

Modeling fMRI data generated by overlapping cognitive processes with unknown onsets using Hidden Process Models

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Abstract

We present a new method for modeling fMRI time series data called Hidden Process Models (HPMs). Like several earlier models for fMRI analysis, Hidden Process Models assume the observed data is generated by a sequence of underlying mental processes that may be triggered by stimuli. HPMs go beyond these earlier models by allowing for processes whose timing may be unknown, and that might not be directly tied to specific stimuli. HPMs provide a principled, probabilistic framework for simultaneously learning the contribution of each process to the observed data, as well as the timing and identities of each instantiated process. They also provide a framework for evaluating and selecting among competing models that assume different numbers and types of underlying mental processes. We describe the HPM framework and its learning and inference algorithms, and present experimental results demonstrating its use on simulated and real fMRI data. Our experiments compare several models of the data using cross-validated data log-likelihood in an fMRI study involving overlapping mental processes whose timings are not fully known.

Key words: functional magnetic resonance imaging, statistical methods, machine learning, hemodynamic response, mental chronometry

1. Introduction

1 Hidden Process Models (HPMs) are a new method
2 for the analysis of fMRI time series data based on the
3 assumption that the fMRI data is generated by a set of
4 mental processes. HPMs model each process with pa-
5 rameters that define both the spatial-temporal signature
6 of fMRI activation generated by the process over some

7 window of time (e.g. a hemodynamic response func-
8 tion (HRF)), and a probability distribution on the on-
9 set time of the process relative to some external event
10 (e.g., a stimulus presentation or behavioral response).
11 By including a probability distribution over process start
12 times, HPMs allow the study of processes whose on-
13 set is uncertain and that may vary from trial to trial.
14 HPMs assume these processes combine linearly when
15 they overlap, and the sum of the HRFs from the active
16 processes defines the mean of a Gaussian probability
17 distribution over observed fMRI data. We present both
18 a learning algorithm to train HPMs from fMRI data,
19 and an inference algorithm that applies an HPM to in-
20 fer the probable identities and start times of processes
21 to explain additional observed data. The HPM learn-

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22 ing algorithm resolves uncertainty about process identities and start times in the training data, while simultaneously estimating the parameters of the processes (the spatial-temporal signature and timing distribution). This probabilistic framework also provides an opportunity for principled comparison of competing models of the cognitive processes involved in a particular fMRI experiment.

30 Hidden Process Models build on a variety of work on fMRI analysis, combining aspects of hemodynamic response function estimation and mental chronometry. A linear systems approach for estimating HRFs is described in Boynton et al. (1996), and Dale & Buckner (1997) describes how to deal with overlapping hemodynamic responses when times and identities of the underlying processes are fully observed. More recently, the problem of asynchronous HRF estimation, in which the stimuli might not align with the image acquisition rate, was addressed in Ciuciu et al. (2003). The major difference between these approaches and HPMs is that all of these methods assume processes generating the HRFs are fully known in advance, as are their onset times, whereas HPMs can estimate HRFs even when there is uncertainty about when the HRF begins.

46 The field of mental chronometry is concerned with decomposing a cognitive task into its component processing stages. Traditionally, mental chronometry has relied on behavioral data such as measured reaction times, but studies have shown that functional MRI can also be used to address this problem (Menon et al. (1998); Formisano & Goebel (2003)). Henson et al. (2002) and Liao et al. (2002) have also proposed methods for estimating the HRF and its latency that use the temporal derivative of an assumed form for the HRF. While these works are not focused on identifying hidden processes, the estimation techniques they describe could potentially be incorporated into the HPM framework.

60 The use of classification techniques from the field of machine learning is becoming widespread in the fMRI domain (see Haynes & Rees (2006) for an overview). Classifiers have been used to predict group membership for particular participants (e.g. drug-addict vs. control, in Zhang et al. (2005)), and a variety of mental states (Kamitani & Tong (2005); Mitchell et al. (2004); Cox & Savoy (2003); Haxby et al. (2001)). HPMs can also be used for classification, but in a more general setting. Whereas the above classification methods assume that the mental processes being classified do not overlap in time, and that their timings are fully known during both training and testing, HPMs remove both of these restrictions. Finally, the current paper also extends preliminary

work on HPMs reported in Hutchinson et al. (2006).

Dynamic Bayesian Networks (DBNs) (Murphy (2002)) are another class of models widely used in machine learning that can be applied to fMRI analysis. Hidden Markov models (HMMs) (Rabiner (1989)) are a type of DBN. HPMs are actually DBNs as well, although it is cumbersome to express HPMs in the standard DBN notation. An example of a DBN that has been used for the spatial-temporal analysis of fMRI is Faisan et al. (2007), which presents hidden Markov multiple event sequence models (HMMESMs). HMMESMs use data that has been pre-processed into a series of spikes for each voxel, which are candidates for association with hemodynamic events. In contrast, we estimate a spatial-temporal response to each process (similar to a hemodynamic event). Additionally, where we estimate a probability distribution over the lag between stimulus and activation, HMMESMs use an optimized, but fixed activation lag. Finally, HMMESMs have only been used to detect activation associated with stimuli, and not to investigate hidden processes.

One of the most widely used methods for analyzing fMRI data is SPM (Friston (2003)). An advantage of SPM is that it produces maps describing the activation throughout the brain in response to particular stimuli. A disadvantage of SPM is that it is massively univariate, performing independent statistical tests for each voxel. In fact, it has been shown that some mental states cannot be detected with univariate techniques, but require multivariate analysis instead (Kamitani & Tong (2005)). HPMs are a multivariate technique that employ data from all voxels, for example, to estimate the onset times of processes. The learned parameters of the HRF for each process can also generate maps to describe the activity over the brain when that process is active (e.g. the average over time of the response for each voxel). This type of map is different from the ones produced by SPM, but still potentially useful.

The ideas discussed in Poldrack (2006) are also relevant to HPMs, especially in interpreting models that include processes that are not well understood. That paper reviews the idea of 'reverse inference,' and the caveats associated with it. Reverse inference occurs when activity of a brain region is taken to imply the engagement of a cognitive process shown in other studies to be associated with that brain region. This line of reasoning is more useful when the region of interest is highly selective for the cognitive process in question. This paper speaks directly to the problem of interpreting unsupervised processes from the parameters of their estimated hemodynamic response functions in HPMs. Also relevant is the companion paper to Poldrack (2006), Henson

(2006), which discusses conditions under which we can distinguish between competing cognitive theories that differ in the presence/absence of a cognitive process. The major contributions of HPMs are the ability to study cognitive processes whose onset times are unknown, the ability to compare different theories of cognitive behavior in a principled way, and the ability to do classification in the presence of overlapping processes. In all of these tasks, HPM parameters can also be used to enhance our understanding of the model.

This paper proceeds as follows. Section 2 introduces HPMs formally, including the algorithms for inference and learning. Section 3 provides results on real and synthetic datasets, and Section 4 discusses these results.

2. Materials and methods

We first present real and synthetic datasets to which we have applied HPMs so that we may use them as examples in the following section. We then describe the HPM formalism and algorithms.

2.1. Data acquisition and pre-processing

2.1.1. Experiment 1: sentence-picture verification

We applied HPMs to an fMRI dataset collected while participants viewed and compared pictures and sentences. In this dataset, 13 normal participants were presented with a sequence of 40 trials (Keller et al. (2001)). In half of the trials participants were shown a picture (involving vertical arrangements of the symbols *, +, and \$) for 4 seconds followed by a blank screen for 4 seconds, followed by a sentence (e.g. “The star is above the plus.”) for 4 seconds. Participants were given 4 seconds to press a button indicating whether the sentence correctly described the picture. The participants then rested for 15 seconds before the next trial began. In the other half of the trials the sentence was presented first and the picture second, using the same timing.

Imaging was carried out on a 3.0 Tesla G.E. Signa scanner. A T2*-weighted, single-shot spiral pulse sequence was used with TR = 500 ms, TE= 18 ms, 50-degree flip angle. This sequence allowed us to acquire 8 oblique axial slices every 500 ms, with an in-plane resolution of 3.125 millimeters and slice thickness of 3.2 mm, resulting in approximately 5000 voxels per participant. The 8 slices were chosen to cover areas of the brain believed to be relevant to the task at hand. More specifically, the eight oblique-axial slices collected in each TR were acquired in two separate non-contiguous four-slice volumes, one positioned superiorly to cover su-

perior parietal and prefrontal areas, and one positioned inferiorly to allow coverage of inferior frontal, posterior temporal, and occipital areas. The spacing between these volumes varied across participants and depended upon individual anatomy. Each participant was also annotated with anatomical regions of interest (ROIs). The data were preprocessed to remove artifacts due to head motion and signal drift using the FIASCO program by Eddy et al. (1998).

2.1.2. Experiment 2: synthetic data

The synthetic data was created to roughly imitate the experiment described above, and was used to evaluate HPMs against ground truth. We created datasets using two synthetic processes (ViewPicture and ReadSentence), and three processes (adding Decide). For each experiment, all of the voxels responded to all of the processes. It is unlikely that all the voxels in the brain would respond to all processes in an experiment, but we wished to test HPMs in the most challenging setting possible: maximal spatial-temporal overlap among the HRFs of different processes.

For each dataset, the HRF for each process was generated by convolving a boxcar function indicating the presence of the stimulus with a gamma function (following Boynton et al. (1996)) with parameters $\{a, \tau, n\}$ of the form

$$h(t) = a * \frac{\left(\frac{t}{\tau}\right)^{n-1} \exp\left(-\frac{t}{\tau}\right)}{\tau(n-1)!}.$$

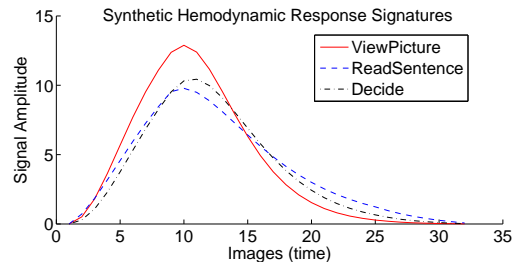


Fig. 1. Noise-free hemodynamic response functions of the processes in the synthetic data.

The parameters for the gamma functions were $\{8.22, 1.08, 3\}$ for ViewPicture, $\{8, 2.1, 2\}$ for ReadSentence, and $\{7.5, 1.3, 3\}$. The processes’ gamma functions were convolved with a 4-second boxcar, matching the experiment timeline. These responses are shown in Figure 1.

The ViewPicture and ReadSentence processes had offset values of $\{0, 1\}$, meaning their onsets could be delayed 0 or 1 images (0 or 0.5 seconds) from their cor-

208 responding stimuli. The Decide process had offset val- 232
 209 ues of $\{0, 1, 2, 3, 4, 5\}$, meaning its onset could be de- 233
 210 layed 0-5 images (0-2.5 seconds) from its corresopding 234
 211 stimulus, which in each case was the second stimulus 235
 212 presentation, whether it was a picture or a sentence.

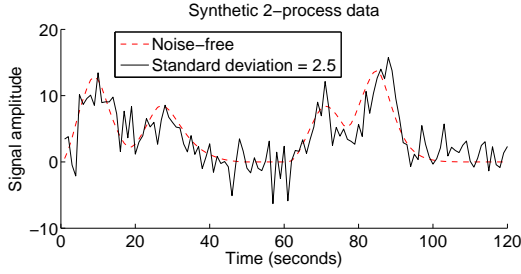


Fig. 2. Two-process synthetic data: a single voxel timecourse for two trials, with and without noise. The first trial is a picture followed by a sentence; the second trial is the reverse.

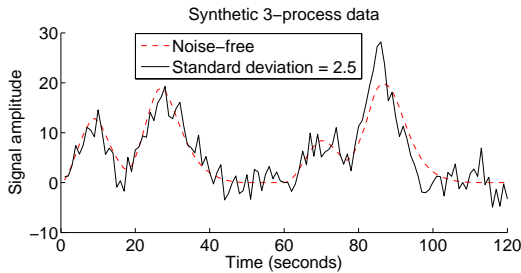


Fig. 3. Three-process synthetic data: a single voxel timecourse for two trials, with and without noise. The first trial is a picture followed by a sentence; the second trial is the reverse. The second peak in each trial is higher than in Figure 2 because the three-process data includes activation for the Decide process.

