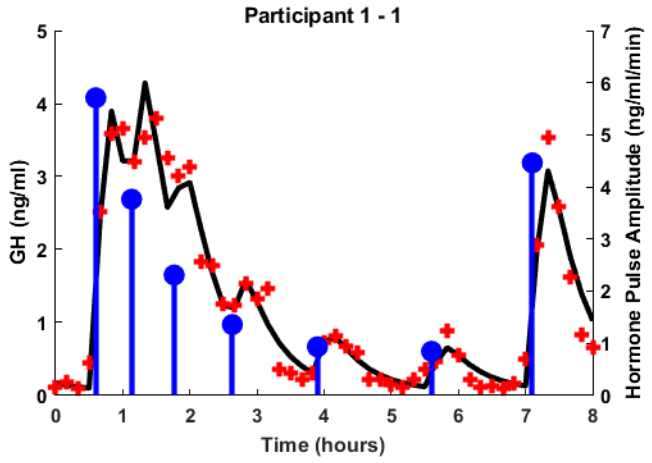
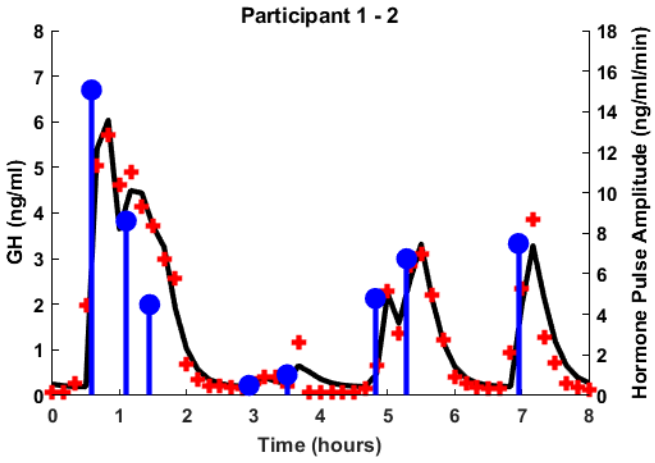
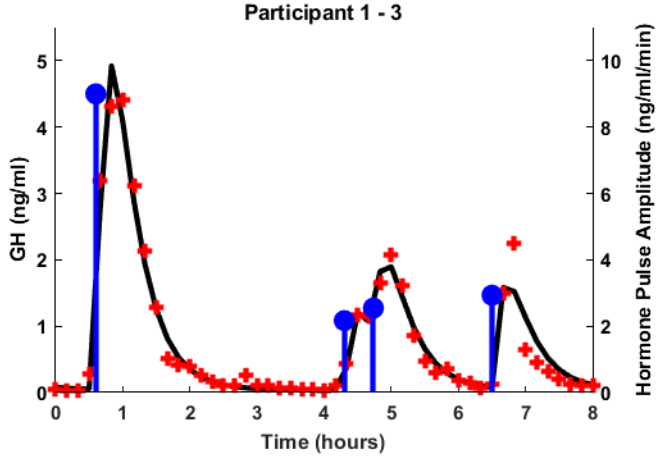
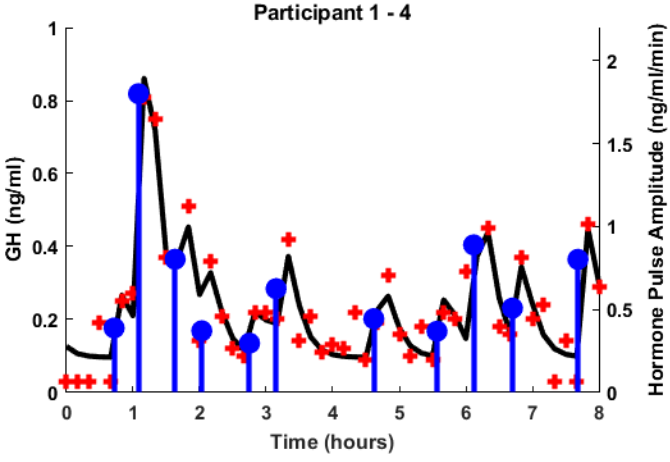
Supplemental Information

