laterality indices, the repetition increases the probability of being left dominant. For repeated measurements close to zero, the probability of left brain dominance will increase, as seen by the repeated measures at −5

Table 2. The table shows the probability of left brain asymmetry after obtaining one, two, three, or four measurements of the same magnitude for a right-handed subject.

	Measurements			
Perceptual laterality measure	1	2	3	4
−40.00	0.09	0.00	0.00	0.00
−30.00	0.25	0.02	0.00	0.00
−20.00	0.54	0.17	0.03	0.01
−10.00	0.80	0.71	0.60	0.48
−5.00	0.88	0.90	0.91	0.92
0.00	0.93	0.97	0.98	0.99
5.00	0.96	0.99	1.00	1.00
10.00	0.98	1.00	1.00	1.00
20.00	0.99	1.00	1.00	1.00
30.00	1.00	1.00	1.00	1.00
40.00	1.00	1.00	1.00	1.00

yielding a slowly increasing probability of left dominance. This is due to the mean dichotic listening score assumed to be 12 for participants with left dominance being closer to -5 than the corresponding mean value -24 for participants with non-left hemispheric dominance Together with Figure 3, this shows how obtaining multiple measurements that tend in the same direction increases the confidence level of classification. Conversely, when multiple measurements tend in opposite directions, the probability of left hemispheric tends toward .5.

Empirical data example

To illustrate the effect of multiple testing on empirical data, we reanalysed data from two longitudinal studies. The Karlsson, Johnstone, and Carey (2019) dataset consisted of 871 participants (485 right-handed, 386 left-handed) for which three perceptual laterality measures were available per participant. The Bless et al. (2013) dataset included data from 33 right-handed participants, but with four measurements available per person. In both studies, the data was collected using the very same consonant-vowel dichotic-listening paradigm as in the above examples so that the used parameters should also apply here.

Regarding the Karlsson et al. (2019) sample, for the classification of the right-handed subsample, we used the same parameters as outlined in Section “Parameter estimates” and a within-subject standard deviation of 14.0 for the retest data (estimated from the empirical data), yielding $r = 17^2/(14^2 + 17^2) = 0.60$. Table 3, left side, provides an overview of the classification results as function of the number of measurements. The following trends get obvious. Firstly, using the first laterality measure only the percentages classified into left or non-left dominance are comparable to the example discussed above (Section “Empirical data example”). That is, 88.9% were classified as left dominant and 3.5% as non-left dominant. Secondly, using three as opposed to one laterality measure reduces the undecided cases by about 50%, increasing both the percentage classified as left and non-left dominant, respectively.

For classification of the left-handed individuals the model parameters had to be adjusted and we used the corresponding estimates reported by Van der Haegen et al. (2013). That is, $\mu_1 = 10$ for left hemispheric dominance and

Table 3. The table shows how the number of classification with 80% probability or higher depends on the number of measurements for left-handers and right-handers.

	Right-handers			Left-handers		
n	Left	Non-left	Undecided	Left	Non-left	Undecided
1	431 (88.9%)	17 (3.5%)	37 (7.6%)	267 (69.2%)	15 (3.9%)	104 (26.9%)
2	440 (90.7%)	21 (4.3%)	24 (4.9%)	287 (74.4%)	19 (4.9%)	80 (20.7%)
3	443 (91.3%)	23 (4.7%)	19 (3.9%)	287 (74.4%)	20 (5.2%)	79 (20.5%)

$\mu_{-1} = 24$ for right hemispheric dominance. Standard deviations for left and non-left dominant left-handed were 22.8 (25 samples) and 28.0 (16 samples), respectively. Hence we use the pooled variance 24.9 as common standard deviation. The antecedent probability of being left-dominant as left handed was set to $\pi_{-1} = .65$ following Carey and Johnstone (2014). The within-subject standard deviation was estimated to 13.8, yielding $r = 24.9^2/(13.8^2 + 24.9^2) = 0.76$. Table 3, right side, provides an overview of the classification results as for the left-handed sample from Karlsson et al. (2019). Again, we see that the number of individuals that cannot be classified conclusively, decreases with the number of measurements, dropping from 26.9% after the first to 20.5% after the third measure. As a result, both the number of individuals classified as left and non-left dominant increases up to 74.4% and 5.2%, respectively.