213 To generate the data for a new trial in the two-process 262
 214 dataset, we first chose which stimulus would come first 263
 215 (picture or sentence). We required that there be an equal 264
 216 number of picture-first and sentence-first trials. When a 265
 217 picture stimulus occurred, we randomly selected an off- 266
 218 set from the ViewPicture offsets and added it to the stimu- 267
 219 lus onset time to get the process start time. Then we 268
 220 added the ViewPicture HRF (over all voxels) to the syn- 269
 221 thetic data beginning at that start time. Sentences were 270
 222 dealt with similarly, where overlapping HRFs summed 271
 223 linearly. Finally, we added Gaussian noise with mean 0 272
 224 and standard deviation 2.5 to every voxel at every time 273
 225 point. The three-process dataset was generated simi- 274
 226 larly, except that each trial included a Decide process as 275
 227 well, whose onset was randomly chosen and added to 276
 228 the second stimulus onset time to get the process start 277
 229 time. Figure 2 shows the timecourse of a single voxel 278
 230 for two trials from the two-process dataset (with and 279
 231 without noise), and Figure 3 shows the same for the 280

three-process dataset. In both cases, the first trial is a
 picture followed by a sentence; the second trial is the
 reverse. The same general process was used to generate
 four-process data.

236 2.2. HPM formalism

237 A Hidden Process Model is a description of a proba-
 238 bility distribution over an fMRI time series, represented
 239 in terms of a set of processes, and a specification of
 240 their instantiations. HPMs assume the observed time
 241 series data is generated by a collection of hidden pro-
 242 cess instances. Each process instance is active during
 243 some time interval, and influences the observed data
 244 only during this interval. Process instances inherit prop-
 245 erties from general process descriptions. The timing of
 246 process instances depends on timing parameters of the
 247 general process it instantiates, plus a fixed timing land-
 248 mark derived from input stimuli. If multiple process in-
 249 stances are simultaneously active at any point in time,
 250 then their contributions sum linearly to determine their
 251 joint influence on the observed data. Figure 4 depicts
 252 an HPM for synthetic sentence-picture data.

253 HPMs make a few key assumptions, some of which
 254 may be relaxed in future iterations of the framework.
 255 For instance, the current version of HPMs uses a pre-
 256 specified and fixed duration for the response signature
 of a process. Additionally, the process offsets are dis-
 crete and tied to specific images. Finally, we adopt the
 commonly used linearity assumption in fMRI and sum
 the response signatures of overlapping process instances
 to predict the signal.

262 More formally, we consider the problem setting in
 263 which we are given observed data \mathbf{Y} , a $T \times V$ matrix
 264 consisting of V time series, each of length T . For exam-
 265 ple, these may be the time series of fMRI activation at
 266 V different voxels in the brain. The observed data \mathbf{Y}
 267 is assumed to be generated nondeterministically by some
 268 system. We use an HPM to model this system. Let us
 269 begin by defining processes:

Definition 1. A process π is a tuple $\langle \mathbf{W}, \Theta, \Omega, d \rangle$. d is
 a scalar called the duration of π , which specifies the
 length of the interval during which π is active. \mathbf{W} is a
 $d \times V$ matrix called the response signature of π , which
 specifies the influence of π on the observed data at each
 of d time points, in each of the V observed time
 series. Θ is a vector of parameters that defines a multinomial
 distribution over a discrete-valued random variable
 which governs the timing of π , and which takes on
 values from a set of integers Ω . The set of all processes
 is denoted by Π .

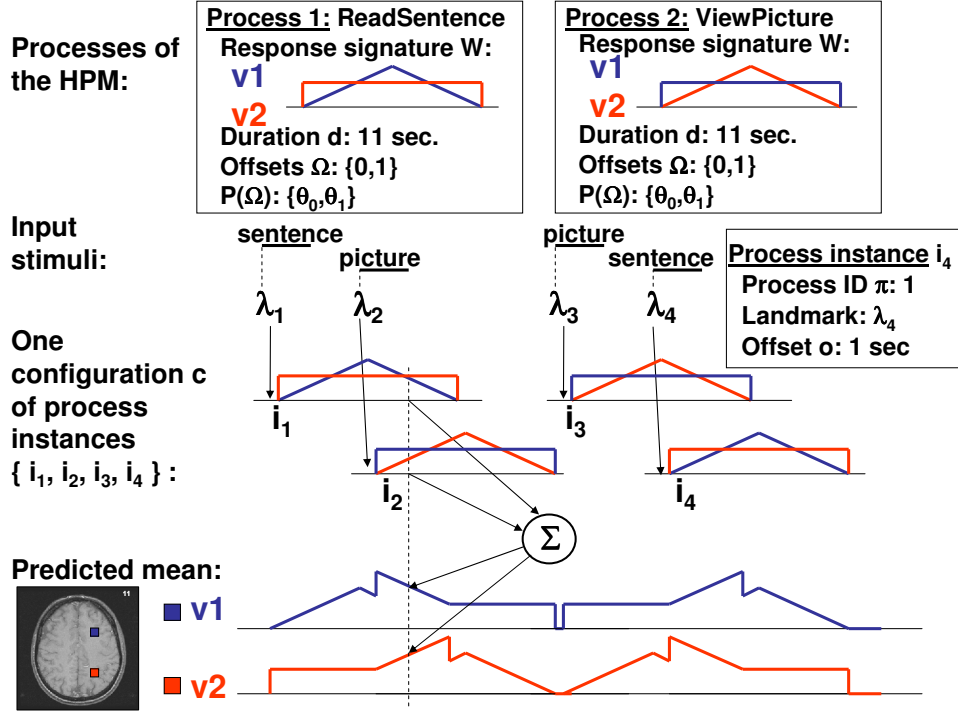


Fig. 4. Example HPM for synthetic 2-process, 2-voxel data. Each process has a duration d , possible offsets Ω and their probabilities Θ , and a response signature W over time (on the horizontal axis) and space (voxels $v1$ and $v2$). They are instantiated 4 times in the configuration c . The start time of a process instance i is its landmark λ plus its offset o . The predicted mean of the data is the sum of the contributions of each process instance at each time point. (The response signatures are contrived rather than realistic in order to more clearly show linearity.)

281 The set of values in Ω is defined by the designer of 305
 282 the HPM, and the length of Θ is the same as the chosen 306
 283 length of Ω . As we will see below, the parameters Θ 307
 284 can be learned from data. 308

285 We will use the notation $\Omega(\pi)$ to refer to the param- 309
 286 eter Ω for a particular process π . More generally, we 310
 287 adopt the convention that $f(x)$ refers to the parameter 311
 288 f affiliated with entity x . 312

289 Each process represents a general procedure which 313
 290 may be instantiated multiple times over the time se- 314
 291 ries. For example, in the sentence-picture fMRI study 315
 292 described above, we can hypothesize general cognitive 316
 293 processes such as ReadSentence, ViewPicture, and De- 317
 294 cide, each of which is instantiated once for each trial. 318
 295 The instantiation of a process at a particular time is 319
 296 called a *process instance*, defined as follows: 320

297 **Definition 2.** A process instance i is a tuple $\langle \pi, \lambda, O \rangle$, 321
 298 where π identifies a process as defined above, λ is a 322
 299 known scalar called a timing landmark that refers to a 323
 300 particular point in the time series, and O is an integer 324
 301 random variable called the offset, which takes on values 325
 302 in $\Omega(\pi)$. The time at which process instance i begins 326
 303 is defined to be $\lambda + O$. The multinomial distribution 327
 304 governing O is defined by $\Theta(\pi)$. The duration of i is 328

given by $d(\pi)$, and the response signature is $W(\pi)$.

The timing landmark λ is a timepoint in the trial, typically associated with an event in the experiment design. For example, the timing landmark for a process instances in the sentence-picture verification task may be the times at which stimuli are presented. λ specifies roughly when the process instance will begin, subject to some variability depending on its offset O , which in turn depends on its process identity π . More specifically, the process starts at $t = \lambda + O$, where O is a random variable whose distribution is a property of the process π . In contrast, the particular value of O is a property of the instance. That is, while there may be slight variation in the offset times of ReadSentence instances, we assume that in general the amount of time between a sentence stimulus (the landmark) and the beginning of the ReadSentence cognitive process follows the same distribution for each instance of the ReadSentence process.

We consider process instances that may generate the data in ordered sets, rather than as individual entities. This allows us to use knowledge of the experiment design to constrain the model. We refer to each possible set of process instances as a *configuration*.

329 **Definition 3.** A configuration c of length L is a set of
 330 process instances $\{i_1 \dots i_L\}$, in which all parameters
 331 for all instances $(\{\lambda, \pi, O\})$ are fully-specified. 376

332 In HPMs, the latent random variable of interest is an
 333 indicator variable defining which of the set of configu- 378
 334 rations is correct. Given a configuration $c = \{i_1 \dots i_L\}$ 379
 335 the probability distribution over each observed data 380
 336 point y_{tv} in the observed data \mathbf{Y} is defined by the 381
 337 Normal distribution: 382

$$y_{tv} \sim \mathcal{N}(\mu_{tv}(c), \sigma_v^2) \quad (1) \quad 383$$

338 where σ_v^2 is the variance characterizing the time- 385
 339 independent, voxel-dependent noise distribution associ- 386
 340 ated with the v^{th} time series, and where

$$\mu_{tv}(c) = \sum_{i \in c} \sum_{\tau=0}^{d(\pi(i))} \delta(\lambda(i) + O(i) = t - \tau) w_{\tau v}(\pi(i)) \quad (2) \quad 387$$

341 Here $\delta(\cdot)$ is an indicator function whose value is 1 if
 342 its argument is true, and 0 otherwise. $w_{\tau v}(\pi(i))$ is
 343 the element of the response signature \mathbf{W} associated with
 344 process $\pi(i)$, for data series v , and for the τ^{th} time step
 345 in the interval during which i is instantiated.

346 Equation (2) says that the mean of the Normal distri-
 347 bution governing observed data point y_{tv} is the sum of
 348 single contributions from each process instance whose 391
 349 interval of activation includes time t . In particular, the 392
 350 $\delta(\cdot)$ expression is non-zero only when the start time 393
 351 $(\lambda(i) + O(i))$ of process instance i is exactly τ time 394
 352 steps before t , in which case we add the element of 395
 353 the response signature $\mathbf{W}(\pi(i))$ at the appropriate de- 396
 354 lay (τ) to the mean at time t . This expression captures 397
 355 a linear system assumption that if multiple processes 398
 356 are simultaneously active, their contributions to the data 399
 357 sum linearly. To some extent, this assumption holds for 400
 358 fMRI data (Boynton et al. (1996)) and is widely used
 359 in fMRI data analysis. 401

360 We can now define Hidden Process Models:

361 **Definition 4.** A Hidden Process Model, HPM, is a tuple
 362 $\langle \Pi, \mathcal{C}, \langle \sigma_1^2 \dots \sigma_V^2 \rangle \rangle$, where Π is a set of processes, \mathcal{C} is a
 363 set of candidate configurations, and σ_v^2 is the variance
 364 characterizing the noise in the v^{th} time series of \mathbf{Y} . 404

365 Note that the set of configurations \mathcal{C} is defined as part
 366 of the HPM and that it is fixed in advance. Each config- 406
 367 uration is an assignment of timings and process types 407
 368 to some number of process instances. If we think of the
 369 hypothesis space of an HPM as the number of ways that
 370 its processes can be instantiated to influence the data,
 371 which is a very large number if any process can occur
 372 at any time, we can see that \mathcal{C} restricts the hypothesis 408
 373 space of the model by allowing the HPM to consider 409

a smaller number of possibilities. These configurations
 facilitate the incorporation of prior knowledge about the
 experiment design like timing constraints as mentioned
 above. For example, if stimulus A was presented at $t =$
 5 then there is no need to consider configurations that
 allow the cognitive process associated with this stimu-
 lus to begin at $t = 4$. This knowledge is contained in \mathcal{C}
 if none of the configurations have an instance of pro-
 cess A beginning at a time earlier than $t = 5$. The al-
 gorithms presented below can compute the probability
 of each configuration in several settings.

An HPM defines a probability distribution over the
 observed data \mathbf{Y} as follows:

$$P(\mathbf{Y}|HPM) = \quad (3)$$

$$\sum_{c \in \mathcal{C}} P(\mathbf{Y}|HPM, C = c)P(C = c|HPM)$$

where \mathcal{C} is the set of candidate configurations associ-
 ated with the HPM, and C is a random variable defined
 over \mathcal{C} . Notice the term $P(\mathbf{Y}|HPM, C = c)$ is defined
 by equations (1) and (2) above. The second term is

$$P(C = c|HPM) = \quad (4)$$

$$\frac{P(\pi(c)|HPM) \prod_{i \in c} P(O(i)|\pi(i), HPM)}{\sum_{c' \in \mathcal{C}} P(\pi(c')|HPM) \prod_{i' \in c'} P(O(i')|\pi(i'), HPM)}$$

where $P(\pi(c)|HPM)$ is a uniform distribution
 over all possible combinations of process IDs.
 $P(O(i)|\pi(i), HPM)$ is the multinomial distribution
 defined by $\Theta(\pi(i))$.

