Respiratory Rate Determination by ECG Monitoring

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1 Introduction

1.1 Background

Pneumonia is the deadliest infectious disease to children under the age of 5, responsible for 740,180 deaths under 5 as of 2019 (World Health Organisation, 2022). The worsening symptoms of pneumonia can rapidly become life-threatening for young children if not treated on time. Nevertheless, the early stage of pneumonia with young children is often confused with other less serious respiratory disease with similar symptoms. On the other hand, a medical institution cannot provide comprehensive monitoring to all its patients for all potential symptoms of pneumonia due to limitation of resources. Thus it is of interest to develop light-weight, non-evasive methods for detecting the most common symptoms of pneumonia, as an early warning to serve as an indication of a need for further medical interventions.

In a research outlined in Shamo'on et al. (2004), tachypnoea (average respiratory rate > 50 per minute) is one of the critical indicators of pneumonia in young children. However, the high volatility of breath rate in children poses a major challenge for manual counting that is both time-consuming and prone to error. In contrary, automated respiratory monitoring often involves machine-measurement of chest/abdomen movement or nasal airflow that are resource-costly and possibly invasive such that the discomfort from wearing the equipment might adversely affect its accuracy.

A potential solution to the problem above arises from the phenomenon of *respiratory sinus arrhythmia*, such that the instantaneous heart rates increase with inspiration and decrease during expiration (Larsen et al., 2010), by monitoring the periodicity of variation in the heart rate, it may be possible to determine one's respiratory rate with a simple, non-evasive method, such as by a pulse oximeter that is resource-friendly. As such, this project attempts to develop an efficient *predictive* algorithm to accurately and precisely determine respiratory rate from heart rate, as well as briefly discuss its limitations and direction for future works.

1.2 The data

The *apnea-ECG database* (Penzel et al., 2000) on *PhysioNet* (Goldberger et al., 2000) provides sufficiently large data sets of approximately eight hours long records of electrocardiogram and respiratory signals for eight subjects in a study for *sleep apnea*. The eight records consist of 100Hz signal from the electrocardiogram (ECG), respiratory effort from chest/abdomen movements, nasal airflow, and blood O_2 saturation over time.

A major concern of using such data is the misalignment of objective for the researches. Study for apnea typically involves subjects with airway obstruction, a factor that must be considered for prior to building our model. Under the presumption that, subjects in our data might sometimes stop breathing, the response variable of interest should be robust from the presence of apnea. Therefore, the model will focus on exploring the algorithm for determining the respiratory rate from the ECG signal as a predictor for the respiratory rate implied by chest movements, assuming that for living humans, respiratory efforts are always present.

This study will divide records from the eight subjects into two sets:

- Subjects a01, a02, a03, a04 and b01 form the *training set*.
- Subjects c01, c02 and c03 form the *test set* for evaluation.

2 Methodologies and implementation

2.1 Data wrangling

2.1.1 Processing ECG signals

The ECG signal does not provide the heart rate directly. Instead, it is a time series of varying electric potential that controls the rhythm of the contraction and relaxation of the heart muscle, with a magnitude of approximately 0.5mV in absolute value. Such a signal is often masked by unwanted noise, such as electric signals from pectoral muscle movement, creating a challenge in computing heart rate from the ECG signal.