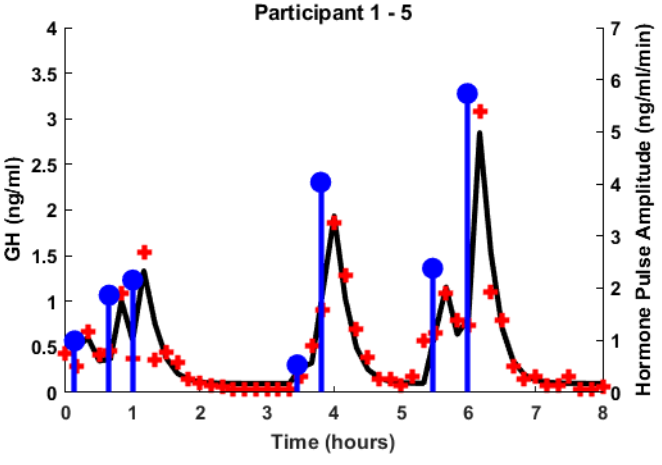
1.1 Supplementary Figures

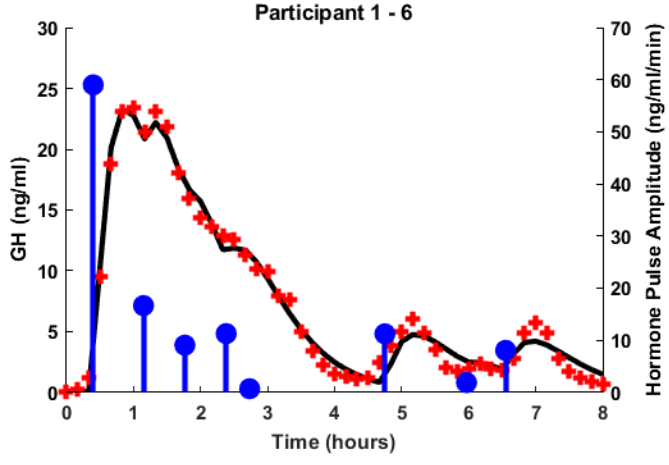


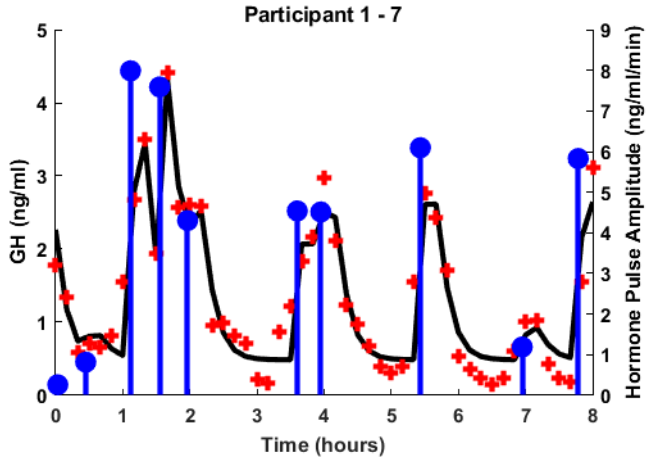


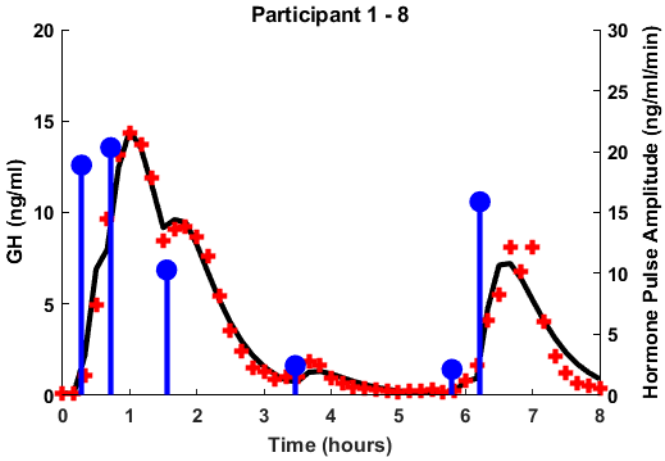


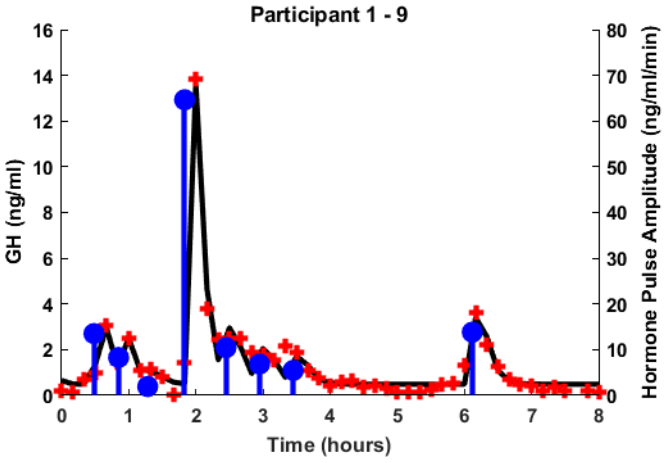


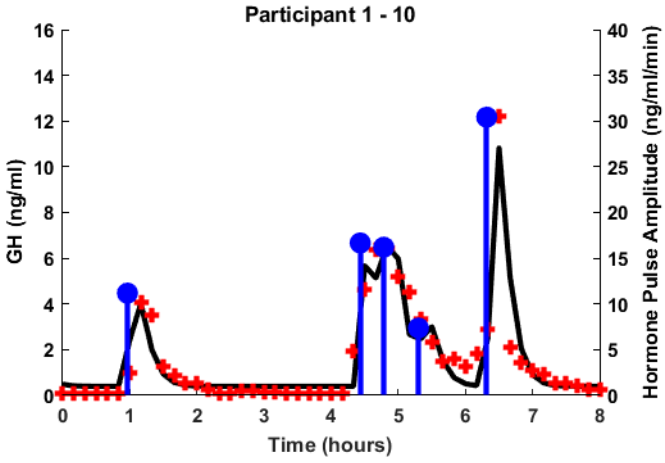


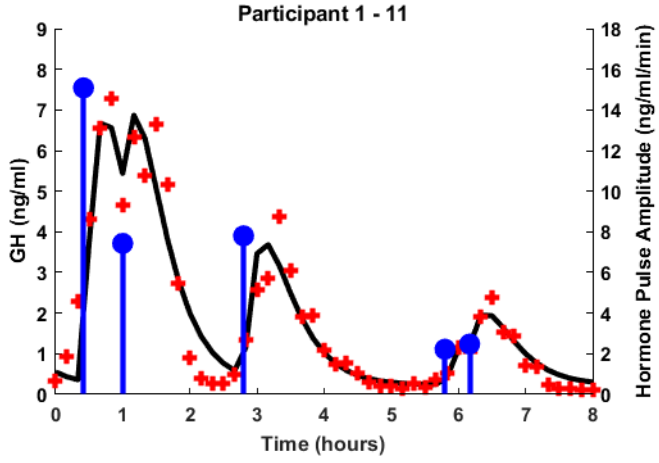


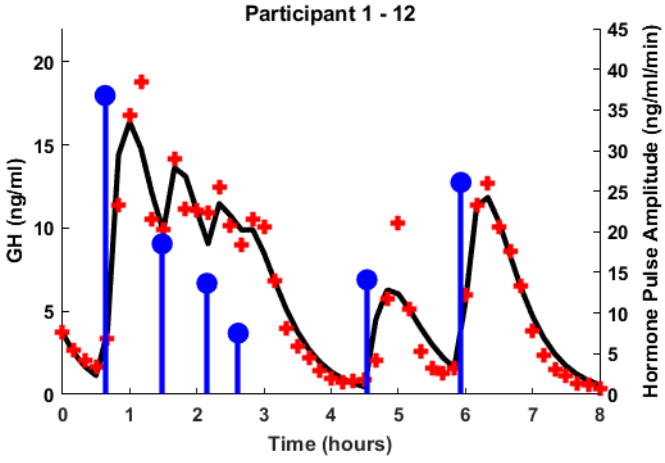












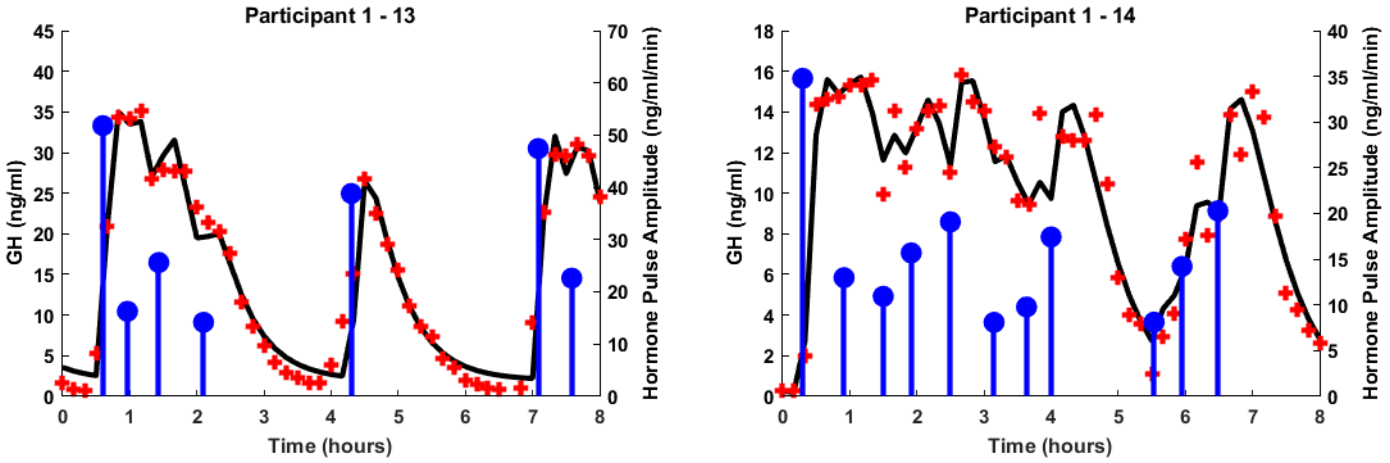


Figure S-1. Estimated deconvolution of observed 8-hour GH levels associated with each of the 14 participants from Dataset 1. Each panel shows the simulated 8-hour GH time series (red crosses), the model-estimated GH levels (black curve) and the model-estimated pulse timing and amplitude (blue vertical lines) for a single participant. The estimated model parameters are provided in Table 1 in the main text.