Thus, the generative model for an HPM involves first
 choosing a configuration $c \in \mathcal{C}$, using the distribution
 given by equation (4), then generating values for each
 time series point using the configuration c of process
 instances and the distribution for $P(\mathbf{Y}|HPM, C = c)$
 given by equations (1) and (2).

2.3. HPM algorithms

2.3.1. Inference: classifying configurations and process instance identities and offsets

The basic inference problem in HPMs is to infer the
 posterior distribution over the candidate configurations
 \mathcal{C} of process instances, given the HPM, and observed
 data \mathbf{Y} . By Bayes theorem we have

$$P(C = c|\mathbf{Y}, HPM) = \quad (5)$$

$$\frac{P(\mathbf{Y}|C = c, HPM)P(C = c|HPM)}{\sum_{c' \in \mathcal{C}} P(\mathbf{Y}|C = c', HPM)P(C = c'|HPM)}$$

where the terms in this expression can be obtained
 using equations (1), (2), and (4).

410 Given the posterior probabilities over the configura- 455
 411 tions $P(C = c|\mathbf{Y}, HPM)$, we can easily compute the 456
 412 marginal probabilities of the identities of the process 457
 413 instances by summing the probabilities of the configura- 458
 414 tions in which the process instance in question takes 459
 415 on the identity of interest. For instance, we can com- 460
 416 pute the probability that the second process instance i_2 461
 417 in a particular trial has identity A by: 462

$$P(\pi(i_2) = A) = \sum_{c \in \mathcal{C}} \delta((\pi(i_2) = A)|c)P(C = c|\mathbf{Y}, HPM) \quad (6)$$

418 Note that other marginal probabilities can be obtained 466
 419 similarly from the posterior distribution, such as the 467
 420 probabilities of particular offsets for each process instan- 468
 421 ce, or the joint probability of two process instances 469
 422 having a particular pair of identities. 470

423 2.3.2. Learning: estimating model parameters 472

424 The learning problem in HPMs is: given an observed 473
 425 data sequence \mathbf{Y} and a set of candidate configurations, 474
 426 we wish to learn maximum likelihood estimates of the 475
 427 HPM parameters. The set Ψ of parameters to be learned 476
 428 include $\Theta(\pi)$ and $\mathbf{W}(\pi)$ for each process $\pi \in \Pi$, and 477
 429 σ_v^2 for each time series v . 478

430 2.3.3. Learning from fully observed data 480

431 First consider the case in which the configuration of 481
 432 process instances is fully observed in advance (i.e., all 482
 433 process instances, including their offset times and pro- 483
 434 cess IDs, are known, so there is only one configura- 484
 435 tion in the HPM). For example, in our sentence-picture 485
 436 brain imaging experiment, we might assume there are 486
 437 only two cognitive processes, ReadSentence and View- 487
 438 Picture, and that a ReadSentence process instance be- 488
 439 gins at exactly the time when the sentence is presented 489
 440 to the participant, and ViewPicture begins exactly when 490
 441 the picture is presented. 491

442 In such fully observable settings the problem of learn- 489
 443 ing $\Theta(\pi)$ reduces to a simple maximum likelihood esti- 490
 444 mate of multinomial parameters from observed data. 491
 445 The problem of learning the response signatures $\mathbf{W}(\pi)$
 446 is more complex, because the $\mathbf{W}(\pi)$ terms from multi-
 447 ple process instances jointly influence the observed data
 448 at each time point (see equation (2)). Solving for $\mathbf{W}(\pi)$
 449 reduces to solving a multiple linear regression problem
 450 to find a least squares solution, after which it is easy to
 451 find the maximum likelihood solution for the σ_v^2 . Our
 452 multiple linear regression approach in this case is based
 453 on the GLM approach described in Dale (1999). One
 454 complication that arises is that the regression problem

can be ill posed if the training data does not exhibit suf-
 ficient diversity in the relative onset times of different
 process instances. For example, if processes A and B
 always occur simultaneously with the same onset times,
 then it is impossible to distinguish their relative contri-
 butions to the observed data. In cases where the problem
 involves such singularities, we use the Moore-Penrose
 pseudoinverse to solve the regression problem.

2.3.4. Learning from partially observed data

In the more general case, the configuration of pro-
 cess instances may not be fully observed, and we face
 a problem of learning from incomplete data. Here we
 consider the general case in which we have a set of
 candidate configurations in the model and we do not
 know which one is correct. The configurations can have
 different numbers of process instances, and differing
 process instance identities and timings. If we have no
 knowledge at all, we can list all possible combinations
 of process instances. If we do have some knowledge, it
 can be incorporated into the set of configurations. For
 example, in the sentence-picture brain imaging exper-
 iment, if we assume there are three cognitive processes,
 ReadSentence, ViewPicture, and Decide, then while it
 is reasonable to assume known offset times for Read-
 Sentence and ViewPicture, we must treat the offset time
 for Decide as unobserved. Therefore, we can set all of
 the configurations to have the correct identities and tim-
 ings for the first two process instances, and the correct
 identity and unknown timing for the third.

In this case, we use an Expectation-Maximization
 algorithm (Dempster et al. (1977)) to obtain locally
 maximum likelihood estimates of the parameters, based
 on the following Q function.

$$Q(\Psi, \Psi^{\text{old}}) = E_{C|\mathbf{Y}, \Psi^{\text{old}}} [P(\mathbf{Y}, C|\Psi)] \quad (7)$$

The EM algorithm, which we will call Algorithm 1,
 finds parameters Ψ that locally maximize the Q func-
 tion by iterating the following steps until convergence.
 Algorithm 1 is shown in Table 1.

The update to \mathbf{W} is the solution to a weighted least
 squares problem minimizing the objective function

$$\sum_{v=1}^V \sum_{t=1}^T \sum_{c \in \mathcal{C}} -\frac{P(C = c|\mathbf{Y}, \Psi^{\text{old}})}{2\sigma_v^2} (y_{tv} - \mu_{tv}(c))^2 \quad (8)$$

where $\mu_{tv}(c)$ is defined in terms of W as given in equa-
 tion (2). We can optionally add a regularization term r
 to this objective function to penalize undesirable prop-
 erties of the the parameters:

ALGORITHM 1

Iterate over the following two steps until the change in Q from one iteration to the next drops below a threshold, or until a maximum number of iterations is reached.

E step: Solve for the probability distribution over the configurations of process instances. The solution to this is given by Equation (5).

M step: Use the distribution over configurations from the E step to obtain new parameter estimates for \mathbf{W} , $\sigma_v^2 \forall v$, and $\theta_{\pi,o} \forall \pi, \forall o$ that maximize the expected log-likelihood of the full (observed and unobserved) data (Equation 7), using Equations 8 (or 9), 11, and 12.

Table 1

Algorithm 1 computes the maximum likelihood estimates of the HPM parameters in the case where the true configuration of process instances is unknown.

$$\sum_{v=1}^V \sum_{t=1}^T \sum_{c \in \mathcal{C}} -\frac{P(C=c|\mathbf{Y}, \Psi^{\text{old}})}{2\sigma_v^2} (y_{tv} - \mu_{tv}(c))^2 + \gamma r \quad (9)$$

Here γ weights the influence of the regularizer r in relation to the original objective function. In our experiments, we penalized deviations from temporal and spatial smoothness by setting r to the squared difference between successive time points within the process response signatures, summed over voxels, plus the squared difference between adjacent voxels, summed over the time points of the process response signatures. That is:

$$r = \sum_{\pi \in \Pi} \sum_{v=1}^V \sum_{\tau=1}^{d(\pi)-1} (w_{v,\tau+1}(\pi) - w_{v,\tau}(\pi))^2 + \sum_{\pi \in \Pi} \sum_{i=1}^{V-1} \sum_{j=i+1}^V \mathbf{A}(i,j) \sum_{\tau=1}^{d(\pi)} (w_{i,\tau}(\pi) - w_{j,\tau}(\pi))^2 \quad (10)$$

where \mathbf{A} is a binary $V \times V$ adjacency matrix ($\mathbf{A}(i,j)$ is 1 if and only if voxel i is adjacent to voxel j , where we consider a voxel adjacent to the 26 surrounding voxels).

The updates to the remaining parameters are given by:

$$\sigma_v^2 \leftarrow \frac{1}{T} \sum_{t=1}^T E_{C|\mathbf{Y}, \Psi^{\text{old}}} [(y_{tv} - \mu_{tv}(C))^2] \quad (11)$$

$$\theta_{\pi,o} \leftarrow \frac{\sum_{c \in \mathcal{C}, i \in \mathcal{C}} \delta(\pi(i) = \pi \wedge O(i) = o) p(c)}{\sum_{c \in \mathcal{C}, i \in \mathcal{C}, o' \in \Omega(\pi(i))} \delta(\pi(i) = \pi \wedge O(i) = o') p(c)} \quad (12)$$

where $p(c)$ is shorthand for $P(C=c|\mathbf{Y}, \Psi^{\text{old}})$.

the model is:

$$l(W, A, \sigma) = \frac{-NTV \log(2\pi)}{2} - NTV \log(\sigma) - \frac{1}{2\sigma^2} l'(W, A) \quad (15)$$

where

$$l'(W, A) = \sum_{n,t,v} (y_{tv}^n - \sum_i a_{iv} w_{(t-\lambda^n(i))i})^2 \quad (16)$$

where y_{tv}^n represents the value of in trial n and $\lambda^n(i)$ represents the start of process i in trial n .

ALGORITHM 2

Let \bar{Y} be the column vector for the values in $\{y_{tv}^n\}$. Start with (\hat{W}, \hat{A}) an initial random guess, then repeat Steps 1 and 2 until they converge to the minimum of the function $l'(\hat{W}, \hat{A})$.

STEP 1: Write $l'(\hat{W}, \hat{A}) = \|U\hat{W} - \bar{Y}\|^2$ where U is a NTV by Kd matrix depending on the current estimate \hat{A} of the scaling constants. Minimize with respect to \hat{W} using ordinary Least Squares to get a new estimate $\hat{P} = (U^T U)^{-1} U^T \bar{Y}$.

STEP 2: Minimize l' with respect to \hat{A} same as in Step 1.

STEP 3: Once convergence is reached by repeating the above two steps, let $\hat{\sigma}^2 = \frac{l'(\hat{W}, \hat{A})}{NVT}$.

Table 2

Algorithm 2 computes the maximum likelihood estimators for parameters in Shared HPMs.

It is easy to see that the function l' does not depend on the variance σ^2 and it is a sum of squares, where the quantity inside each square is a linear function in both W and A . Based on this observation, we describe a method to compute the maximum likelihood estimators for the parameters that are shared across the voxels in our set, which we call Algorithm 2, shown in Table 2.

In general it is difficult to specify a priori which voxels share their process response signature parameters. Algorithm 3, shown in Table 3 introduces Hierarchical Hidden Process Models, which use a nested cross-validation hierarchical approach to both partition the brain into clusters of voxels that will share parameters and simultaneously estimate those parameters. For each fold of training data, the algorithm starts by partitioning the voxels into their anatomical ROIs. It then iteratively evaluates the current partitioning scheme with an incremental modification to the partition created by splitting one existing subset into 16 smaller subsets using equally spaced planes in all three directions. If the average cross-validated log-likelihood of the model using the new partition is higher than that of the old, the new partition is kept. Otherwise the subset that the algorithm

ALGORITHM 3

STEP 1: Split the examples into n folds $F = F_1, \dots, F_n$.

STEP 2: For all $1 \leq k \leq n$, keep fold F_k aside and learn a model from the remaining folds using Steps 3-5.

STEP 3: Start by partitioning all voxels in the brain into their ROIs and mark all subsets as *Not Final*.

STEP 4: While there are subsets in the partition that are *Not Final*, take any such subset and try to split it using equally spaced planes in all three directions (in our experiments we split each subset into $16 = 4 \times 2 \times 2$ smaller subsets). If the cross-validation average log-likelihood of the model learned from these new subsets using Algorithm 2 (based on folds $F \setminus F_k$, where \setminus denotes set minus) is lower than the cross-validation average log-likelihood of the initial subset for folds in $F \setminus F_k$, then mark the initial subset as *Final* and discard its subsets. Otherwise remove the initial subset from the partition and replace it with its subsets which then mark as *Not Final*.

STEP 5: Given the partition computed by Step 3 and 4, based on the data points in $F \setminus F_k$, learn a Hidden Process Model that is shared for all voxels inside each subset of the partition. Use this model to compute the log score for the examples/trials in F_k .

STEP 6: In Steps 2-4 we came up with a partition for each fold F_k . To come up with one single model, compute a partition using Steps 3 and 4 based on all n folds together, then, based on this partition learn a model as in Step 5 using all examples. The average log score of this last model can be estimated by averaging the numbers obtained in Step 5 over the folds.

