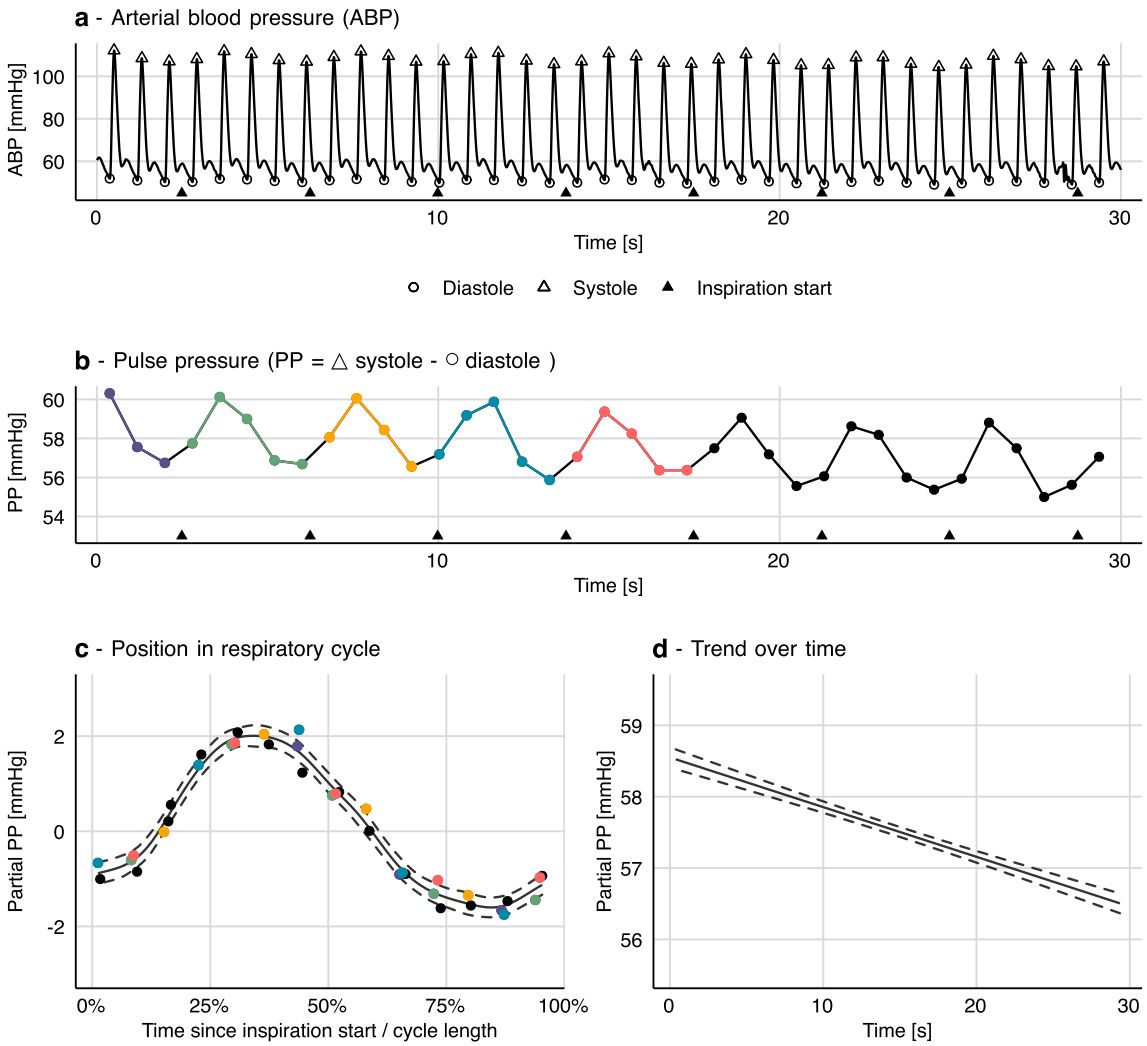

Fig. 2 How a generalized additive model (GAM) can be fitted to a series of pulse pressure measurements (derived from the arterial waveform). **a** and **b** For each beat, systolic and diastolic pressure are detected, and pulse pressure (PP) is calculated. A GAM with two smooths **c** and **d** is fitted to the PP time series (**b**). **c** This first smooth represents the variation in PP explained by the beats' position in the respiratory cycle. Coloured points (beats) correspond between panels **b** and **c**. **d** The second smooth represents the trend in PP over time with the model constant (α) added. The sum of these two smooths (**b** and **c**) gives the model prediction. Residuals of the model (ε) are the vertical distance from the smooth to the points in panel **c** (i.e. the scatters are partial residuals). Dashed curves represent 95% confidence intervals

$f\left(pos_{ventilationcycle}\right)$ describes the relationship between a heart beat's position in the respiratory cycle and the produced PP at that heart beat. $f(time)$ represents the trend in PP over time, and α is the mean PP over the entire sample. ϵ represents the remainder: noise, 'random' fluctuation, etc.

The individual observations in this analysis are heart beats. For each heart beat, we need to know the time it occurred, its position in the respiratory cycle (time since the start of the latest inspiration/respiratory cycle length) and the pulse pressure of the beat. The timing of each beat was assigned the time of the diastole,[1] and pulse pressure was calculated as systolic minus diastolic pressure (see Fig. 2a and b). With this data, the model can be fitted as a GAM where $f\left(pos_{ventilationcycle}\right)$ is a cyclic cubic spline and $f(time)$ is a natural cubic spline.

[1] Alternatively, QRS-complexes from the ECG could be used to mark the time of each heart beat. Pulse transit time is around 200 ms and it varies approximately 10–20 ms with ventilation [16]. Therefore, using QRS-complexes to time each heart beat would create a slight leftwards phase shift of the respiratory cycle smooth (Fig. 2c) and a probably unnoticeable effect of the variation in pulse transit time. For patients with cardiac arrhythmia, using QRS-complexes could aid the analysis. Both because it may be difficult to identify individual heart beats from the ABP waveform alone, and because pulse transit time might vary significantly between beats.