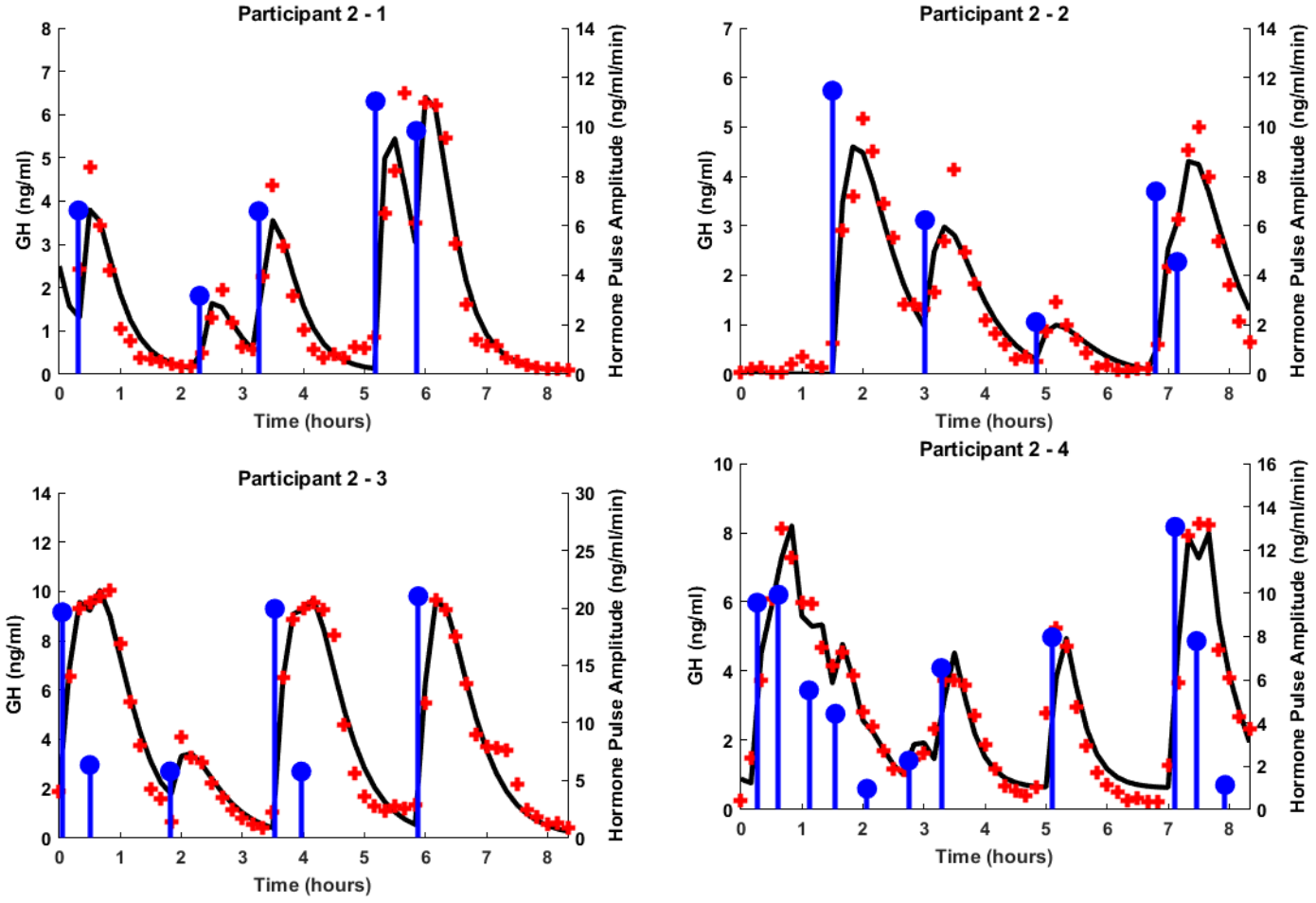
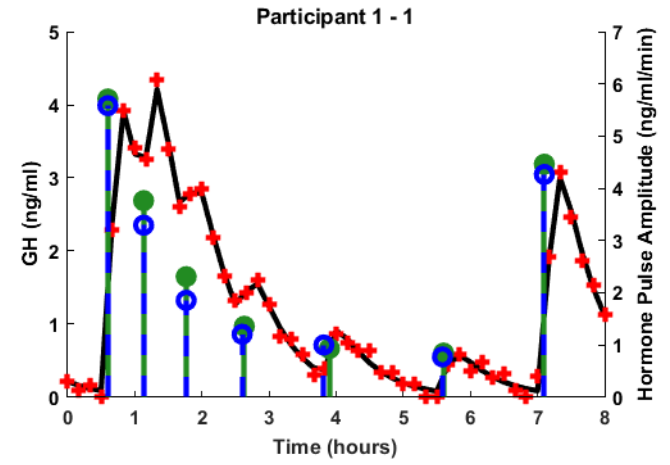
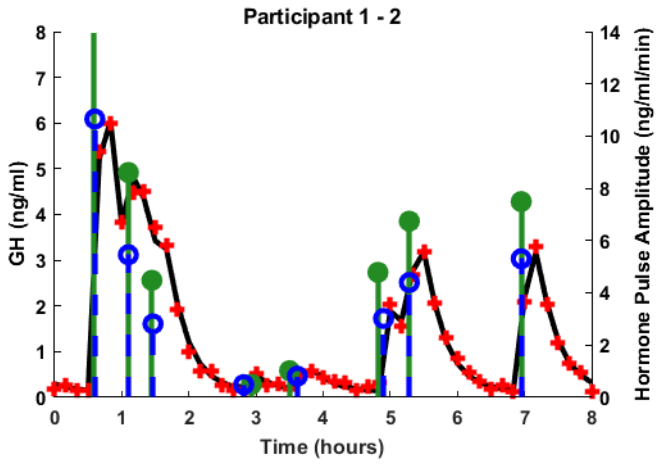
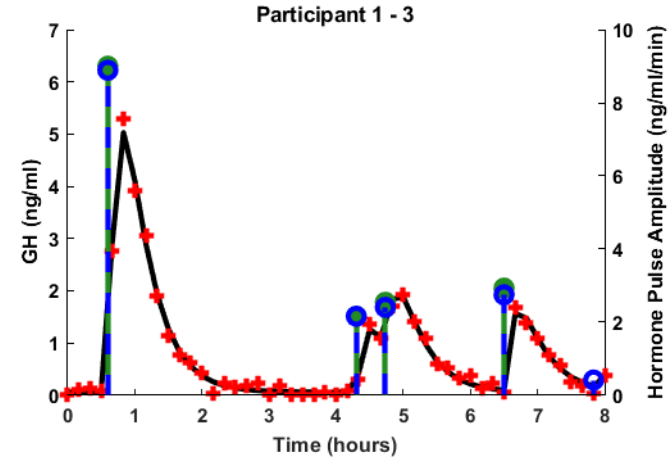
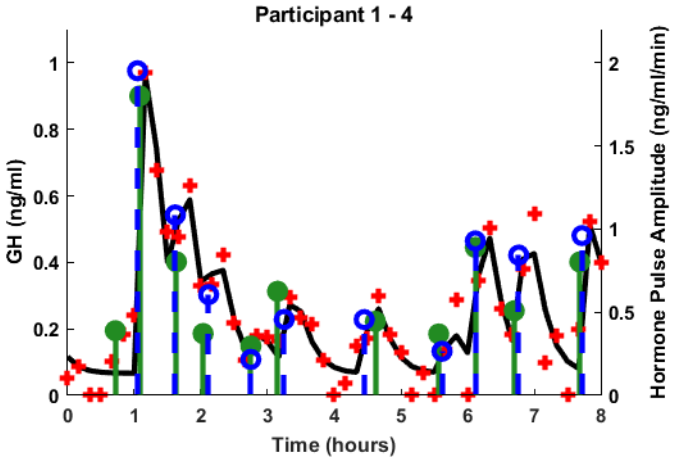