Table 3

Algorithm 3 performs nested cross-validation to partition the brain into clusters of voxels that share their process response signature parameters and simultaneously estimate those parameters.

attempted to split is placed into the final partition, and the algorithm iterates over the other subsets. The final partition is used to compute a score for the current fold of the training set, and then the process is repeated for the other folds. Finally, a model unifying all the folds can be computed, whose performance can be estimated from the cross-validation. (See Table 3 for details.)

3. Results

In this section, we present results on both synthetic data and fMRI data from the sentence-picture verification experiment. Our results on synthetic data show that we can accurately recover the true process response

signatures from training data using Algorithm 1, that we can correctly classify which of a set of configurations truly generated the test data, and that we can reliably choose the number of processes underlying the data. Our results on the real sentence-picture fMRI data demonstrate the use of HPMs for model comparison in the sentence-picture study, and give examples of the results of the trained models, including spatial and temporal views of an estimated response signature, and an estimated timing distribution. Finally, we present results showing that Shared HPMs can improve data log-likelihood, especially when the training set is small, and show clusters of voxels learned by Algorithm 3.

Some of our results are compared in terms of the log-likelihood of the data under the model. To compute the log-likelihood, we use the log of Equation 3 with a slight modification. Equation 3 takes an average of the data likelihood under each configuration, weighted by the probability of that configuration. To compute the likelihood of the configuration, we use Equations 1 and 2. Since different configurations can be active for windows of time with different lengths, we replace inactive timepoints in $\mu_{tv}(c)$ with the mean over all trials of the training data for timepoint t and voxel v , replacing zeros in the predicted mean where no process instances were active. This process helps to minimize the advantage of longer configurations over shorter ones in terms of data log-likelihood. These log-likelihood scores can be averaged over multiple test sets when performing cross-validation to get an estimate of the overall performance of the model.

3.1. Synthetic data**3.1.1. Estimation of the hemodynamic responses**

To test whether HPMs can accurately recover the true process response signatures underlying the data, we compared the learned response signatures to the true responses in the two and three-process synthetic datasets. These datasets each had only 2 voxels (the small number of voxels was chosen to easily show the learned responses, even though the learning problem is easier with more informative voxels). In each case, we trained the HPM on 40 trials (the number of trials we have in the real data) using Algorithm 1. For the synthetic data experiments we did not use regularization.

In both datasets, the identity of the process instances in each trial were provided to the learning algorithm via the configurations, but their timings were not. This corresponds to reasonable assumptions about the real fMRI data. Since we know the sequence of the stimuli, it is

618 reasonable to assume that the process instances match 668
619 that sequence. However, we do not know the delay be- 669
620 tween the stimulus presentation and the beginning of 670
621 the cognitive process(es) associated with it. 671

622 Two trials of the two-process data are shown in Fig- 672
623 ure 5, and the learned responses for each process in 673
624 each voxel are shown in Figure 6. Note that the learned 674
625 responses are reasonably smooth, even though this as- 675
626 sumption was not provided to the learner. The mean 676
627 squared error between the learned and true responses av-
628 eraged over timepoints, processes, and voxels is 0.2647,
629 and the estimated standard deviations for the voxels are 677
630 2.4182 and 2.4686 (compare with the true value, 2.5). 678
631 The EM training procedure converged in 16 iterations. 679
632 Figures 7 and 8 are the corresponding plots for the 680
633 three-process data. In this case, the mean squared error 681
634 between the learned and true responses averaged over 682
635 timepoints, processes, and voxels is 0.4427, and the es- 683
636 timated standard deviations for the voxels are 2.4316 684
637 and 2.4226. The EM training procedure converged in 685
638 24 iterations. 686

639 The identifiability of the model from the data is a sig- 687
640 nificant factor in estimating the HRFs of the processes. 688
641 A system is identifiable if there is a unique set of param- 689
642 eters that optimally reconstruct the data. For instance, 690
643 if the cognitive processes never overlap, we can easily 691
644 deconvolve the contributions of each one. However, if 692
645 two processes are fully-overlapping every time they oc- 693
646 cur in the data, there are an infinite number of response 694
647 signature pairs that could explain the data equally well. 695
648 Note that the two-process data is identifiable, whereas 696
649 the three-process data is not. 697

650 3.1.2. *Classification of configurations* 700

651 To test whether these learned HPMs could correctly 701
652 classify the process instance configurations in a new 702
653 trial, we ran a similar experiment, again using synthetic 703
654 data. In this case, the training set was again 40 trials, 704
655 and the test set consisted of 100 trials generated inde- 705
656 pendently from the same model. This time, we used 500 706
657 voxels, all of which responded to both stimuli, in both 707
658 the training and test sets, which is a reasonable number 708
659 of voxels in which we might be interested. 709

660 The uncertainty in the process configurations in the 710
661 training set again reflected the real data. That is, the pro- 711
662 cess identities were provided in the configurations for 712
663 the training data, but the timing was unknown. In the 713
664 test set however, we allowed more uncertainty, assum- 714
665 ing that for a new trial, we did not know the sequence 715
666 of the first two stimuli. Therefore, the third process was 716
667 known to be Decide, but the first two could be either 717

ReadSentence followed by ViewPicture, or ViewPicture
followed by ReadSentence. Based on our knowledge of
the experiment design, the first two instances could not
have the same parent process (i.e. ReadSentence fol-
lowed by ReadSentence was not allowed). For all three
instances in the test set trials, the timing was unknown.
For both the two-process and three-process data, HPMs
predicted the correct configuration on the test data with
100% accuracy.

3.1.3. *Choosing the number of processes to model*

Another interesting question to approach with syn-
thetic data is whether or not HPMs can be used to de-
termine the number of processes underlying a dataset.
One might be concerned that HPMs would be biased in
favor of more and more processes by using extra pro-
cesses to fit noise in the data more closely. We do ex-
pect to fit the training data better by using more pro-
cesses, but we can use independent test data to evaluate
whether the extra processes are indeed fitting noise in
the training data (which we would not expect to help fit
the test data) or whether the extra process contain ac-
tual signal that helps fit the test data. In fact, there can
be a slight bias, even when using separate test data, in
favor of models that allow a larger number of possible
configurations. As we show below, the impact of this
bias in our synthetic data experiments does not prevent
HPMs from recovering the correct model.

To investigate this question, we generated training
sets of 40 examples each using 2, 3, and 4 processes
in the same fashion as the previous experiments. For
each training set, we trained HPMs with 2, 3, and 4
processes each. Additionally, we generated test sets of
100 examples each using 2, 3, and 4 processes. Every
training and test set had 100 voxels. For each test set,
we used each of the HPMs trained on its correspond-
ing training set to evaluate the log-likelihood of the test
data under the model. In each case, the model selected
by the algorithm based on this score was the one with
the correct number of processes. We performed this ex-
periment with independently generated training and test
sets 30 times with consistent results. The average test-
set log-likelihoods are shown in Table 4, along with fur-
ther repetitions of this experiment with decreasing train-
ing set sizes. As expected, we see increased variability
with smaller training sets, but even for small numbers
of examples, the HPM with the highest test data log-
likelihood has the same number of processes as were
used to generate the data.

When using real data instead of synthetic data, we
do not have an independent test set on which to verify

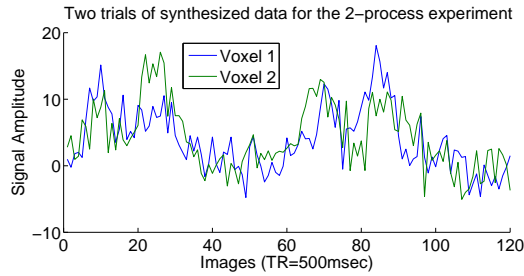


Fig. 5. Two trials of synthetic data for the 2-process experiment using 2 voxels. The first trial (the left half of the time series) is a picture followed by a sentence; the second trial is the reverse.

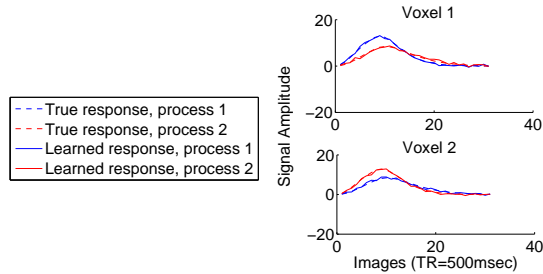


Fig. 6. Comparison of the learned vs. true process response signatures in the two-process data for two voxels. The mean squared error between the learned and true responses averaged over timepoints, processes, and voxels is 0.2647.

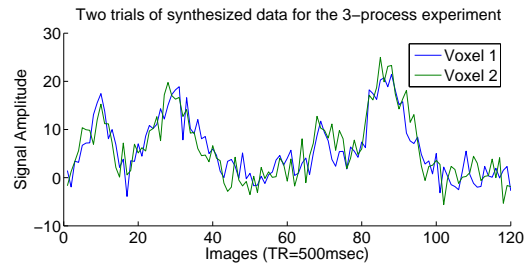


Fig. 7. Two trials of synthetic data for the 3-process experiment using 2 voxels. The first trial (the left half of the time series) is a picture followed by a sentence; the second trial is the reverse.

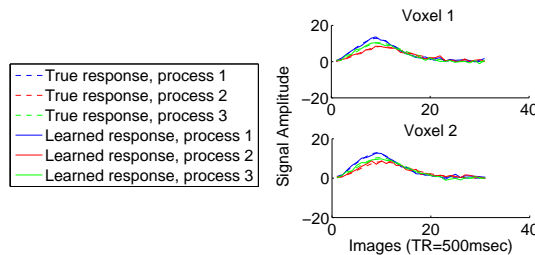


Fig. 8. Comparison of the learned vs. true process response signatures in the synthetic two-process data for two voxels. The mean squared error between the learned and true responses averaged over timepoints, processes, and voxels is 0.4427.

718 the number of processes to use. Instead, we can modify 723
 719 our method by using cross-validation. We can separate 724
 720 the dataset into n non-overlapping pieces, leave one of 725
 721 them out as the independent test set, and train HPMs 726
 722 with different numbers of processes on the remaining 727

pieces. For each left-out piece, we can compute the log-likelihood of the data for each HPM, and average these log-likelihoods over the left-out pieces. This average log-likelihood is then a measure of how well each HPM performs on unseen data. This process avoids overfitting

Number of Training Trials	Number of Processes in HPM	2 Process Data	3 Process Data	4 Process Data
40	2	-5.64 ± 0.00444	-7.93 ± 0.0779	-7.72 ± 0.0715
40	3	-7.47 ± 0.183	-5.66 ± 0.00391	-5.72 ± 0.00504
40	4	-7.19 ± 0.0776	-5.687 ± 0.00482	-5.65 ± 0.00381
20	2	-2.87 ± 0.204	-3.80 ± 0.192	-3.70 ± 0.606
20	3	-4.00 ± 0.0461	-2.86 ± 0.00597	-2.87 ± 0.00276
20	4	-3.91 ± 0.0319	-2.89 ± 0.00320	-2.85 ± 0.00364
10	2	-1.44 ± 0.245	-2.07 ± 0.0653	-1.96 ± 0.0665
10	3	-1.99 ± 0.119	-1.47 ± 0.0231	-1.47 ± 0.00654
10	4	-1.95 ± 0.0872	-1.49 ± 0.0195	-1.46 ± 0.00427
6	2	-2.87 ± 0.204	-1.32 ± 0.0363	-1.34 ± 0.297
6	3	-4.00 ± 0.0461	-0.923 ± 0.0130	-0.928 ± 0.0126
6	4	-3.91 ± 0.0319	-0.933 ± 0.0149	-0.921 ± 0.00976
2	2	-3.75 ± 0.00710	-7.23 ± 0.0456	-4.62 ± 0.0383
2	3	-5.36 ± 0.0689	-6.99 ± 0.0823	-3.96 ± 0.0252
2	4	-5.08 ± 0.0704	-7.02 ± 0.0853	-3.91 ± 0.0241

Table 4

For each training set, the table shows the average (over 30 runs) test set log-likelihood of each of 3 HPMs (with 2, 3, and 4 processes) on each of 3 synthetic data sets (generated with 2, 3, and 4 processes). Each cell is reported as mean \pm standard deviation. NOTE: All values in this table are $\times 10^5$.

728 the noise in the training set because the model must do
729 well on data it has not seen in training.