To illustrate the effect of using four measures, we classified the data from Bless et al. (2013). As all participants were right-handed, we here used the model parameters outlined in Section "Parameter estimates". Within-subject standard deviation was 20.3, yielding $r = 0.41$. As can be seen in Table 4 the percentage of left dominant classified individual varies between 84.8% for one laterality index, 90.9% for two laterality indices, 87.9% for three laterality indices, and back to 84.8% for four laterality indices. The number of subjects classified as right dominant, on the other hand, increases from 3% after a single measure to 9.1% after four measures. At the same time the number that cannot be classified is reduced from 12.1% to 6.1%. The step-wise progress of the classification is illustrated in Figure 4.

Simulation experiment

In order to more quantitatively examine the benefit of additional measurements, a simulation experiment was conducted in which we simulated the measurement process. For each combination of hemispheric dominance (left/non-left) and handedness (left/right), a sample with 10 repeated measurements of 2,000 subjects was simulated. First, one "true laterality" for each simulated subject was sampled around the mean obtained from Van der Haegen et al. (2013). The true laterality values were truncated such that subjects with left hemispheric dominance had values in [0, 100] and subjects with right hemispheric dominance had values in $[-100, 0]$. This

Table 4. The table shows how the number of classification with 95% probability or higher depends on the number of measurements for the Bless App data.

n	Left	Non-left	Undecided
1	28 (84.8%)	1 (3%)	4 (12.1%)
2	30 (90.9%)	1 (3%)	2 (6.1%)
3	29 (87.9%)	2 (6.1%)	2 (6.1%)
4	28 (84.8%)	3 (9.1%)	2 (6.1%)

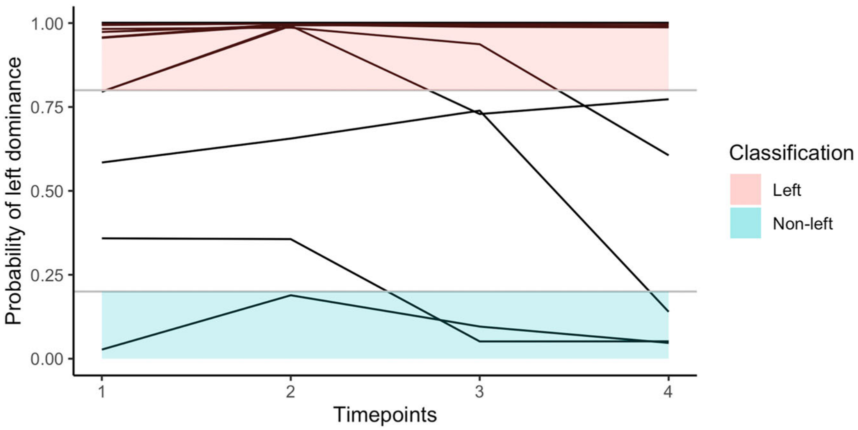

Figure 4. How an individual subject's probability of being left dominant (black lines) changes by successively entering 1, 2, 3, and 4 laterality measures into the prediction. [To view this figure in color, please see the online version of this journal.]

restriction is in line with Kimura's structural model of dichotic listening (Kimura, 1967), or other accepted models explaining the relationship between perceptual preference in dichotic listening and hemispheric dominance (for review see Hiscock & Kinsbourne, 2011). Next, the actual measurements for each subject were randomly sampled around the subject's true laterality values. In the data from Bless et al. (2013) used in Section "Empirical data example" the within-subject standard deviation was 20.3, and using this as a guideline, we set the standard deviation of the repeated measurements of each individual to 20.

Each subject in each sample was classified 10 times according to the methods developed in this paper, first time using only one measurement, the second time using two measurements, until the 10th time in which all measurements were used. For each combination of hemispheric dominance and handedness, the correlation *r* used in the covariance matrix in Equation (4) was estimated from the sampled data.