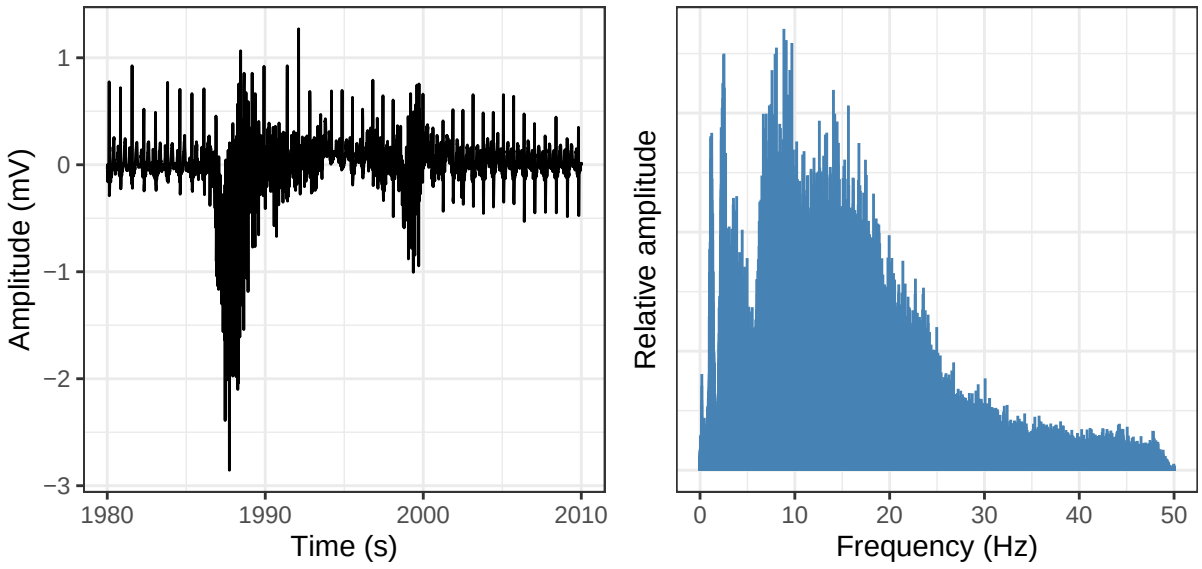


Figure 1: Left: sudden spike in noise; right: frequency spectrum of the ECG signal

Algorithm 1 5-20Hz band-pass filter with fast Fourier transform

Take $\mathbf{x} \in \mathbb{R}^n$ as the 100-Hz input
Obtain $\mathbf{y}$ by fast Fourier transform on $\mathbf{x}$
for $t = 1, ..., n$ **do**
    $y_t \leftarrow \sum_{k=1}^{n} x_k \exp(-2\pi i(k-1)(t-1)/n)$
end for
Zero corresponding (Nyquist) frequency bins for 0-5, 20-50Hz
for $t = 1, ..., n \wedge (t \in (0.2n, 0.8n) \vee t > 0.95n \vee t < 0.05n)$ **do**
    $y_t \leftarrow 0 + 0i$
end for
Obtain $\mathbf{z}$ by normalised inverse fast Fourier transform on $\mathbf{y}$
for $t = 1, ..., n$ **do**
    $z_t \leftarrow \sum_{k=1}^{n} y_k \exp(2\pi i(k-1)(t-1)/n)/n$
end for
return $\mathrm{Re}(\mathbf{z}) \in \mathbb{R}^n$ as the 100-Hz output