730 3.2. Real data

731 3.2.1. HPMs for model comparison

732 In this section, we create several HPMs for the
733 sentence-picture fMRI data and evaluate them in terms
734 of the log-likelihood of the data under each model.
735 This evaluation is done in the context of 5-fold cross-
736 validation, meaning that the 40 trials are split into 5
737 folds of 8 trials each. Each fold is held out in turn as a
738 test set while the models are trained on the other 32 tri-
739 als. The training was done using Algorithm 1 with reg-
740 ularization, with weight $\gamma = 20$. Since log-likelihood
741 does not have concrete units, we compare the score of
742 each model to the log-likelihood score achieved by the
743 naive method of averaging all training trials together
744 and predicting this average trial for each test trial.

745 Table 5 presents the improvement of 4 models over a
746 baseline, averaged over 5 folds of cross-validation. Fig-
747 ure 9 presents the same information graphically. The
748 baseline is computed by predicting the mean of the train-

749 ing trials for each test trial. The 4 models are an HPM
750 with 2 processes (ReadSentence and ViewPicture) with
751 non-overlapping responses (HPM-GNB), HPMs with 2
752 processes (ReadSentence and ViewPicture) with known
753 and unknown timing for ReadSentence and ViewPicture
754 (HPM-2-K and HPM-2-U respectively), and an HPM
755 with 3 processes (ReadSentence, ViewPicture, and De-
756 cide) with known timing for ReadSentence and View-
757 Picture (HPM-3-K). Note that all of the models used
758 all available voxels for each participant. More details of
759 each model are explained below.

The HPM-GNB model approximates a Gaussian Naive Bayes model (Mitchell (1997)) through the HPM framework. It has two processes: ReadSentence and ViewPicture. The duration of each process is 8 seconds (16 images) so that they may not overlap. HPM-GNB has a variance for each voxel, and incorporates the knowledge that each trial has exactly one instance of ReadSentence and exactly one of ViewPicture. It is the same as HPM-2-K (presented in the next section) except that the processes are shorter so that they may not overlap.

HPM-2-K is a 2-process HPM containing just ReadSentence and ViewPicture, each of which has a dura-

Participant	HPM-GNB	HPM-2-K	HPM-2-U	HPM-3-K
A	14040 ± 3304	12520 ± 1535	14720 ± 1970	11780 ± 3497
B	14460 ± 2555	14580 ± 1011	15960 ± 1790	7380 ± 2439
C	12860 ± 4039	14080 ± 1794	15460 ± 2542	7500 ± 1329
D	12140 ± 1276	13700 ± 943	15720 ± 1264	10360 ± 1408
E	14340 ± 1941	17140 ± 1236	17560 ± 1484	10100 ± 4909
F	16180 ± 3671	17400 ± 4064	18040 ± 4060	8180 ± 1886
G	12160 ± 680	14680 ± 942	14940 ± 1358	5740 ± 1820
H	14120 ± 1281	14860 ± 811	16160 ± 1699	7360 ± 4634
I	11460 ± 2201	13080 ± 2572	14260 ± 2384	10420 ± 2046
J	12140 ± 2509	12840 ± 1301	14420 ± 3391	7960 ± 2907
K	14080 ± 2983	14620 ± 2190	17120 ± 2410	8800 ± 3044
L	17820 ± 2716	20200 ± 1580	19980 ± 2494	13700 ± 3519
M	12940 ± 1205	12680 ± 1796	14560 ± 1236	9240 ± 1677

Table 5

Improvement of test-set log-likelihood for 4 models over predicting the average training trial computed using 5-fold cross validation for 13 subjects. Each cell reports the mean plus or minus 1 standard deviation of the model log-likelihood minus the naive method log-likelihood over the 5 folds.

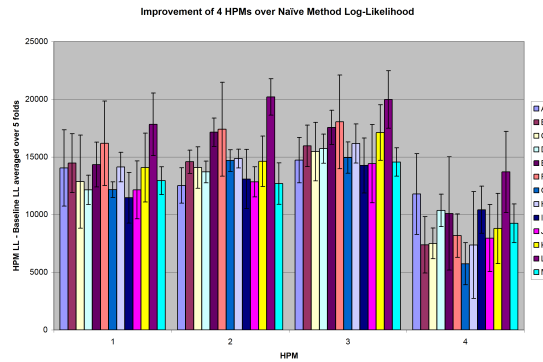


Fig. 9. Improvement in all 13 participants (A-M in different colors) of 4 HPMs over a baseline method that predicts the average training trial for every test trial. The values plotted are the mean over 5 folds of cross validation of the model log-likelihood minus the baseline log-likelihood, and the error bars represent one standard deviation. From left to right on the x-axis, the models are HPM-GNB, HPM-2-K, HPM-2-U, HPM-3-K.

773 tion of 12 seconds (a reasonable length for the hemody-
774 namic response function). The 'K' stands for 'known,'
775 meaning that the timing of these two processes is as-
776 sumed to be known. More specifically, it is assumed
777 that each process starts exactly when its corresponding
778 stimulus is presented. In other words, $\Omega = \{0\}$ for both
779 processes. For a given test set trial, the configurations
780 for HPM-2-K are shown in Table 6. The configurations
781 for a training set trial are restricted to those containing
782 the correct order of the processes (based on the order
783 of the stimuli).

784 HPM-2-U is also a 2-process HPM containing just

c	$\pi(i_1)$	$\lambda(i_1)$	$O(i_1)$	$\pi(i_2)$	$\lambda(i_2)$	$O(i_2)$
1	S	1	0	P	17	0
2	P	1	0	S	17	0

Table 6

Configurations for a test set trial under HPM-2-K. i_1 is the first process instance in the trial, and i_2 is the second process instance. $\pi(i)$, $\lambda(i)$, and $O(i)$ are the process ID, landmark, and offset, respectively, for process instance i . For supervised training, there is only one configuration for each training trial.

785 ReadSentence and ViewPicture. In this case though, the
786 'U' stands for 'unknown,' meaning that we allow a small
787 amount of uncertainty about the start times of the pro-

cesses. In HPM-2-U, the Ω for each process is $\{0, 1\}$, which translates to delays of 0 or 0.5 seconds (0 or 1 images) following the relevant stimulus presentation. The configurations for the test set in this case are in Table 7. Again, during supervised training, the configurations for a given training trial are limited to those that have the correct process ordering. Since the true offset for the processes are unknown even during training, there are still 4 configurations for each training trial.

c	$\pi(i_1)$	$\lambda(i_1)$	$O(i_1)$	$\pi(i_2)$	$\lambda(i_2)$	$O(i_2)$
1	S	1	0	P	17	0
1	S	1	1	P	17	0
1	S	1	0	P	17	1
1	S	1	1	P	17	1
2	P	1	0	S	17	0
2	P	1	1	S	17	0
2	P	1	0	S	17	1
2	P	1	1	S	17	1

Table 7
Configurations for a test set trial using HPM-2-U. For supervised training where we assume the order of the stimuli is known, there will be only four configurations for each training trial.

HPM-3-K adds a Decide process to the previous 2 models, also with a duration of 12 seconds. The Decide process has $\Omega = \{0, 1, 2, 3, 4, 5, 6, 7\}$, allowing the process to start with a delay of 0 to 3.5 seconds from the second stimulus presentation. For these HPMs, we can use the information we have about the participant’s reaction time by assuming that the Decide process must begin before the participant pushes the button. This means that for each trial, we can also eliminate any configurations in which the Decide process starts after the button press; that is, any configurations for which $o_3 > reaction_time$. Note that this implies that different trials can have different sets of configurations since reaction times varied from trial to trial. If the participant did not press the button for some trial, all offsets are considered for the Decide process. The test set configurations for HPM-3-K for a trial with a reaction time of 2.6 seconds are given in Table 8. Since the nearest preceding image to the button press corresponds to offset 5, we have removed configurations with $o_3 \in \{6, 7\}$. To do supervised training, we only use the configurations with the correct ordering of ReadSentence and ViewPicture.

The first thing to note about Figure 9 is that all 4 HPMs show significant improvement over the naive baseline method of predicting the mean training trial for all test trials. While the differences between models for

c	$\pi(i_1)$	$\lambda(i_1)$	$O(i_1)$	$\pi(i_2)$	$\lambda(i_2)$	$O(i_2)$	$\pi(i_3)$	$\lambda(i_3)$	$O(i_3)$
1	S	1	0	P	17	0	D	17	0
2	S	1	0	P	17	0	D	17	1
3	S	1	0	P	17	0	D	17	2
4	S	1	0	P	17	0	D	17	3
5	S	1	0	P	17	0	D	17	4
6	S	1	0	P	17	0	D	17	5
7	P	1	0	S	17	0	D	17	0
8	P	1	0	S	17	0	D	17	1
9	P	1	0	S	17	0	D	17	2
10	P	1	0	S	17	0	D	17	3
11	P	1	0	S	17	0	D	17	4
12	P	1	0	S	17	0	D	17	5

Table 8
Configurations for a test set trial under HPM-3-K. The reaction time for this trial is 2.6 seconds, which corresponds to offset 5 for the Decide process, so all configurations with offsets greater than 5 for this process have been eliminated for this trial.

each individual subject are not all significant, the cross-subject trend indicates that HPM-2-K slightly outperforms HPM-GNB, implying that modeling the overlap of the ReadSentence and ViewPicture process response signatures can be advantageous. HPM-2-U generally performs even better, indicating that it can be helpful to allow some uncertainty as to the onset of the process instances. Interestingly, HPM-3-K shows the least improvement over the naive method, despite the fact that some kind of third process must be occurring in this experiment. One possible explanation for the relatively poor performance of this model could be that the possible offsets for Decide are not modeled properly. Another possibility is that the added complexity of HPM-3-K requires more training data than is available.

3.2.2. Interpreting HPMs

In the previous section, we estimated how well different HPMs would predict unseen test data using cross-validation. In this section, we examine the parameters of the HPMs to try to understand what the models are learning better. For the results below, we trained HPM-3-K on all trials for Participant L.

The learned timing distribution for the Decide process is shown in Table 9. The distribution is similar to the distribution of reaction times for this subject. For trials where the subject did not press the button, the program tended to choose the last possible offset for the Decide process.

We can also visualize the model by looking at the

Offset	Θ
0	0.2713
1	0.0762
2	0.1006
3	0.1006
4	0.0762
5	0.1250
6	0.0030
7	0.2470

Table 9

Learned timing distribution for the Decide process for Participant L using HPM-3-K, for offsets from the second stimulus presentation 0-7 images (0-3.5 seconds). The Θ values are the parameters of the multinomial distribution over these offsets.

learned process response signatures. Since a response signature contains parameters over space and time, one option is to average the parameters of each voxel over time. This value with respect to the ReadSentence process is plotted for each voxel (in that voxel’s location) in Figure 10, for the View Picture process in Figure 11, and for the Decide process in Figure 12. We can also plot the time courses for individual voxels. For instance, the time course of the darkest red voxel from Figure 12 (in the top middle slice) is shown in Figure 13.

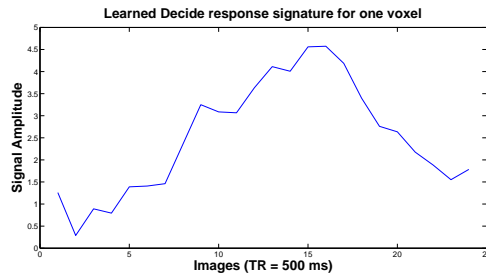


Fig. 13. The time course of the darkest red voxel in Figure 12, for the Decide process in participant L under HPM-3-K.

3.2.3. Improvement of data log-likelihood with Shared HPMs

In this section we report experiments on the same sentence-picture dataset using the methods in Section 2.4, which attempt to share, when appropriate, process parameters across neighboring voxels. Since the results reported in this section are intended to be only a proof of concept for incorporating sharing of HPM parameters across spatially contiguous voxels in HPM learning, they are limited to data from a single human participant, consisting of 4698 voxels (participant D). For

each trial, we considered only the first 32 images (16 seconds) of brain activity.

We model the activity in the brain using a Hidden Process Model with two processes, ReadSentence and ViewPicture. The start time of each process instance is assumed to be known in advance (i.e., the offset values for each process are $\{0\}$), so each process instance begins exactly at the landmark corresponding to the relevant stimulus). This is equivalent to HPM-GNB from the previous section. We evaluated the performance of the models using the average log-likelihood over the held-out trials in a leave-two-out cross-validation approach, where each fold contains one example in which the sentence is presented first, and one example in which the picture is presented first.

Our experiments compared three HPM models. The first model, which we consider a baseline, consists of a standard Hidden Process Model (StHPM) learned independently for each voxel (or equivalently, a standard HPM with no parameter sharing). The second model is a Hidden Process Model where all voxels in an ROI share their Hidden Process parameters (ShHPM). ShHPM is learned using Algorithm 2. The third model is a Hierarchical Hidden Process Model (HieHPM) learned using Algorithm 3.