Figure 5 shows the number of correctly and incorrectly classified subjects at an 80% threshold, as well as the number of undecided subjects, as a function of the number of measurements. For left dominant right-handed participants, the proportion of correctly classified subjects gets very close to 100% as the number of measurements increases. For left dominant left-handers, the proportion of correctly classified subjects increases quickly from 71% after a single measurement to 87% after 4 measurements and 90% after 8 measurements. The number of not classified individuals accordingly decreases. However, the adding of additional laterality measures revealed diminishing returns. That is, the gain in correct classifications and reduction of unclassified

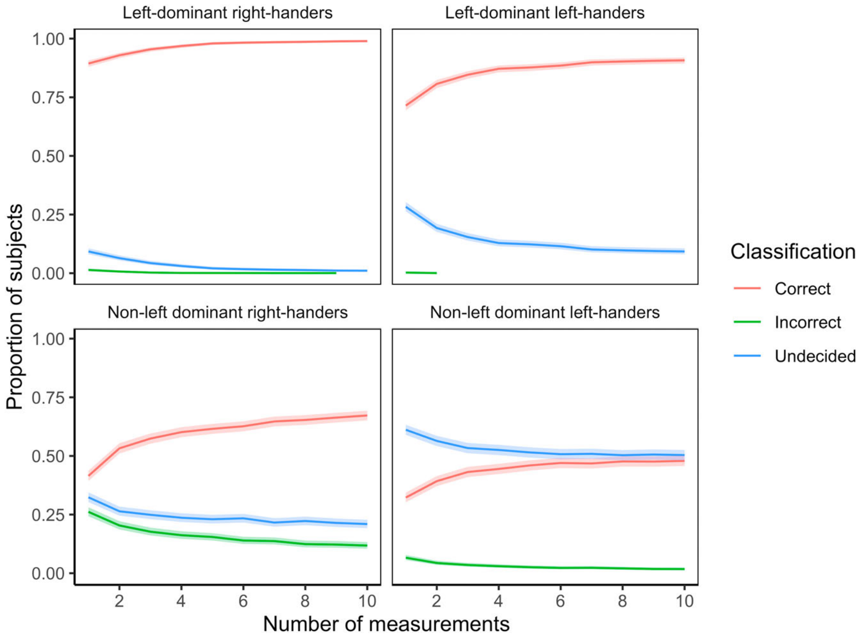

Figure 5. Results of the simulation experiment described in Section "Simulation experiment." The figures show the proportion of subjects classified correctly, incorrectly, or undecided at an 80% threshold. Shaded regions represent 95% confidence bands. [To view this figure in color, please see the online version of this journal.]

individuals that is achieved by an additional measurement is largest when the number of measurements is low.

Figure 5, bottom, also illustrates once more that correctly classifying subjects with non-left hemispheric dominance is a much harder task. For non-left dominant right-handers, the proportion of correctly classified subjects starts at 42% after a single measurement and reaches 67% after 10 measurements, while for left-handed individuals, the number starts at 32% after a single measurement, and increases to 48% after 10 measurements. The number of non-left dominant subjects that are incorrectly classified, however, does decrease rapidly with the number of measurements: for right-handers it is still 12% after 10 measurements, while for left-handers the proportion gets down to 1.8%. Hence, while the majority of subjects with non-left hemispheric dominance end up as correctly classified, a large proportion are still undecided after obtaining 10 measurements.

The chosen probability threshold for classification, which was set to 80% here, determines the minimum classification probability according to the Bayesian model for which subjects are given a classification. Using the simulation results, we can investigate how the classification depends on the