2.1.2 Heart rate derivation from ECG signals

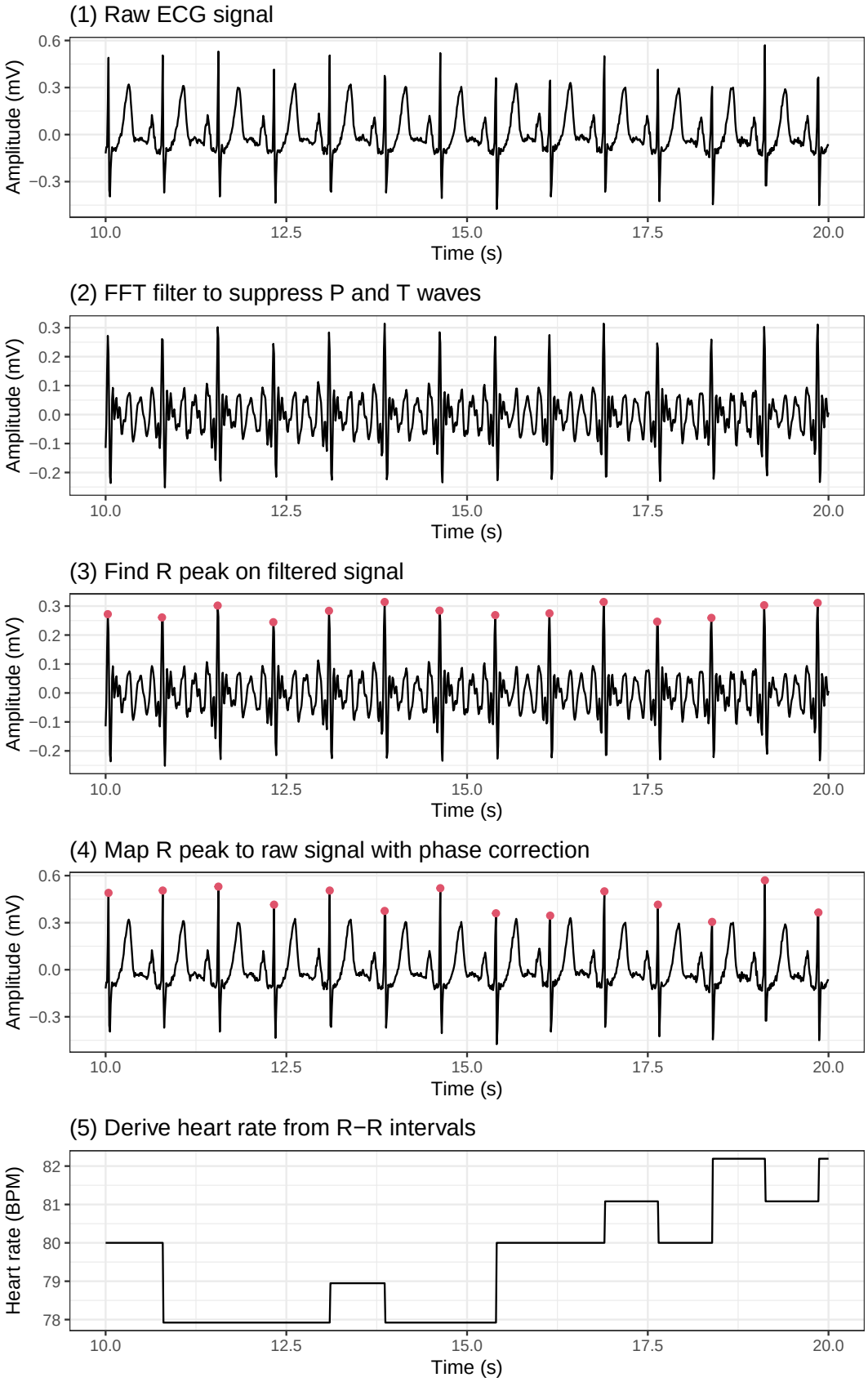
Algorithm 2 R peak timestamping with phase correction

Take the original $\mathbf{x} \in \mathbb{R}^n$ and the filtered $\mathbf{z} \in \mathbb{R}^n$ as the 100-Hz inputs
Set moving threshold $\mathbf{b}$ as half of rolling maximum
$(b_t | t = 1, ..., 100) \leftarrow (+\infty)_{\times 100}$
for $t = 101, ..., n$ **do**
    $b_t \leftarrow \frac{1}{2}\max\{z_{t-100}, ..., z_t\}$
end for
Create thresholding indicator $\boldsymbol{\iota}^{(\mathbf{1})}$
for $t = 1, ..., n$ **do**
    $\iota_t^{(1)} \leftarrow I(z_t > \max\{b_t, F_Z^{-1}(0.95)\})$
end for
Create concave-peak indicator $\boldsymbol{\iota}^{(\mathbf{2})}$
for $t = 1, n$ **do**
    $\iota_t^{(2)} \leftarrow 0$
end for
for $t = 2, ..., n-1$ **do**
    $\iota_t^{(2)} \leftarrow I[I(z_{t+1} - z_t > 0) - I(z_t - z_{t-1} > 0) = -1]$
end for
Preliminary timestamps for R peak $\mathbf{p} \leftarrow (t = 1, ..., n | \iota_t^{(1)} \wedge \iota_t^{(2)}$ is True)
Remove abnormal timestamps in $\mathbf{p}$ with R-R intervals of < 300ms
Correct phase-shifts caused by fast Fourier transform
for $t \in \{\mathbf{p}\}$ **do**
    $p | p = t \leftarrow \text{argmax}_{i=t-4,...,t,...,t+4} x_i$
end for
return $\mathbf{p}$ the timestamps of the R peak