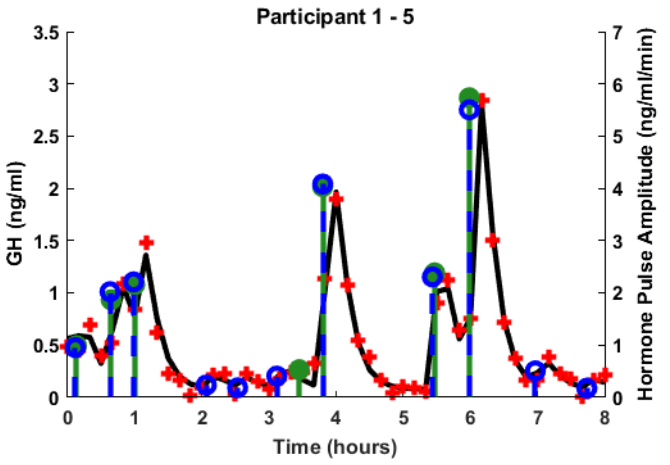
Figure S-2. Estimated deconvolution of observed 8-hour GH levels associated with each of the 4 participants from Dataset 2. Each panel shows the simulated 8-hour GH time series (red crosses), the model-estimated GH levels (black curve) and the model-estimated pulse timing and amplitude (blue vertical lines) for a single participant. The estimated model parameters are provided in Table 2 in the main text.

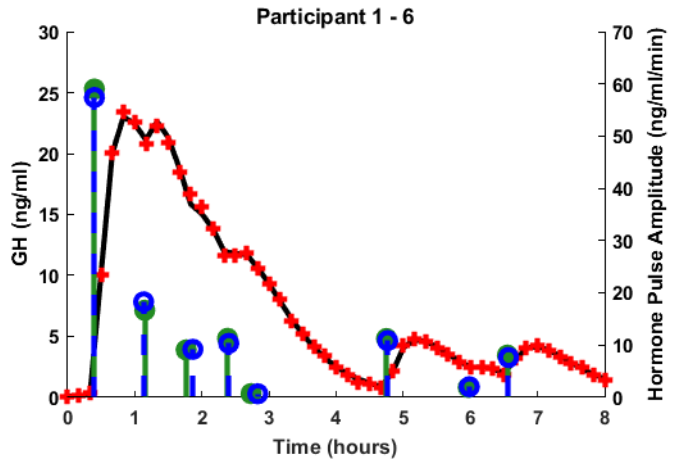

Participant 1 - 1
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)

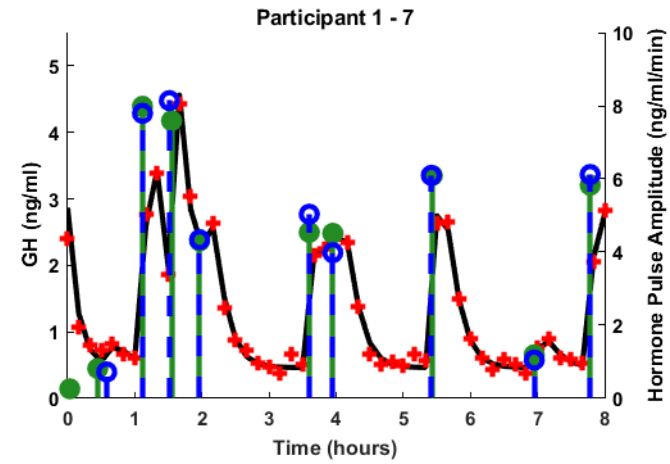

Participant 1 - 2
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)

