## Supplementary Material

## A lightweight learning-based decoding algorithm for intraneural vagus nerve activity classification in pigs

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|       | RRC15 | TVC125% | RRC20 | TVC200% |
|-------|-------|---------|-------|---------|
| p2-t2 | x     | x       |       |         |
| p3-s1 |       |         | X     | x       |
| p4-s3 |       |         | X     | x       |
| p4-s4 |       |         | X     | x       |
| p5-t3 | Х     | x       |       |         |
| p5-t4 | Х     | x       |       |         |
| p6-t5 | Х     | х       |       |         |
| p6-t6 | Х     | Х       |       |         |

Figure S1: Information about which animals underwent which physiological challenges. The Blood Pressure Challenge is not listed because it was the same for all animals. RRC = Respiratory Rate Challenge; TVC = Tidal Volume Challenge.

Table S1: Median,  $1^{st}$  and  $3^{rd}$  quartiles of the SVM classifier across the 10 folds for all animals when using  $w_s=500~{\rm ms}$ 

|                                | p2-t2              | p3-s1              | p4-s3                 | p4-s4              |
|--------------------------------|--------------------|--------------------|-----------------------|--------------------|
| Median (%)                     | 100.0              | 88.84              | 98.61                 | 82.96              |
| 25th percentile (%)            | 99.58              | 85.36              | 96.63                 | 79.81              |
| 75th percentile (%)            | 100.0              | 91.86              | 99.47                 | 85.84              |
|                                |                    |                    |                       |                    |
|                                | p5-t3              | p5-t4              | p6-t5                 | p6-t6              |
| Median (%)                     | <b>p5-t3</b> 63.48 | <b>p5-t4</b> 72.18 | <b>p6-t5</b><br>85.69 | <b>p6-t6</b> 82.43 |
| Median (%) 25th percentile (%) |                    |                    |                       |                    |

Table S2: Median,  $1^{st}$  and  $3^{rd}$  quartiles of the MLP classifier across the 10 folds for all animals when using  $w_s = 500$  ms

|                                | p2-t2              | p3-s1                          | p4-s3              | p4-s4              |
|--------------------------------|--------------------|--------------------------------|--------------------|--------------------|
| Median (%)                     | 100.0              | 84.5                           | 99.79              | 81.87              |
| 25th percentile (%)            | 99.79              | 81.28                          | 98.91              | 78.67              |
| 75th percentile (%)            | 100.0              | 85.87                          | 100.0              | 84.31              |
|                                |                    |                                |                    |                    |
|                                | p5-t3              | $\mathbf{p}$ 5- $\mathbf{t}$ 4 | p6-t5              | p6-t6              |
| Median (%)                     | <b>p5-t3</b> 84.09 | <b>p5-t4</b> 77.53             | <b>p6-t5</b> 86.32 | <b>p6-t6</b> 82.87 |
| Median (%) 25th percentile (%) |                    |                                |                    |                    |

Table S3: Median,  $1^{st}$  and  $3^{rd}$  quartiles of the KNN classifier across the 10 folds for all animals when using  $w_s = 500$  ms

|                                | p2-t2              | p3-s1             | p4-s3              | p4-s4              |
|--------------------------------|--------------------|-------------------|--------------------|--------------------|
| Median (%)                     | 97.07              | 77.14             | 85.59              | 64.54              |
| 25th percentile (%)            | 96.74              | 75.55             | 82.36              | 62.41              |
| 75th percentile (%)            | 98.64              | 80.26             | 88.67              | 65.08              |
|                                |                    |                   |                    |                    |
|                                | p5-t3              | p5-t4             | p6-t5              | p6-t6              |
| Median (%)                     | <b>p5-t3</b> 37.91 | <b>p5-t4</b> 31.8 | <b>p6-t5</b> 65.27 | <b>p6-t6</b> 68.09 |
| Median (%) 25th percentile (%) |                    |                   |                    |                    |