Algorithm 3 Deriving instantaneous heart rates from R peak timestamps

Take $\mathbf{p}$ the timestamps of the R peak as the input, and ν as an argument for the frequency unit of $\mathbf{p}$
$m \leftarrow \dim(\mathbf{p})$ dimension of $\mathbf{p}$
Compute the R-R intervals $\mathbf{d}$
$(d_t | t = 1, ..., p_1) \leftarrow (\text{NA})_{\times p_1}$
$(d_t | t = p_1 + 1, ..., p_m) \leftarrow ((p_2 - p_1)_{\times (p_2 - p_1)}, (p_3 - p_2)_{\times (p_3 - p_2)}, ..., (p_m - p_{m-1})_{\times (p_m - p_{m-1})})^\top$
Convert R-R intervals into heart rates per minute $\mathbf{h}$
$\mathbf{h} \leftarrow 60 \cdot \nu / \mathbf{d}$
return $\mathbf{h}$ the heart rates per minute at frequency ν

2.1.3 Visualising ECG signal processing



2.2 Modelling rate of breathing by heart rate

2.2.1 The smoothing spline crossing algorithm

Algorithm 4 Smoothing spline crossing for counting cycles of nonstationary pseudosinusoidal oscillations, for varying heart rates/chest movements

Take a time series vector $\mathbf{a}$ at any frequency, and the optional argument λ the regularisation parameter
$\mathbf{t} \leftarrow (1, ..., \dim(\mathbf{a}))^\top$ as the indexing vector
Construct B-spline bases $\mathbf{B}$ derived from natural cubic spline bases about all possible knots of $\mathbf{t}$
Penalty matrix $\mathbf{\Omega} \leftarrow \{\omega_{jk} = \int_T B_j^{''}(s) B_k^{''}(s) ds | B_j(t_i) = (\mathbf{B})_{ij}\}$
if argument λ is missing **then**
    $\lambda \leftarrow \text{argmin}_{\lambda>0}(1 - \text{tr}(\mathbf{B}(\mathbf{B}^\top\mathbf{B} + \lambda\mathbf{\Omega})^{-1}\mathbf{B}^\top)/\dim(\mathbf{a}))^{-2} ||(\mathbf{I} - \mathbf{B}(\mathbf{B}^\top\mathbf{B} + \lambda\mathbf{\Omega})^{-1}\mathbf{B}^\top)\mathbf{a}||^2$
end if
$\hat{\mathbf{a}} \leftarrow \mathbf{B}(\mathbf{B}^\top\mathbf{B} + \lambda\mathbf{\Omega})^{-1}\mathbf{B}^\top\mathbf{a}$
Count the number of times the curves $(\mathbf{t}, \mathbf{a})$ and $(\mathbf{t}, \hat{\mathbf{a}})$ cross (equivalent to zero-crossing for $(\mathbf{t}, \mathbf{a} - \hat{\mathbf{a}})$)
return half of the count obtained above as the approximated cycles