The first set of experiments, summarized in Table 10, compares the three models based on their performance in the calcarine sulcus of the visual cortex (CALC). This is one of the ROIs actively involved in this cognitive task, containing 318 voxels for this participant. The training set size was varied from 6 examples to all 40 examples, in increments of two. Sharing parameters for groups of voxels proved beneficial, especially for small training sets. As the training set size increased, the performance of ShHPM degraded because the bias in the inaccurate assumption that all voxels in CALC share parameters was no longer outweighed by the corresponding reduction in the variance of the parameter estimates. However, we will see that in other ROIs, this assumption holds and in those cases the gains in performance may be quite large.

As expected, the hierarchical model HieHPM performed better than both StHPM and ShHPM because it takes advantage of shared Hidden Process Model parameters while not making the restrictive assumption of sharing across all voxels in a ROI. The largest difference in performance between HieHPM and StHPM is observed at 6 examples, in which case StHPM fails to learn a reasonable model while the highest difference between HieHPM and ShHPM occurs at the maximum number of examples, presumably when the bias of ShHPM is most harmful. As the number of training ex-

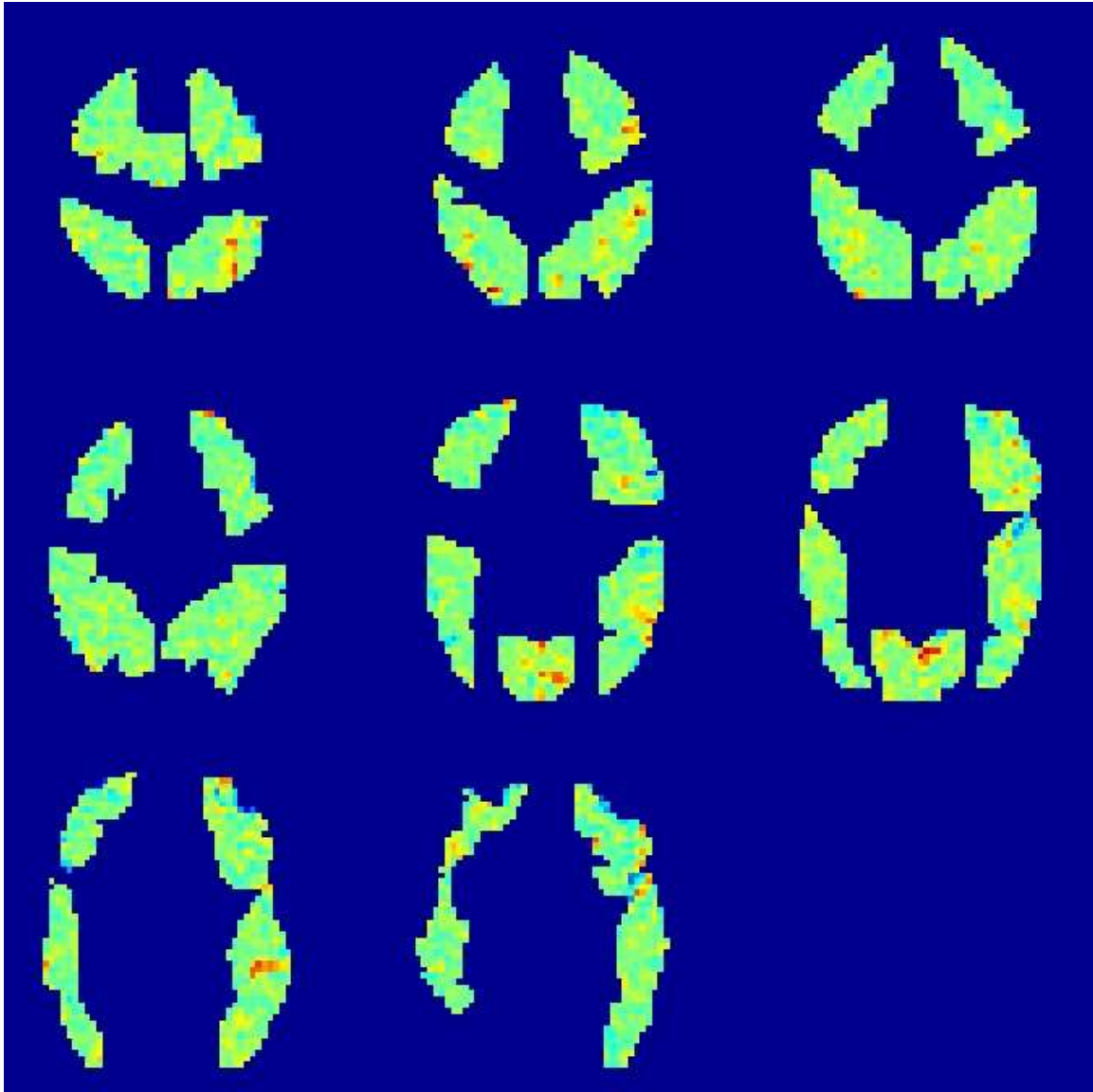


Fig. 10. The learned spatial-temporal response for the ReadSentence process in participant L under HPM-3-K, averaged over time. Red corresponds to higher values, blue to lower values. Images are displayed in radiological convention (the left hemisphere is on the right of each slice). Anterior is higher, posterior is lower.

925 amplex increases, both StHPM and HieHPM tend to per- 936
 926 form better and better and one can see that the marginal 937
 927 improvement in performance obtained by the addition 938
 928 of two new examples tends to shrink as both models 939
 929 approach convergence. While with an infinite amount 940
 930 of data, one would expect both StHPM and HieHPM to 941
 931 converge to the true model, at 40 examples, HieHPM 942
 932 still outperforms the baseline model StHPM by a differ- 943
 933 ence of 106 in terms of average log-likelihood, which 944
 934 is an improvement of e^{106} in terms of data likelihood. 945
 935 Perhaps the best measure of the improvement of 946

HieHPM over the baseline StHPM is the number of
 examples needed by StHPM to achieve the same per-
 formance as HieHPM. These results show that on
 average, StHPM needs roughly 2.9 times the number
 of examples needed by HieHPM in order to achieve
 the same level of performance in CALC.

The last column of Table 10 displays the number
 of clusters into which HieHPM partitioned CALC. At
 small sample sizes HieHPM uses only one cluster of
 voxels and improves performance by reducing the vari-
 ance in the parameter estimates. However, as the train-

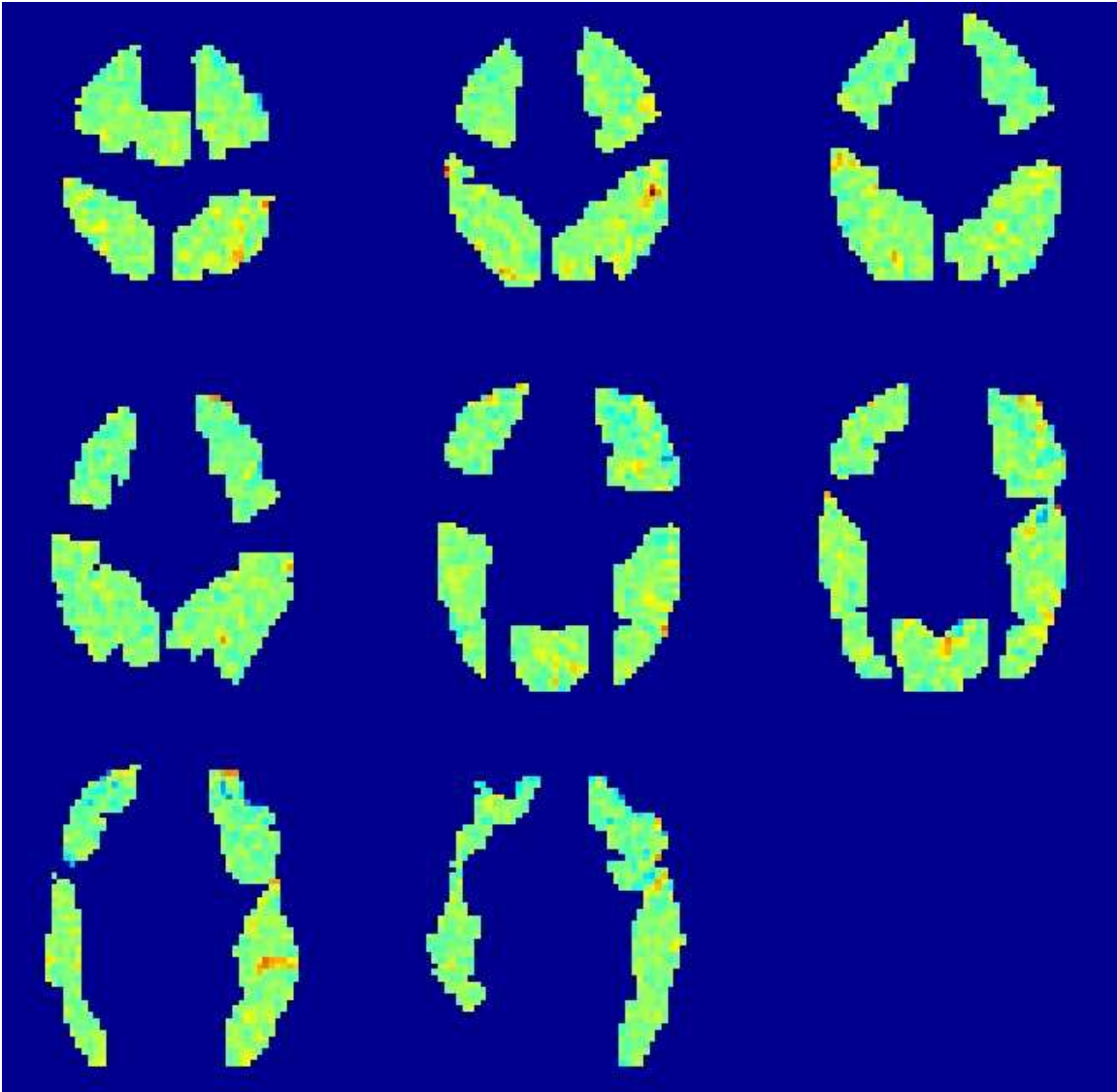


Fig. 11. The learned spatial-temporal response for the ViewPicture process in participant L under HPM-3-K, averaged over time. Red corresponds to higher values, blue to lower values. Images are displayed in radiological convention (the left hemisphere is on the right of each slice). Anterior is higher, posterior is lower.

947 ing set size increases, HieHPM improves by finding 959
 948 more and more refined partitions. This number of shared 960
 949 voxel sets tends to stabilize around 60 clusters once the 961
 950 number of examples reaches 30, which yields an aver- 962
 951 age of more than 5 voxels per cluster in this case. For 963
 952 a training set of 40 examples, the largest cluster has 41 964
 953 voxels while many clusters consist of only one voxel. 965
 954 The second set of experiments (see Table 11) de- 966
 955 scribes the performance of the three models for each 967
 956 of the 24 individual ROIs of the brain, and also when 968
 957 trained over the entire brain. While ShHPM was biased 969
 958 in CALC, we see here that there are several ROIs in 970

which it makes sense to assume that all voxels share
 parameters. In fact, in most of these regions, HieHPM
 finds only one cluster of voxels. ShHPM outperforms
 the baseline model StHPM in 18 out of 24 ROIs while
 HieHPM outperforms StHPM in 23 ROIs. One may ask
 how StHPM can possibly outperform HieHPM on any
 ROI, since StHPM is a special case of HieHPM. The
 explanation is that the hierarchical approach is subject
 to local minima since it is a greedy process that does
 not look beyond the current potential split for a finer
 grained partition. Fortunately, this problem is very rare
 in our experiments.