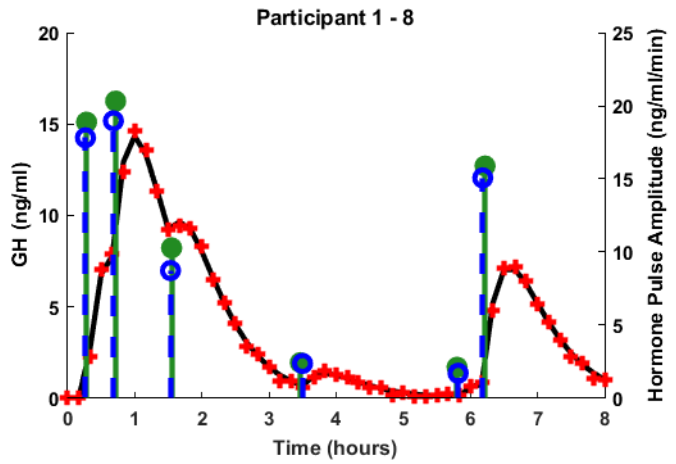

Participant 1 - 3
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)


Participant 1 - 4
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)


Participant 1 - 5
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)


Participant 1 - 6
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)


Participant 1 - 7
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)


Participant 1 - 8
GH (ng/ml)
Hormone Pulse Amplitude (ng/ml/min)
Time (hours)

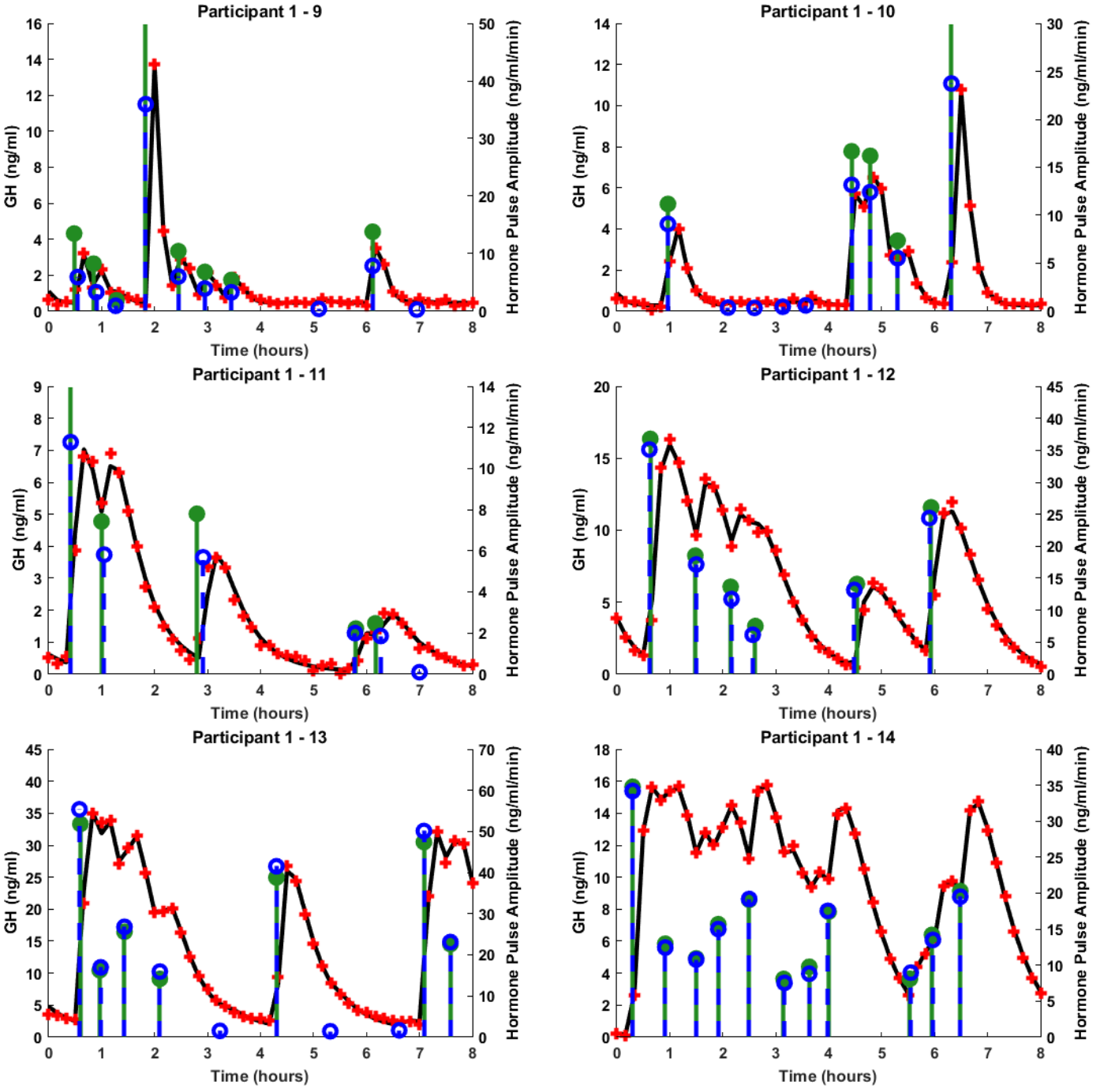


Figure S-3. Estimated deconvolution of simulated 8-hour GH levels associated with each of the 14 participants from Dataset 1 at a SNR of 20 dB. Each panel shows the simulated 8-hour GH time series (red crosses) generated from the "ground truth" pulse timing and amplitude (green vertical lines), the model-estimated GH levels (black curve), and the estimated pulse timing and amplitude (blue vertical lines) for a single participant. The estimated model parameters are provided in Table 3 in the main text.