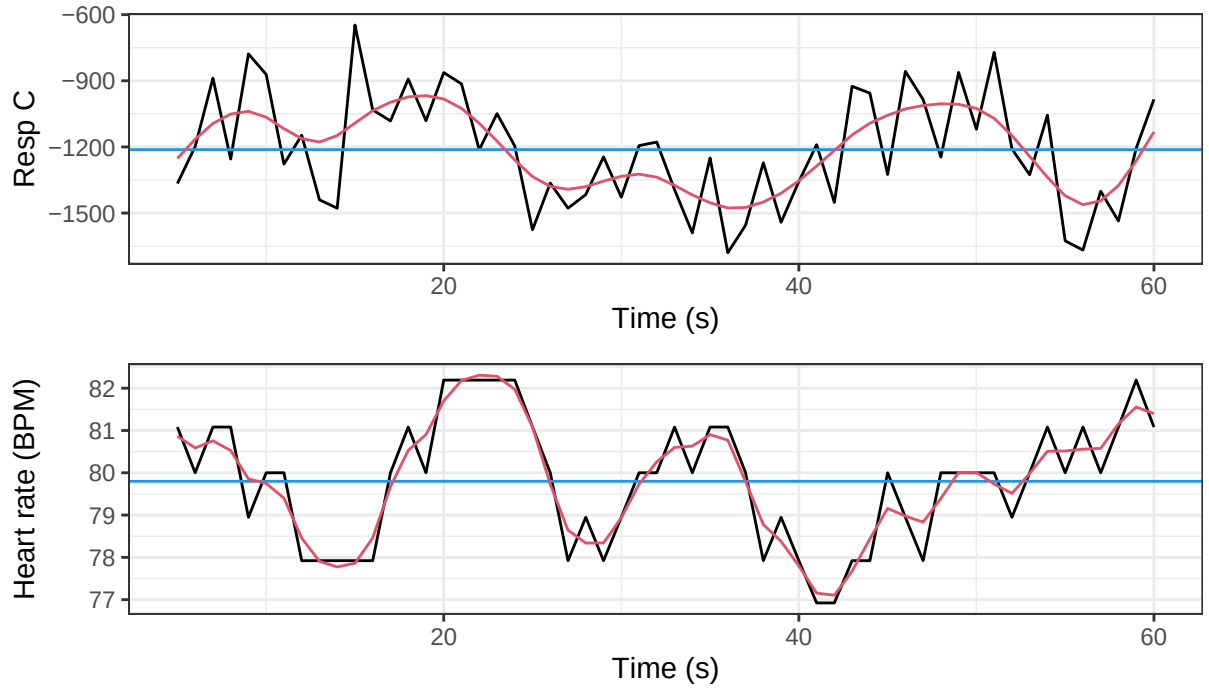


Figure 2: Time series of chest movement (top) and heart rates (bottom) at 1Hz for 1 minute. Blue: naive zero-crossing gives a count of 11.5 and 6 breaths; red: smoothing spline crossing gives a count of 19.5 and 16.5 breaths. We can clearly see that smoothing spline performs much better in counting breaths.

2.2.2 Model training

Algorithm 5 Deriving breath rate from heart rate based on chest movements

1: Take $\mathbf{h}$ the heart rates per minute and $\mathbf{c}$ the chest movements signal (either at 100Hz or down-sampled) where both time series have aligned indices and identical frequency; and optional argument λ_{opt} (only in model evaluation with test data)
2: For both $\mathbf{h}$ and $\mathbf{c}$, remove elements of index where $c_t = \text{NA}$
3: **for** each record of all the subjects **do**
4: Partition each of $\mathbf{h}$ and $\mathbf{c}$ into segments of 60-second data
5: **end for**
6: Drop the remainder (last segment), which is less than 60 seconds
7: **if** $\mathbf{h}$ and $\mathbf{c}$ for more than one subject is input **then**
8: Bind $\mathbf{h}$ and $\mathbf{c}$ of all subjects together
9: **end if**
10: **for** each 60-second segment of $\mathbf{c}$ **do**
11: Pass each minute of $\mathbf{c}$ into Algorithm 4 (the smoothing spline crossing, without specifying λ) to compute the true rate of breath based on chest movements, and output $\rightarrow \mathbf{r}$
12: **end for**
13: **if** argument λ_{opt} is missing **then**
14: $\lambda_{\text{opt}} \leftarrow \text{argmin}_{\lambda>0}||\mathbf{r} - \hat{f}(\mathbf{h}; \lambda)||^2$ where $\hat{f}$ is the Algorithm 4: applied on each minute of $\mathbf{h}$ given λ
15: **end if**
16: $\hat{\lambda}_{\text{opt}} \leftarrow \lambda_{\text{opt}}$: if its value is obtained by Step 14 $\hat{\lambda}_{\text{opt}}$ is the estimate of λ_{opt} derived from the training data; otherwise, if λ_{opt} is passed as an argument, then the purpose of this algorithm is model testing
17: **for** each 60-second segment of $\mathbf{h}$ **do**
18: Pass each minute of $\mathbf{h}$ into Algorithm 4 (with argument of $\lambda = \hat{\lambda}_{\text{opt}}$) to compute the derived rate of breath from heart rate, and output $\rightarrow \hat{\mathbf{r}}$ which is the model's estimate of $\mathbf{r}$: the chest rate of breath
19: **end for**
20: **return** data matrix $(\mathbf{r}, \hat{\mathbf{r}})$, a bi-variate time series (minutely), $\mathbf{r}$:= "count of breaths by chest movements (observations)" and $\hat{\mathbf{r}}$:= "number of breaths derived by cardio-activities of that minute (fitted values)", and most importantly $\hat{\lambda}_{\text{opt}}$ the trained parameter for our final model!