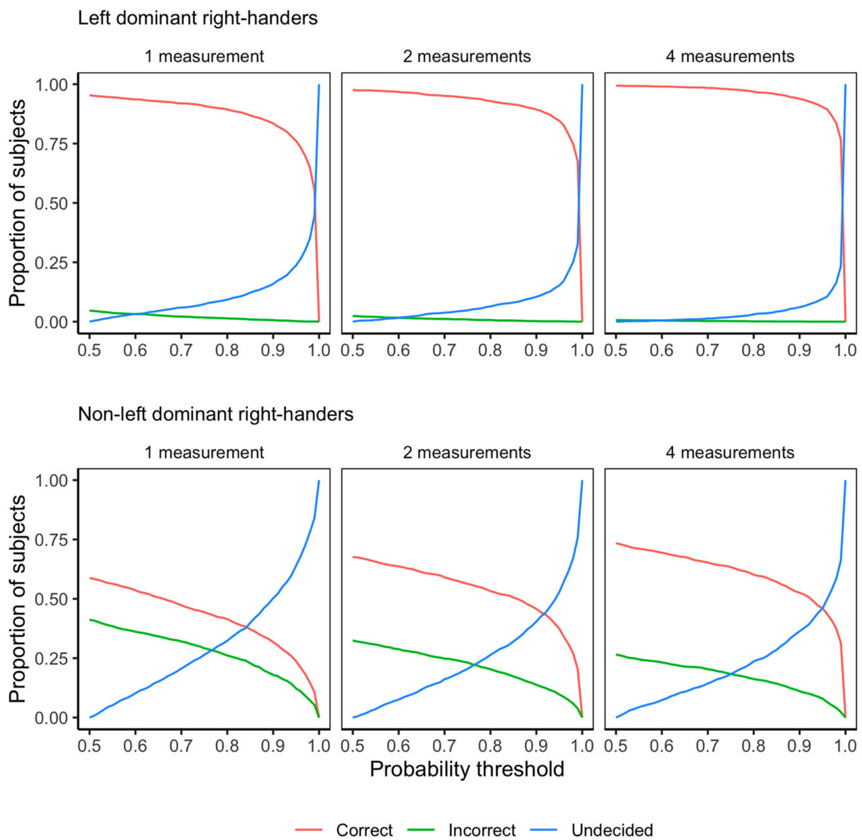

Figure 6. Proportion correctly classified, incorrectly classified and undecided subjects as a function of the chosen probability threshold for classification. [To view this figure in color, please see the online version of this journal.]

chosen threshold. Figure 6 shows this for right-handers, after 1, 2, or 4 measurements. For example, for left dominant right-handers using one measurement, setting the threshold to 60% leads to 3.2% incorrectly classified and 93.6% correctly classified subjects, setting it to 80% leads to 1.4% incorrectly classified and 89.4% correctly classified, while setting it to 95% leads to 0.2% incorrectly classified and 76.1% correctly classified. These numbers illustrate the trade-off between ensuring a sufficiently large sample with a given hemispheric dominance (low threshold) and having a sufficiently small proportion of incorrectly classified subjects (high threshold).

For non-left dominant right-handers the corresponding numbers are 36.2% incorrectly classified and 53.6% correctly classified subjects when using a 60% threshold, 26.2% incorrectly classified and 41.5% correctly classified subjects when using an 80% threshold, and 12.2% incorrectly classified and 23.8% correctly classified when using a 95% threshold.

Discussion

Satz (1977) demonstrated that using the sign of observed laterality scores to infer underlying hemispheric dominance leads to invalid conclusions in conditions in which the antecedent probabilities of hemispheric dominance are strongly skewed to one side. In particular, his example shows that a classification of an individual into the low probability *atypical* right hemisphere dominance group is not valid. In the present work, we revisited this inference problem by theoretically extending Satz' Bayesian approach in two ways: we incorporated (a) the magnitude of the observed laterality index and (b) the possibility of multiple measures of laterality in the classification model. Applying our extended Bayesian classification on the case of using dichotic listening data, we made a couple of observations, which might be considered useful for future studies that attempt to draw conclusions about latent hemispheric differences.