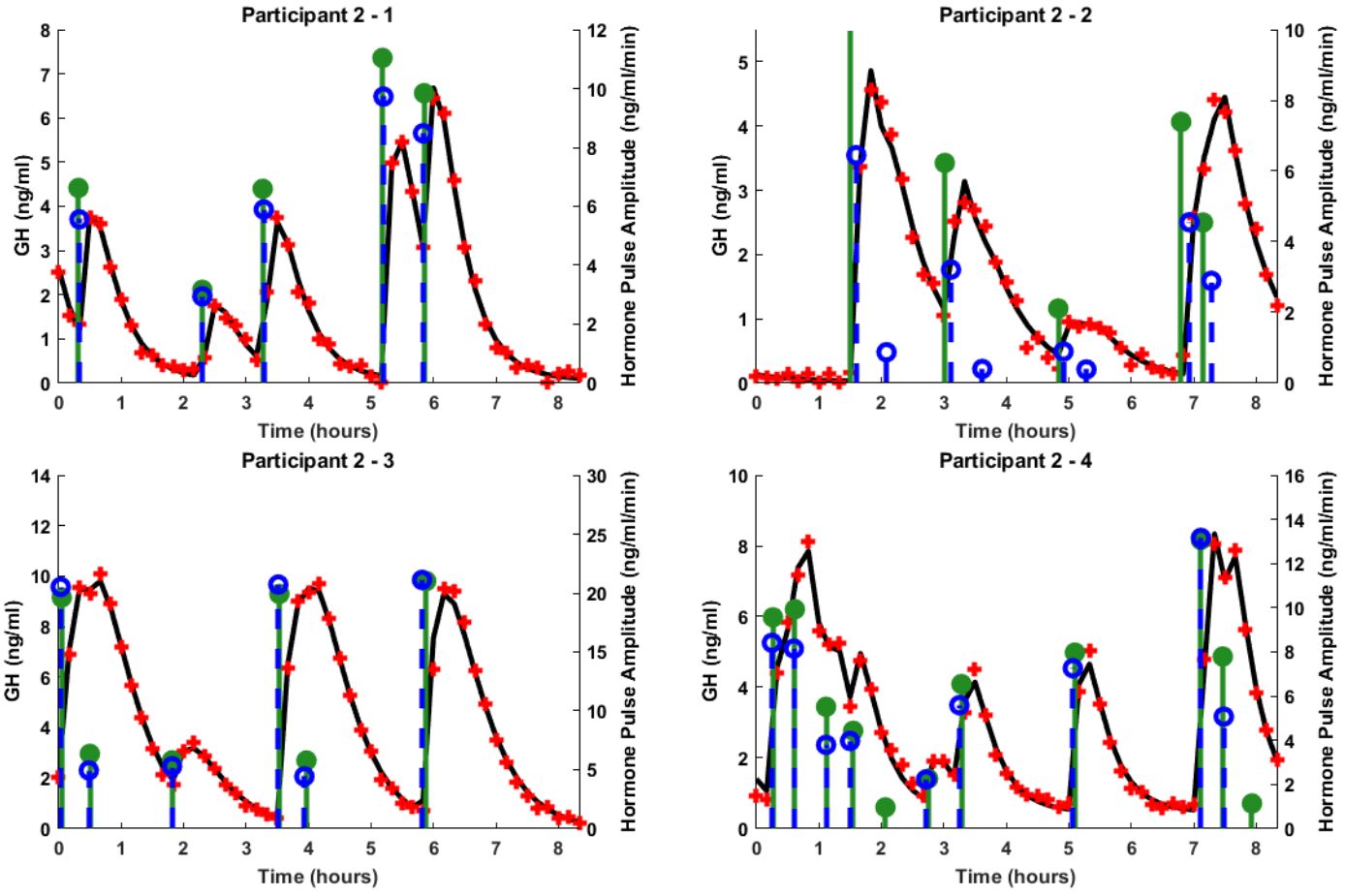


Figure S-4. Estimated deconvolution of simulated 8-hour GH levels associated with each of the 4 participants from Dataset 2 at a SNR of 20 dB. Each panel shows the simulated 8-hour GH time series (red crosses), generated from the "ground truth" pulse timing and amplitude (forest green vertical lines), the model-estimated GH levels (black curve), and the model-estimated pulse timing and amplitude (blue vertical lines) and the ground truth pulse timing and amplitude (green vertical lines) for a single participant. The estimated model parameters are provided in Table 4 in the main text.

1.2 Listwise Deletion

If there are missing values in the GH time series data, then subsequent analyses must be suitable for both our proposed algorithm and the missingness of the data.