2.3 Model diagnostics

The trained model implied that one's heart rate is useful for inferring the rate of breath, and the results are statistically significant based on the regularisation result. If there is null relationship between the heart rate and rate of breath, the trained model should have returned a *least-complex fit*, such the L_2 loss function (cross-validated MSE) is minimised at large λ and is monotonically decreasing. Hence, the obvious inverted bell curve exhibited by the regularised L_2 loss with one minimum gives evidence against a *null-model fit*.

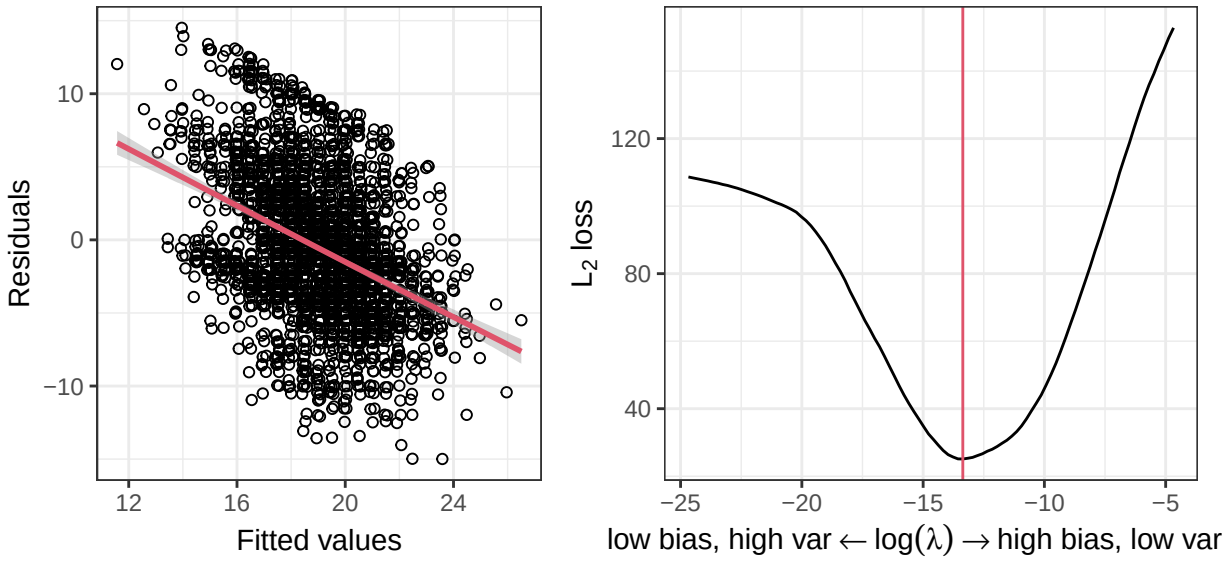


Figure 3: Left: the existence of residual trend, indicates a nonzero bias; right: visual representation of the bias-variance tradeoff via regularisation, the result indicates that the model is more useful than null model.