Firstly, Satz neglected that the magnitude of the laterality index provides additional information about the security of the statistical inference. As outlined in the introduction, a larger as compared to smaller (absolute) laterality score, makes it less likely that the direction (sign) of the laterality score is due to measurement error. Incorporating the magnitude of the laterality index, we were able to determine statistical boundaries in which confident inferences about latent hemispheric differences may be drawn. Importantly, in the present examples these boundary values deviate from zero, suggesting that the common praxis of using a laterality index of zero as cut-off to split samples into hemispheric dominance subgroups or to exclude individuals of unwanted lateralization is questionable. For example, as the boundary laterality above which an individual can be classified as left dominant for speech processing is actually below zero (see Figure 1), using zero as threshold would lead to a heterogeneous "below-zero group" which includes both left and non-left dominant individuals. At the same time, the "above-zero" group will be homogenous for speech dominance but exclude a substantial proportion of the sample. Given the latter observation, it appears little surprising that dichotic-listening studies using zero as threshold, typically underestimate the percentage of individuals with left hemispheric speech processing dominance by about 15 to 20% compared to direct measures of lateralization (cf. Bryden, 1988; Westerhausen & Kompus, 2018). Using the here determined Bayesian laterality boundaries for classification this gap disappears, at least when using an 80% confidence threshold. That is, for the two large data sets of right-handed individuals examined here we yield estimates between 88.2% and 88.9% of left hemispheric dominance (using one laterality measure) which are comparable with estimates obtain from Wada test or other more direct measures of hemispheric dominance (Carey & Johnstone, 2014). Likewise, in the left-handed sample, the percentage of left dominance was estimated to be 69.2% so that it was slightly elevated compared to the expected 65%. However, it has to be noted that these percentage estimates depend on the confidence threshold applied and a more conservative threshold (i.e., using 95% instead of 80%) will obviously lead to reduction in participants classified as left dominant (or classified at all; see Figure 6). Nevertheless, whenever the aim is to confirm or secure that a given participant is left-dominant for language processing, the here suggested Bayesian laterality boundaries might be seen as an improvement compared to the use of zero as a cut-off value. At the same time, rather than classifying individuals based on a cut-off value, the present model might also be used to determine the likelihood of being left or non-left dominant on an individual level. These estimates may well be used as weights in analyses comparing groups.

We also show that the suggested laterality thresholds for non-right hemispheric dominance yield conservative proportion estimates and prevent a conclusive classification of a significant amount of individuals. At the same time, this outcome already represents a substantial improvement compared to the analysis by Satz (1977), as his implicit conclusion was that atypical dominance cannot be inferred from individual laterality measures. According to Satz, having a left-ear advantage did not increase the likelihood of being right dominant above 10%. Here, we can classify between 5% and 9% of the right-handed and ≈5% in left-handed individuals as non-left dominant with a confidence of at least 80%. Nevertheless, these estimates are well below the assumed 12% and 25%, respectively (Carey & Johnstone, 2014), and the classified individuals, showing comparatively strong laterality indices, likely represent and extreme group of the population. Thus, the findings illustrate again that inferring membership of the less likely class is statistically more challenging, when the antecedent probabilities are strongly skewed.

The second theoretical extension to Satz's approach was the inclusion of multiple laterality measures in the Bayesian classification. As expected, the inclusion of multiple measures step-wise decreases the amount of individuals that could not be conclusively classified by the empirical data. However, as can be seen already after three measures in Table 3, adding additional measurements appears to yield diminishing returns for the classification rate. That is, the classification rate increase from the second to the third laterality measure is smaller than the increase from the first to the second measure. This observation was confirmed in the simulation experiment indicating that the major improvement in classification rates is attained within the first three laterality measures. Beyond four or five measures, the increase in classification rates appear negligible. However, the simulation also indicates that the classification of the low likelihood class (i.e., non-left dominance) benefits most from including additional measures, as the initial increase appears steeper than in the high-likelihood class. The proportion of correct classifications as right-dominant reaches an asymptote at around .70 and .50 for right- and left-handed simulation sample, respectively, again illustrating the difficulty of classifying the groups of low antecedent probability. Nevertheless, at least considering the present data, using two or three laterality measures for the classification appears to improve the classification rates compared to using a single laterality measure.

In summary, one might criticise that the here introduced framework for Bayesian inference does not solve the inference problem. While this is certainly true, we here argue that the present approach substantially improves the classification outcome compared with the standards currently applied in literature. Importantly, however, it is not only the statistical model but also the inserted parameters that determine the quality of the classification outcome. In the present case—inferring latent speech dominance from dichotic-listening laterality measures—the assumed distributions of laterality measures were characterized by comparatively large standard deviations, resulting in a substantial overlap of the distribution of left and non-left dominant individuals. This might well reflect true interindividual difference in the population, but substantial intra-individual difference in the repeated-measure examples suggest that at least some of the variance can be attributed to low reliability of the used dichotic-listening paradigm (for discussion see also Westerhausen, 2019). Thus, one way of further improving the classification certainly is to improve the available paradigms and obtain a better data basis. If we, as laterality researchers, are interested in drawing valid conclusions about latent hemispheric dominance from observed laterality differences, it is crucial to establish a good knowledge about the relationship of these variables. This applies for behavioural measures of laterality as much as electrophysiological, near-infrared spectroscopy, functional MRI or any other laterality measures.