In our estimation algorithm, we apply a least squares approach, modelling v_i as a Gaussian random variable, where $v_i = y_i - F_{\beta_i} H_d[0] - D_{\beta_i} u_i$ and $i = \{1,2,3,\cdots,M\}$. We can represent the probability density function of v_i as $P_1(v_i|\sigma^2)$ where $P_1(v_i|\sigma^2) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{\frac{(v_i)^2}{2\sigma^2}}$. Assuming the missing GH data are randomly distributed, we then represent the probability density function of missing values as $P_2(x)$ with unknown parameters denoted x. If the probability density function of a missing response, $P_2(x)$, is unrelated to the either the actual value missing from the data or the set of observed responses, then that response is said to be Missing Completely At Random (MCAR) [1]. Furthermore, if the set of missing responses is MCAR, then the likelihood function of P_1 and P_2 can be represented as $P_1(v_i|\sigma^2) \cdot P_2(x)$. We take the negative log of the likelihood function of P_1 and P_2, resulting in

$$
\begin{aligned}
&-\log\big(P_1(v_i|\sigma^2)\big) - \log\big(P_2(x)\big) \\
&= \frac{1}{2\sigma^2}\left\|y_i - F_{\beta_i} H_d[0] - D_{\beta_i} u_i\right\|_2^2 - \log\big(P_2(x)\big) \qquad (17)
\end{aligned}
$$

We can see in (17) that the Gaussian distribution of measurement error is independent from the uniform distribution of missing values. The distribution of missing values does not depend on observed data and as such the missing data is considered MCAR.

We perform listwise deletion, as opposed to imputation, because (i) the temporal resolution of our GH data does not lend itself to imputation, (ii) listwise deletion will yield an unbiased estimate of mean response trends, because the missingness of GH data is MCAR [1], and (iii) our proposed algorithm accounts for missing sample data. Additionally, methods of imputation like linear interpolation tend to produce biased estimates of parameters [2].

We perform listwise deletion by reformulating the optimization problem in (12) as:

$$
\min \frac{1}{2} \sum_{i \in \{1,2,\cdots,M\} \setminus \{\boldsymbol{S}\}} \big(y_i - F_{\beta_i} H_d[0] - D_{\beta_i} u_i\big)^2 \qquad (18)
$$

where $\boldsymbol{S}$ represents the set of indices in which sample data is missing.

Listwise deletion introduces no bias in the

approximation of model parameters or of the timing and amplitude of secretory events. Therefore, maximizing the fit of available data via our estimation algorithm also improves the estimation of missing data, where $\mathbf{y_j} = \mathbf{F_{\beta_j}H_d}[\mathbf{0}] + \mathbf{D_{\beta_j}u_j}$ and $\boldsymbol{j} \in \{\boldsymbol{S}\}$.

1.3 Participant Information

The sex, age, and BMI of each participant from Dataset 1 are listed in Table S-1. The sex, age, BMI and Apnea-Hypopnea Index (AHI) for each participant from Dataset 2 are in Table S-2.

TABLE S-1
PARTICIPANT SEX, AGE AND BMI FOR DATASET 1.

Participant No.	Sex	Age [years]	BMI $\left[\frac{kg}{m^2}\right]$
1	F	12.5	18.6
2	F	12.3	19.2
3	F	12.3	17.9
4	F	11.6	16.5
5	F	12.3	19.8
6	M	13.4	17.9
7	F	13.4	20.5
8	F	13.2	25
9	M	11.3	26.1
10	M	12.0	22.9
11	M	12.2	29.3
12	M	13.8	18.7
13	M	13.4	17.9
14	M	14.1	21.6

TABLE S-2
PARTICIPANT SEX, AGE AND BMI FOR DATASET 2.

Participant No.	Sex	Age [years]	BMI $\left[\frac{kg}{m^2}\right]$	AHI	
				off cpap	on cpap
1	F	12.3	25.9	5.4	4.1
2	M	14.4	40.4	2.2	0.2
3	M	13.4	18.2	1.2	0.0
4	M	11.8	14.9	0.0	0.0

1.4 Alternative Method: Peak Detection

We used the *findpeaks*() function within MATLAB for detecting secretion events. We apply the relevant constraints of our problem (i.e., the maximum number of secretory events) to estimate a physiologically plausible solution and the minimum distance between secretory events based on this constraint in our method. While this peak detection method can identify significant peaks in serum GH data, it cannot recover the model parameters or accurate GH pulse locations, because this method lacks a physiological interpretation of GH secretion. This peak detection method also does not provide the infusion and clearance rates. Additionally, the location of serum GH peaks identified by the peak detection method is not the location of the GH secretion event. Rather, the peak detection provides the location of the maximum level of serum GH after a secretion event. This peak detection method also identified two small noise spikes (near 0 and 6.5 hours) as a GH peak, as indicated in Figure S-5.

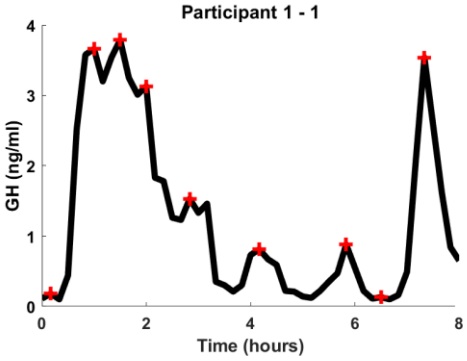


Figure S-5. Detected peaks of Participant 1-1 (red crosses) and the experimental GH data (black curve).

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