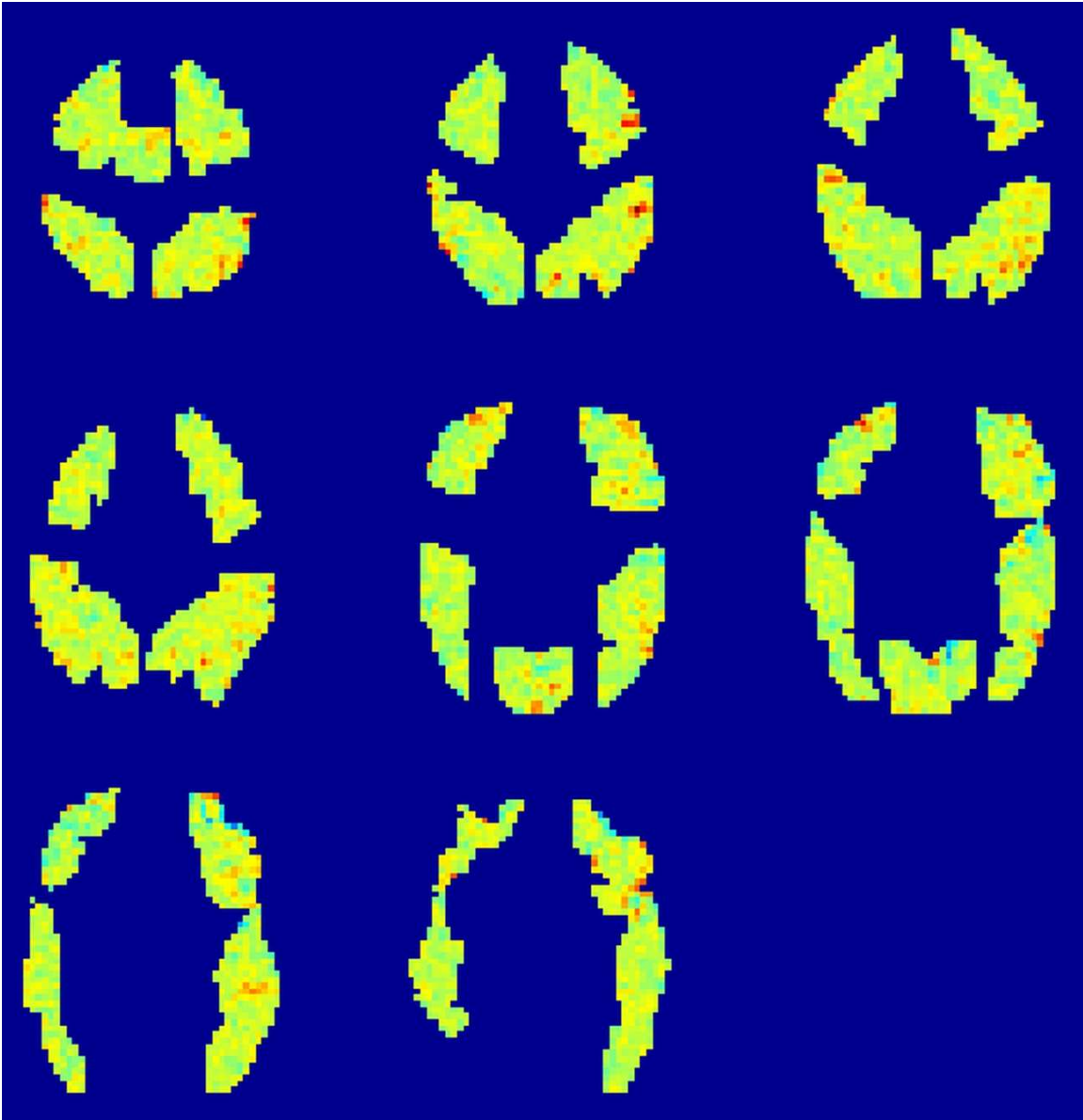


Fig. 12. The learned spatial-temporal response for the Decide process in participant L under HPM-3-K, averaged over time. Red corresponds to higher values, blue to lower values. Images are displayed in radiological convention (the left hemisphere is on the right of each slice). Anterior is higher, posterior is lower.

971 Over the whole brain, HieHPM outperforms StHPM 981
 972 by 1792 in terms of log-likelihood while ShHPM out- 982
 973 performs StHPM only by 464. ShHPM also makes a 983
 974 restrictive sharing assumption and therefore HieHPM 984
 975 emerges as the recommended approach. 985
 976 As mentioned above, HieHPM automatically learns 986
 977 clusters of voxels that share their process response sig- 987
 978 nature parameters. Figure 14 shows these learned clus- 988
 979 ters in slice five of the eight slices. Neighboring voxels 989
 980 that were assigned by HieHPM to the same cluster are 990

pictured in the same color. Note that there are several very large clusters in this picture. This may be because it makes sense to share voxel parameters at the level of an entire ROI if the cognitive process does not activate voxels in this ROI. However, large clusters are also found in areas like CALC, which we know is directly involved in visual processing.

In Figure 15 we present the learned ReadSentence process for the voxels in slice five of CALC. The graphs corresponding to voxels that belong to the same cluster

Trials	StHPM	ShHPM	HieHPM	Cells
6	-30497	-24020	-24020	1
8	-26631	-23983	-23983	1
10	-25548	-24018	-24018	1
12	-25085	-24079	-24084	1
14	-24817	-24172	-24081	21
16	-24658	-24287	-24048	36
18	-24554	-24329	-24061	37
20	-24474	-24359	-24073	37
22	-24393	-24365	-24062	38
24	-24326	-24351	-24047	40
26	-24268	-24337	-24032	44
28	-24212	-24307	-24012	50
30	-24164	-24274	-23984	60
32	-24121	-24246	-23958	58
34	-24097	-24237	-23952	61
36	-24063	-24207	-23931	59
38	-24035	-24188	-23921	59
40	-24024	-24182	-23918	59

Table 10

The effect of training set size on the average log-likelihood (higher numbers/lower absolute values are better) of the three models in the calcarine sulcus of the visual cortex (CALC), and the number of clusters into which the algorithm segmented the ROI.

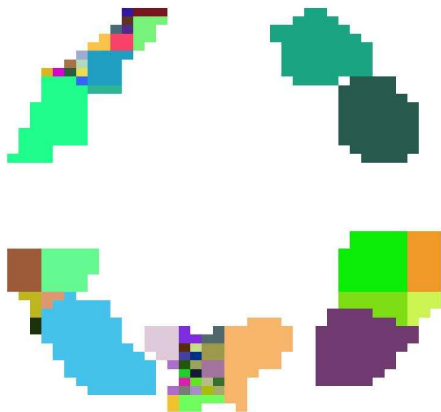


Fig. 14. Clusters learned by HieHPM in slice 5 of the brain

991 have the same color as in Figure 14. For readability, we 1005
 992 only plot the base processes, disregarding the learned 1006
 993 scaling constants which specify the amplitude of the 1007
 994 response in each voxel within a given cluster. The in- 1008
 995 creased smoothness of these learned time courses sug- 1009
 996 gest that the discontinuities from figure 13 may be par- 1010
 997 tially due to the sparsity of data that occurs when each 1011

ROI	Voxels	StHPM	ShHPM	HieHPM	Cells
CALC	318	-24024	-24182	-23918	59
LDLPFC	440	-32918	-32876	-32694	11
LFEF	109	-8346	-8299	-8281	6
LIPL	134	-9889	-9820	-9820	1
LIPS	236	-17305	-17187	-17180	8
LIT	287	-21545	-21387	-21387	1
LOPER	169	-12959	-12909	-12909	1
LPPREC	153	-11246	-11145	-11145	1
LSGA	6	-441	-441	-441	1
LSPL	308	-22637	-22735	-22516	4
LT	305	-22365	-22547	-22408	18
LTRIA	113	-8436	-8385	-8385	1
RDLPFC	349	-26390	-26401	-26272	40
RFEF	68	-5258	-5223	-5223	1
RIPL	92	-7311	-7315	-7296	11
RIPS	166	-12559	-12543	-12522	20
RIT	278	-21707	-21720	-21619	42
ROPER	181	-13661	-13584	-13584	1
RPPREC	144	-10623	-10558	-10560	1
RSGA	34	-2658	-2654	-2654	1
RSPL	252	-18572	-18511	-18434	35
RT	284	-21322	-21349	-21226	24
RTRIA	57	-4230	-4208	-4208	1
SMA	215	-15830	-15788	-15757	10
Full Brain	4698	-352234	-351770	-350441	299

Table 11

Performance of the three models over whole brain and in several ROIs when learned using all 40 examples

998 voxel is estimated independently.

999 3.2.4. SPM analysis

1000 For comparison, we provide an SPM analysis of the
 1001 sentence-picture dataset. To detect activation in each of
 1002 the conditions the data for each participant were fit to a
 1003 general linear model using SPM2 software (<http://www.fil.ion.ucl.ac.uk/spm/spm2.html>).
 1004 The data were first corrected for slice acquisition tim-
 ing using sinc-interpolation, and then modeled using
 regressors for each stimulus condition and run consist-
 ing of a box-car representing the onset and duration of
 each stimulus presentation convolved with the canon-
 ical double-gamma HRF model available in SPM2.
 Additional covariates implemented a high-pass filter

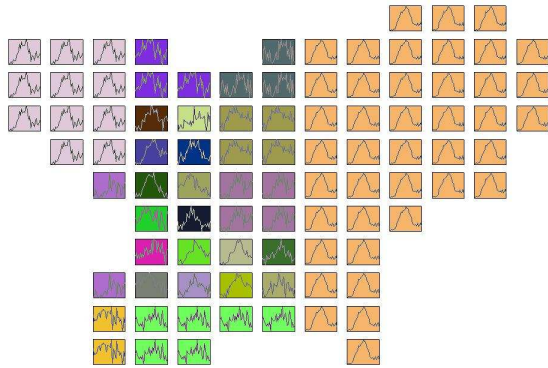


Fig. 15. Learned ReadSentence process for all voxels in slice 5 of the Visual Cortex

(cutoff at 128 s) and serial correlations in the errors were modeled with an AR(1) process. No spatial smoothing, resampling, or 3D motion correction of the data were employed in SPM2, for the sake of consistency with the real and synthetic data that were used in the Hidden Process Models. Parameter estimates and their contrasts were evaluated on a voxel-wise basis for statistical significance by t-tests, at a threshold of $p < 0.05$, corrected for multiple comparisons using Gaussian random field theory. The activation map for Participant L for the sentence stimuli (minus fixation) is shown in Figure 16 and the corresponding map for the picture stimuli is in Figure 17.

Consistent with previous imaging studies of sentence-picture verification (Carpenter et al. (1999); Reichle et al. (2000)), this participant showed activation reliably related to sentence presentation in left parietal cortex (Fig. 16, slices 1-4), consistent with the requirement to process the visuo-spatial content of the sentences, as well as in a network of reading-related areas including occipital cortex (slices 5-8), left temporal cortex (Wernicke’s area, slices 5-7), and left inferior frontal gyrus (Broca’s area, slices 7-8). Activation reliably related to picture presentation was found in the same areas of left parietal cortex in this participant (Fig. 17, slices 1-4), but there was less evidence of activation in the occipital-temporal-frontal reading network for this condition.

Note the differences among the figures we have presented in Section 3. Figures 10, 11, and 12 show the parameters of the process response signatures of the three processes in HPM-3-K averaged over time for participant L. Figures 14 and 15 show the clustering and time courses of the process response signatures learned for participant D under HPM-GNB. These signatures are

combined based on the timing of the process instances to predict fMRI data. Figures 16 and 17 show activity maps for responses to the sentence and picture stimuli for participant L. These maps show the voxels whose data are significantly correlated with each type of stimuli. The differences among these figures reflect the different objectives of the methods that produced them.

4. Discussion

In this paper, we have presented Hidden Process Models, a generative model for fMRI data based on a set of assumed mental processes. We have given the formalism for the model, algorithms to infer characteristics of the processes underlying a dataset, and algorithms for estimating the parameters of the model from data under various levels of uncertainty. Additionally, we presented a preliminary approach to improve HPMs by taking advantage of the assumption that some neighboring voxels share parameters, including an algorithm to automatically discover sets of spatially contiguous voxels whose HPM parameters can be shared. We presented experimental results on synthetic data demonstrating that our algorithms can estimate HPM parameters, classify new data, and identify the number of processes underlying the data. We explored a real sentence-picture verification dataset using HPMs to demonstrate that HPMs can be used to compare different cognitive models, and to show that sharing parameters can improve our results.

HPMs facilitate the comparison of multiple theories of the cognitive processing underlying an fMRI experiment. Each theory can be specified as an HPM: a set of processes, each with a timing distribution and response signature parameters, and a set of configurations, each specifying a possible instantiation of the processes that may explain a window of data. The parameters of the processes may be learned from an fMRI dataset. The models may then be compared in terms of their data log-likelihood on a separate test set, or using cross-validation.