Notwithstanding the model being shown useful for predicting the rate of breath using the heart rate, it gives biased estimates for predictions. For all *best linear unbiased estimators* (BLUE), such as *least square estimators*, residuals: $\mathbf{r} - \hat{\mathbf{r}}$, are orthogonal (therefore, independent) to the fitted values: $\hat{\mathbf{r}}$. But, the final model gives $\hat{\text{Corr}}(\hat{\mathbf{r}}, \mathbf{r} - \hat{\mathbf{r}}) = -0.3976376$ implying $\text{Bias}(\hat{\mathbf{r}}) = \mathbb{E}(\hat{\mathbf{r}}) - \mathbf{r} \neq \mathbf{0}$. Such bias is introduced intentionally due to regularisation to reduce variance of the estimator $\hat{\mathbf{r}}$. More comparatively:

$$\text{BLUE minimises } \text{Var}(\hat{\mathbf{r}}) \text{ subject to } \text{Bias}(\hat{\mathbf{r}}) = \mathbf{0}$$
$$\text{Regularised estimator minimises } \text{MSE}(\hat{\mathbf{r}}) = \mathbb{E}((\mathbf{r} - \hat{\mathbf{r}})^2) = \text{Var}(\hat{\mathbf{r}}) + \text{Bias}(\hat{\mathbf{r}})^2$$

While BLUE has constraints $\text{Bias}(\hat{\mathbf{r}}) = \mathbf{0}$ (always aims for maximising accuracy first), it unwantedly inflates the variance of the estimator. Whereas regularised estimator appeals to the *bias-variance tradeoff* seeks to directly minimise the cross-validated prediction error (as a function of L_2 loss), that is decomposable to the sum of variance (imprecision) and bias-squared (inaccuracy) for any estimator (Hastie et al., 2009). It follows that, we relaxed the requirement of zero bias via introducing a small bias (sacrificed some accuracy) for a substantially larger drop in variance (massively improved precision) to achieve better predictive performance.

Despite prior anticipation of the bias being nonzero, it is of interest to test for its statistical and practical significance and see if it is acceptably low. For heart-rate-derived breath rate: $\hat{\mathbf{r}}$, as an estimator for breath rate based on chest movements: $\mathbf{r}$, we can draw a hypothesis test for $\mathbf{r} = \beta\hat{\mathbf{r}}$, and due to the linear nature in projecting the estimator (see Algorithm 4), we have the null and alternative hypotheses:

$$H_0 : \text{The estimator } \hat{\mathbf{r}} \text{ is unbiased } \iff \beta = 1$$
$$H_1 : \text{The estimator } \hat{\mathbf{r}} \text{ is biased } \iff \beta \neq 1$$

Therefore, under H_0 :

$$\frac{1}{\sigma^2}(1-\hat{\beta})^\top \hat{\mathbf{r}}^\top \hat{\mathbf{r}}(1-\hat{\beta}) = \sigma^{-2}\hat{\mathbf{r}}^\top \hat{\mathbf{r}}(1-\hat{\beta})^2 \sim \chi_1^2 \text{ where } \hat{\beta} = (\hat{\mathbf{r}}^\top \hat{\mathbf{r}})^{-1}\hat{\mathbf{r}}^\top \mathbf{r}$$

Which gives the Wald's statistic (Wald, 1943):

$$W = (n-1)||(\mathbf{1} - \hat{\mathbf{r}}(\hat{\mathbf{r}}^\top \hat{\mathbf{r}})^{-1}\hat{\mathbf{r}}^\top)\mathbf{r}||^{-2}(\hat{\mathbf{r}}^\top \hat{\mathbf{r}} - \hat{\mathbf{r}}^\top \mathbf{r})^2$$

Applied to the results of our final model, we have the Wald's p-value $\mathbb{P}(\chi_1^2 > W) = 2.983174 \times 10^{-13}$, which provides a very strong evidence for the estimator $\hat{\mathbf{r}}$ being biased. However, a further assessment on the 95% asymptotic confidence interval of β, (0.9521173, 0.9724053), indicates the bias is acceptable.