Finally, while we defined perceptual laterality as a continuous variable, we followed Satz (1977) approach of classifying the underlying hemispheric dominance into two groups by following the distinction of left or non-left dominant individuals used by Carey and Johnstone (2014). This might be seen at odds with a series of Wada test studies which classify hemispheric dominance into three classes by also allowing for a "bilateral" group (Benbadis, Dinner, Chelune, Piedmonte, & Lüders, 1995; Carey & Johnstone, 2014), i.e., individuals which show speech arrest neither after left nor right hemisphere amytal perfusion, or who showed some residual speech production after both left and right amytal perfusion. We here decided to keep Satz's binary classification because reliable antecedent probabilities for the bilateral group are missing. Snyder, Novelly, and Julius (1990) in their review found large variability in the prevalence of the bilateral group which ranged from 0% to 60% and was attributed to disagreement in the defining criteria and in the assessment procedures during testing. As consequence, also the relationship between bilateral speech processing and performance in laterality tests is not clear, and necessary antecedent probabilities are missing. However, should this data be available in the future, Appendix 2 provides formulas for trichotomous classification, which are also implemented in the accompanying R package and Shiny app.

In conclusion, we here take a more positive stance than Paul Satz in his original publication: inductive inference from laterality measures to underlying hemispheric dominance is not "unwarranted and reckless" (Satz, 1977, p. 208). If the antecedent probabilities are considered appropriately, for example, within the here presented extended Bayesian framework model, valid inferences are possible also regarding low probable hemispheric dominance classes. The here provided R (R Core Team, 2019) package (Supplementary Material) and Shiny (Chang et al., 2018) app (Supplementary Material) implementations of the model, may be used to statistically explore the boundaries of valid inference.

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Data availability statement

R scripts for reproduction of all numerical examples and simulation results, including figures and tables, are available at the Open Science Framework, https://osf.io/mkwcr. The data from Bless et al. (2013) analysed in Section "Empirical data example" is also available at https://osf.io/mkwcr. We cannot share the data from Hugdahl et al. (2009) and Bless et al. (2015) analysed in Section "Empirical data example" nor the data from Karlsson et al. (2019) analysed in "Empirical data example ."

Disclosure statement

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Appendices

Appendix 1. Satz's approach with updated prior probabilities

For reference, we also computed parameters for Satz's model (Satz, 1977), using updated prior probabilities defined in Section "Parameter estimates". Satz computed probabilities for right-handers only, but given the availability of prior probabilities for both left- and right-handers, we computed both. The resulting probabilities are shown in Tables A1 and A2, respectively. Satz's model assumes a binary classification of perceptual laterality, using a cut-off at 0. Table A3 shows the classification scheme derived from this model. Note that only the sign of the speech laterlisation score impacts the probability of left or right brain asymmetry in this model.

Table A1. Satz's model for right-handers, using updated prior information.

	Left dominance	Non-left dominance	Total
Left ear adv.	0.21	0.12	0.33
Right ear adv.	0.66	0.01	0.67
Total	0.87	0.13	1.00

Table A2. Satz's model for left-handers, using updated prior information.

	Left dominance	Non-left dominance	Total
Left ear adv.	0.22	0.29	0.51
Right ear adv.	0.43	0.06	0.49
Total	0.65	0.35	1.00

Table A3. Probabilities of left or right brain dominance in Satz's model, using updated prior information.

Handedness	Ear advantage	P(Left dom.)	P(Right dom.)
Left	Left	$0.22/0.29 = 0.43$	$0.29/0.22 = 0.57$
Left	Right	$0.43/0.06 = 0.88$	$0.06/0.43 = 0.12$
Right	Left	$0.21/0.12 = 0.64$	$0.12/0.21 = 0.36$
Right	Right	$0.66/0.01 = 0.98$	$0.01/0.66 = 0.02$