Another contribution of Hidden Process Models is the ability to estimate the spatial-temporal response to events whose timing is uncertain. While the responses for simple processes that are closely tied to known stimulus timings can be reasonably estimated with the General Linear Model (Dale & Buckner (1997)) (like ViewPicture and ReadSentence), HPMs allow processes whose onset is uncertain (like Decide). Note that this is not equivalent to letting the GLM search for the Decide process by running it once for each start time in

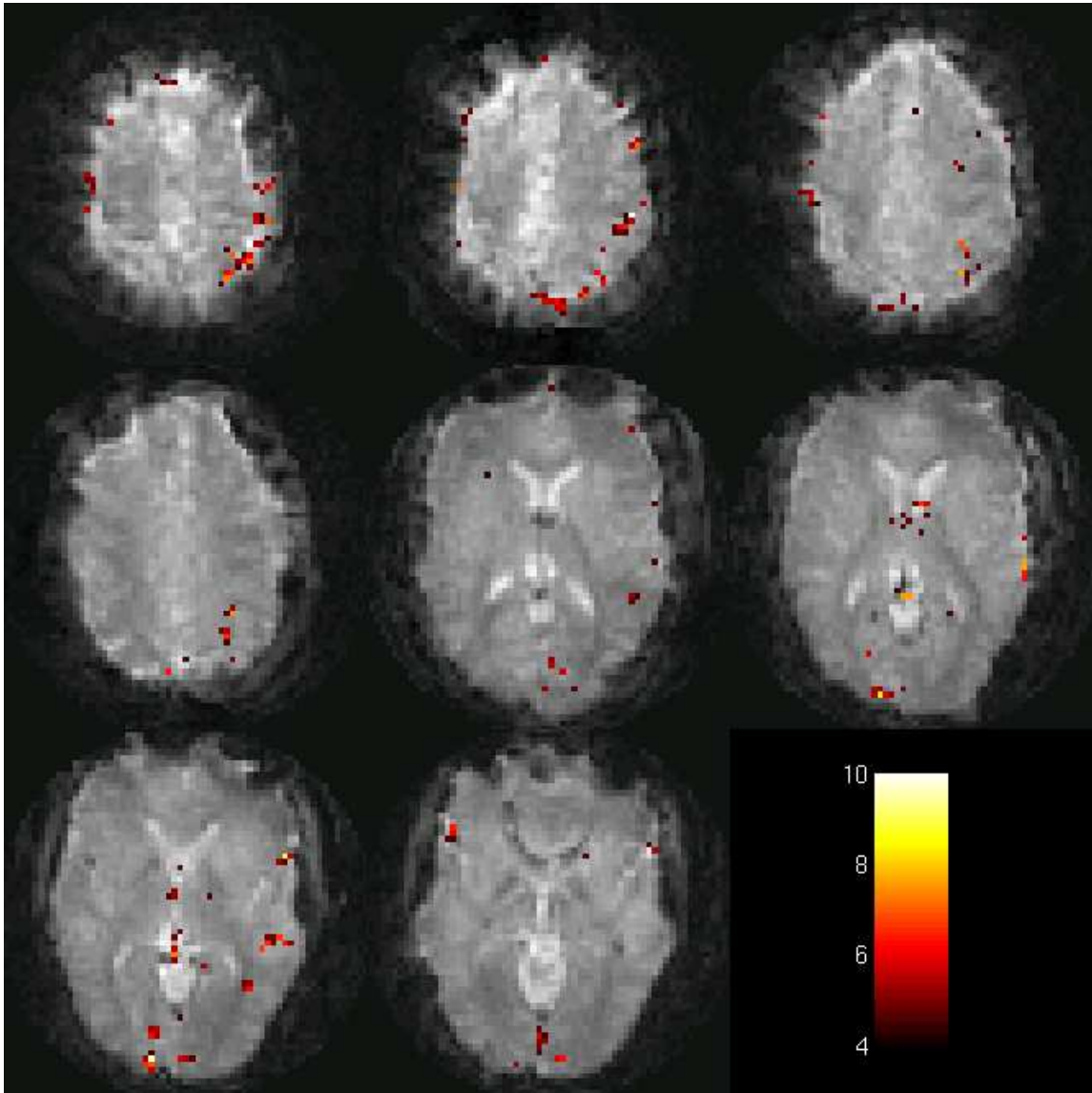


Fig. 16. The SPM activation map for Participant L for the sentence stimuli minus fixation. Images are displayed in radiological convention (the left hemisphere is on the right of each slice).

1096 the window. HPMs allow the start time to vary accord-1108
 1097 ing to a probability distribution; this means that the start1109
 1098 time can change from trial to trial within the experiment1110
 1099 to help model trials with varying difficulty or strategy1111
 1100 differences for example. In practice, we have observed1112
 1101 that HPMs do indeed assign different onsets to process1113
 1102 instances in different trials. 1114

1103 In the interest of comparison and placing HPMs in the1115
 1104 field, let us highlight three major differences between1116
 1105 analysis with HPMs and analysis with SPM (Friston1117
 1106 (2003)). A conventional analysis of the sentence-picture1118
 1107 data using SPM convolves the timecourse of the sen-1119

tence and picture stimuli with a canonical hemodynamic
 response, evaluating the correlation of the timecourse of
 each voxel with that convolved signal, and thresholding
 the correlations at an appropriate level. This analysis
 would support claims about which regions were acti-
 vated for each type of stimulus (e.g. region R is more
 active under condition S than condition P). It is not clear
 how an SPM analysis would treat any of the cognitive
 processes presented above with uncertain timings. The
 first major difference between this SPM approach and
 HPM analysis is that HPMs estimate a hemodynamic
 response instead of assuming a canonical form. Sec-

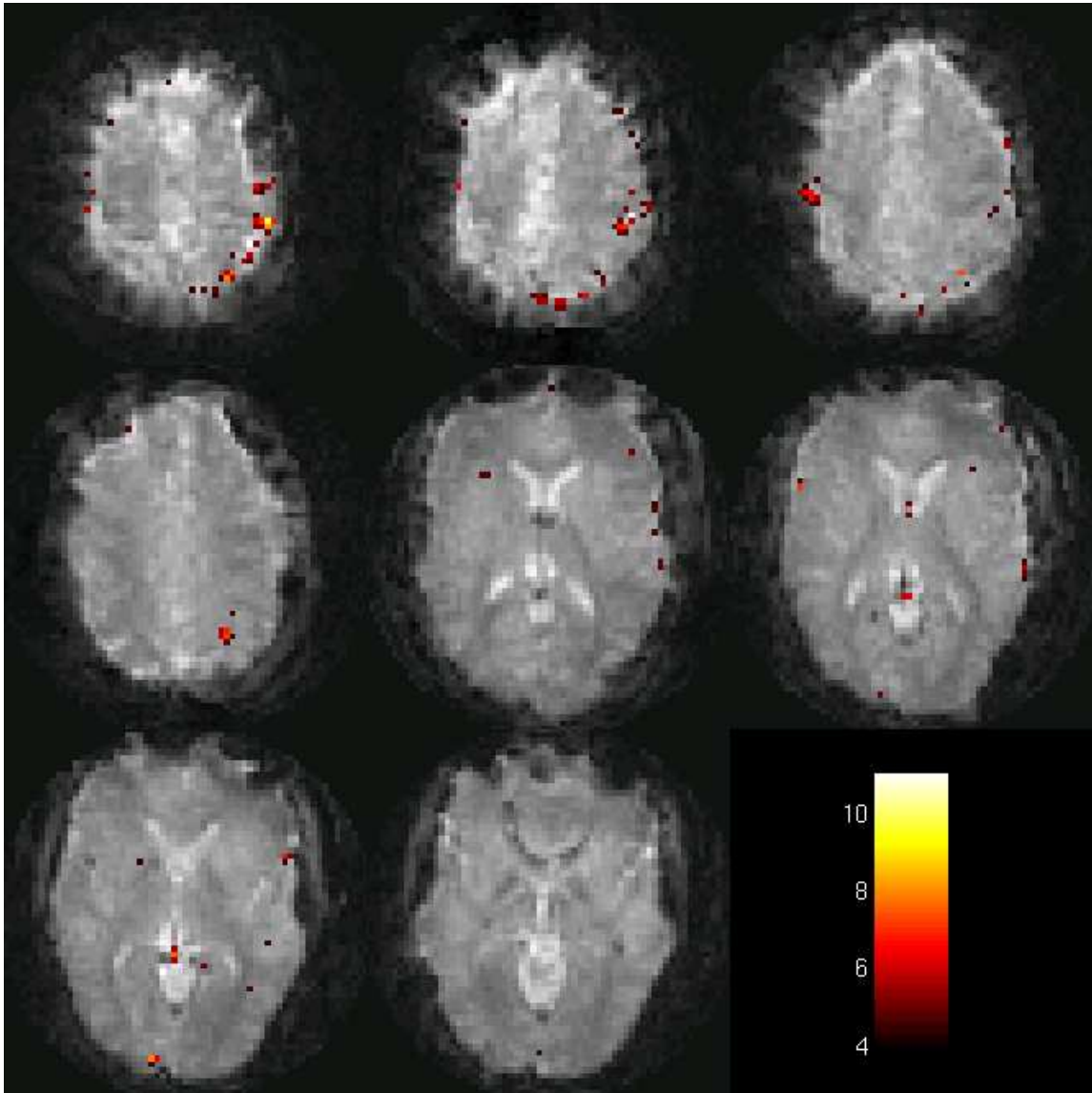


Fig. 17. The SPM activation map for Participant L for the picture stimuli minus fixation. Images are displayed in radiological convention (the left hemisphere is on the right of each slice).

1120 only, HPMs allow unknown timing for cognitive pro-1132
 1121 cesses, and estimate parameters of a probability distri-1133
 1122 bution describing the timing. Finally, the key claim that1134
 1123 HPMs attempt to make is fundamentally different from1135
 1124 that of SPM. HPMs provide evidence for claims about1136
 1125 competing models of the mental processes underlying1137
 1126 the observed sequence of fMRI activity (e.g. model M1138
 1127 outperforms model N). We believe that HPMs and SPM1139
 1128 can be complementary approaches for fMRI data anal-1140
 1129 ysis. 1141

1130 Based on our experience, we can provide a few pieces1142
 1131 of advice to those interested in using HPMs. First, since1143

HPMs are an exploratory tool, one must be careful not to jump to conclusions about the processes learned from them. In this paper, we have named a number of processes (ViewPicture, Decide, etc.). These names are only for convenience. Processes are defined by their offset values, the probability distribution over the offset values, and their response signatures. Furthermore, the parameters learned also depend on the configurations used for the training data. The set of configurations associated with an HPM reflects the prior knowledge and assumptions built into the learning algorithm; this set is part of the bias of the model. Changing the set of config-

1144 urations could result in learning different parameters for 1196
1145 each process. The response signature for each process 1197
1146 should be carefully examined to determine whether the 1198
1147 name it was given for convenience is a good descriptor. 1199

1148 A second suggestion for researchers interested in ap- 1200
1149 plying HPMs to fMRI data regards the benefit of de- 1201
1150 signing experiments with HPMs in mind. HPMs per- 1202
1151 form best if the arrangement of process instances in 1203
1152 the data renders the processes identifiable by isolating 1204
1153 and/or varying the overlap between processes. For ex- 1205
1154 ample, two processes that are always instantiated si-
1155 multaneously cannot be uniquely separated, so this case 1206
1156 should be avoided in the experiment design. Experiment
1157 designs that provide natural choices for landmarks like
1158 stimulus presentation times and behavioral data are also
1159 helpful for limiting the window of possible start times 1207
1160 for processes. For example, without recording partici- 1208
1161 pants' reaction times in the picture and sentence data, 1209
1162 we might model the button press with a similar range of
1163 offsets to the Decide process instead of just two offsets
1164 corresponding to the button press, which would result
1165 in more configurations, and thus more complexity. Fi-
1166 nally, HPMs are of most interest for studying processes
1167 of uncertain onset. If the timing of all processes of in-
1168 terest is known to be directly tied to stimuli, there are
1169 a number of other analysis methods that will perform
1170 just as well as HPMs.

1171 A third note about the application of HPMs is that
1172 the main computational complexity issue to address is
1173 the number of configurations that must be created to
1174 encode the prior knowledge we have from the experi-
1175 ment design, since adding configurations increases the
1176 size of the linear system to be solved in training HPMs.
1177 The number of configurations can be lessened by lim-
1178 iting the number of offsets for any given process and
1179 providing the sequence of some subset of processes (as
1180 we have done with ViewPicture and ReadSentence).

1181 Finally, we conclude with a discussion of future work.
1182 Hidden Process Models show promise as a new method
1183 for fMRI data analysis, and will become even more use-
1184 ful as they become more general. We are working to pro-
1185 vide more modeling options for scientists using HPMs,
1186 including regularization options for allowing priors on
1187 the areas of the brain in which we expect a process to
1188 be active. We are trying to reduce the sample complex-
1189 ity of the model by allowing the process response sig-
1190 natures to be modeled using weights on a set of basis
1191 functions, which could significantly reduce the num-
1192 ber of parameters to be estimated in training an HPM.
1193 Modelling the process response signatures with contin-
1194 uous functions could also allow us to model process
1195 instance onsets at a finer temporal resolution than the

experiment TR, and potentially relax the assumption of
fixed-duration responses. We are also looking into ways
to relax the linearity assumption present in the current
version of HPMs so that models can reasonably incor-
porate more overlapping processes. We would of course
like to explore ways of combining data from multiple
participants, and finally, we hope to relax the simplify-
ing assumptions of the parameter sharing approach to
accommodate uncertainty in the onset times of the pro-
cesses.

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