3 Model evaluation

4 Appendix: model training workflow, code and output

4.1 Source code

The source codes for the functions used in the workflow are in the `.R` files at /R.

4.2 Data wrangling and signal processing

```
training_set <- c("a01", "a02", "a03", "a04", "b01")
test_set <- c("c01", "c02", "c03")
hr <- fuse_data(map(
  sprintf("../data-bin/%s.dat", training_set),
  function(ecg_file) {
    ecg_file |>
      read_ecg() |>
      find_r_peaks() |>
      frequency() |>
      down_sample()
  }
))
resp <- fuse_data(map(
  sprintf("../data-bin/%sr.dat", training_set),
  function(resp_file) down_sample(read_resp(resp_file))
))
hr_test <- fuse_data(map(
  sprintf("../data-bin/%s.dat", test_set),
  function(ecg_file) {
    ecg_file |>
      read_ecg() |>
      find_r_peaks() |>
      frequency() |>
      down_sample()
  }
))
resp_test <- fuse_data(map(
  sprintf("../data-bin/%sr.dat", test_set),
  function(resp_file) down_sample(read_resp(resp_file))
))
write_rds(hr, "../R/hr.rds")
write_rds(resp, "../R/resp.rds")
write_rds(hr_test, "../R/hr-test.rds")
write_rds(resp_test, "../R/resp-test.rds")
```

4.3 Model training

```
hr <- read_rds("../R/hr.rds")
resp <- read_rds("../R/resp.rds")
resp_df <- resp_dataset(hr, resp)
```

```
attributes(resp_df)$opt_lambda
```

```
#>   opt_lambda
#> 1.571851e-06
```

```
resp_df
```

```
#> # A tibble: 2,526 x 2
#>    breath_chest breath_ecg
#>  *        <dbl>      <dbl>
#>  1         19.5       15
#>  2         22.5       16
#>  3         23.5       17.5
#>  4         20.5       18
#>  5         20.5       18
#>  6         23         15
#>  7         16         18
#>  8         20         21.5
#>  9         20         17.5
#> 10         18         16.5
#> # i 2,516 more rows
```

```
summary(resp_df)
```

```
#>   breath_chest     breath_ecg
#>  Min.   : 5.50   Min.   :11.50
#>  1st Qu.:15.00   1st Qu.:17.50
#>  Median :18.50   Median :19.00
#>  Mean   :18.46   Mean   :18.96
#>  3rd Qu.:21.38   3rd Qu.:20.50
#>  Max.   :29.00   Max.   :26.50
```

4.4 Model diagnostics

```
c("R-F cor" = with(resp_df, cor(breath_chest - breath_ecg, breath_ecg)))
```

```
#>    R-F cor
#> -0.3976376
```

```
test <- lm(breath_chest ~ 0 + breath_ecg, resp_df)
c("p-value" = unname(pchisq(
  sum(resp_df$breath_ecg^2) * (coef(test) - 1)^2 *
    (nrow(resp_df) - 1) / sum(residuals(test)^2), 1,
  lower.tail = FALSE
)))
```

```
#>      p-value
#> 2.983174e-13
```

```
confint(test)
```

```
#>                2.5 %    97.5 %
#> breath_ecg 0.9521173 0.9724053
```

4.5 Model evaluation

```
hr_test <- read_rds("../R/hr-test.rds")
resp_test <- read_rds("../R/resp-test.rds")
resp_dt <- resp_dataset(hr_test, resp_test, 1.571851e-06)
c("RMSEP" = with(resp_dt, sqrt(mean((breath_chest - breath_ecg)^2))))
```

```
#>    RMSEP
#> 5.489861
```

References

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