Appendix 2. Extension to the trichotomous case

We here present an extension of the model to the trichotomous case, which is also implemented in the R package and Shiny app referenced above. Firstly, the underlying hemispheric dominance α now takes on values -1, 0, and 1, indicating left dominance, no dominance (bilaterality), and right dominance, respectively. Apart from this, Equations (1) and (2) remain unchanged. Normalization of the posterior distribution (2) is now obtained by the condition

$$p(\alpha = -1 \mid \mathbf{x})p(\alpha = -1) + p(\alpha = 0 \mid \mathbf{x})p(\alpha = 0) + p(\alpha = 1 \mid \mathbf{x})p(\alpha = 1) = 1.$$

Next, the model for observed laterality and hemispheric dominance, Equation (3) becomes

$$p(\mathbf{x} \mid \alpha; \mu_{-1}, \mu_0, \mu_1, \Sigma, a, b) = \begin{cases} N_n(\mu_{-1}, \Sigma, a, b) & \text{if } \alpha = -1 \\ N_n(\mu_0, \Sigma, a, b) & \text{if } \alpha = 0 \\ N_n(\mu_1, \Sigma, a, b) & \text{if } \alpha = 1, \end{cases}$$

where μ_0 represents the mean observed laterality for subjects with no dominance. Furthermore, the probability of belonging to group α now is modeled using a multinomial distribution with three classes, where $p(\alpha) = \pi_\alpha$, $\alpha \in \{-1, 0, 1\}$, subject to the constraint $\pi_{-1} + \pi_0 + \pi_1 = 1$.

Appendix 3. Extension to multiple experimental paradigms

The model presented can be extended to allow for predictions based on measurements obtained with different experimental paradigms. Consider Equation (3), which represents the probability distribution of laterality measurements for a given individual. The parameters μ_{-1}, μ_1, Σ, a, and b describe the means (μ_{-1}, μ_1), covariances (Σ), and upper and lower limits (a,b) of measurements obtained within the experimental paradigm. A generalization to G experimental paradigms indexed by $g = 1, \ldots, G$ would require a different set of parameters for each paradigm, which we denote by μ_{-1}^g, μ_1^g, $\Sigma^{g,g}$, a^g, and b^g, as well as covariance matrices describing how measurements in paradigm g are correlated with measurements in paradigm g', for $g \neq g'$, which we denote $\Sigma^{g,g'}$.

As a concrete example, consider the case of $G = 2$ paradigms and a total of $n = 4$ measurements of each individual. Assume $\mathbf{x} = (x_1, x_2, x_3, x_4)'$ is ordered such that measurements x_1 and x_2 were obtained with paradigm 1 and x_3 and x_4 with paradigm 2. The joint probability distribution of the four measurements is now a truncated multivariate normal distribution with means $(\mu_{-1}^1, \mu_{-1}^1, \mu_{-1}^2, \mu_{-1}^2)'$ for left-dominant subject and $(\mu_1^1, \mu_1^1, \mu_1^2, \mu_1^2)'$ for right-dominant subjects, lower limits $(a^1, a^1, a^2, a^2)'$, and upper limits $(b^1, b^1, b^2, b^2)'$. The full covariance matrix is

$$\Sigma = \begin{pmatrix} \Sigma^{1,1} & \Sigma^{1,2} \\ \Sigma^{2,1} & \Sigma^{2,2} \end{pmatrix},$$

consisting of submatrices

$$\Sigma^{1,1} = \sigma_1^2 \begin{pmatrix} 1 & r_{1,1} \\ r_{1,1} & 1 \end{pmatrix}, \quad \Sigma^{1,2} = \Sigma^{2,1} = \sigma_1 \sigma_2 \begin{pmatrix} r_{1,2} & r_{1,2} \\ r_{1,2} & r_{1,2} \end{pmatrix}, \quad \Sigma^{2,2} = \sigma_2^2 \begin{pmatrix} 1 & r_{2,2} \\ r_{2,2} & 1 \end{pmatrix},$$

in which $r_{1,1}$ denotes the correlation between measurements obtained using paradigm 1, $r_{2,2}$ the correlation between measurements obtained using paradigm 2, $r_{1,2}$ the correlation between a measurement obtained using paradigm 1 and another measurement obtained using paradigm 2, σ_1 the standard deviation of measurements obtained using paradigm 1, and σ_2 the standard deviation of measurements obtained using paradigm 2.