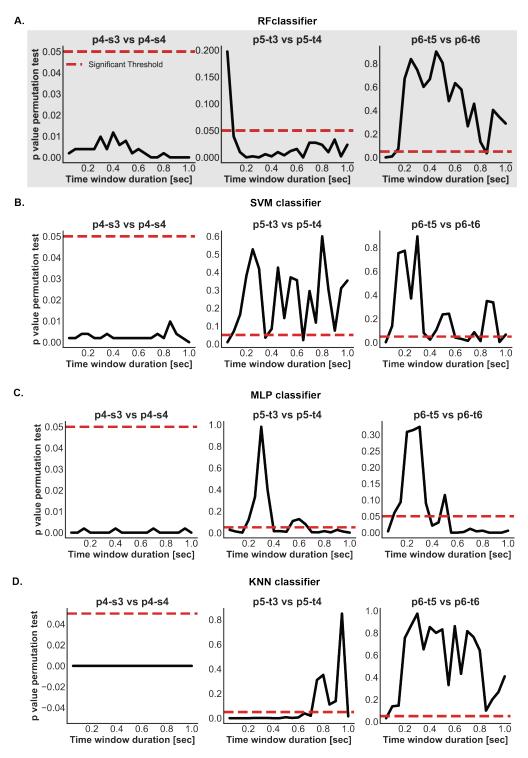
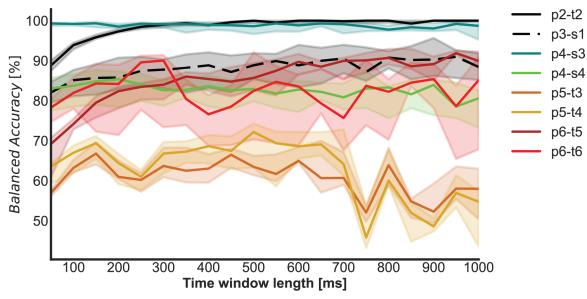


Figure S2: Results of the permutation test performed for all models tested, for each animal being implanted with two different electrodes, and for each time window investigated (values ranging from 50 ms to 1 sec with steps of 50 ms): **A.** Random Forest, **B.** Support Vector Machines, **C.** Multi Layer Perceptron, and **D.** K-Nearest Neighbors. The faded gray area in **A.** indicates that RF was the model we first selected for the classification task. The dashed line represents the significant threshold set at  $\alpha = 0.05$ . The number of permutations was 1024.





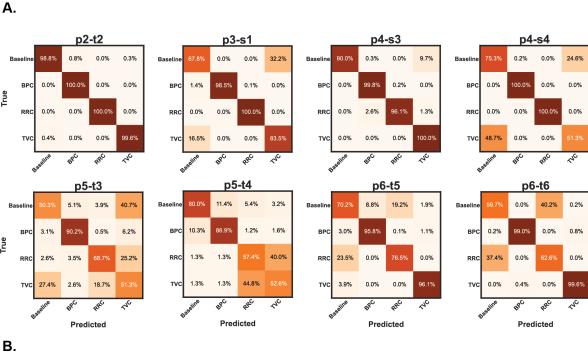
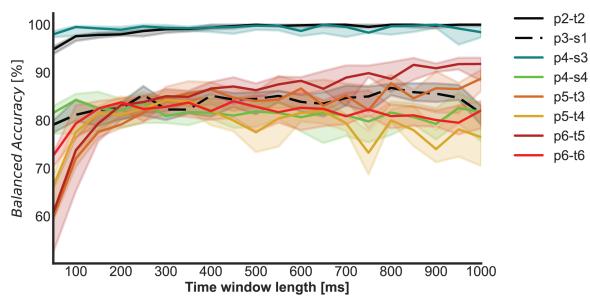


Figure S3: Overall classification results obtained with a SVM classifier. **A:** Balanced Accuracy obtained by the SVM classifier for each animal and for each time window tested. The duration of the time windows extracted from the signals was incremented by 50 ms starting from an initial duration of 50 ms and reaching a final duration of 1 second. A constant overlap of 20% between consecutive time windows was used. Bold lines indicate median performance, while the faded colored area spans the range from the  $1^{st}$  to the  $3^{rd}$  quartiles across the 10 test folds. **B:** Confusion matrices for all 4 classes and for each animal indicating the performance of the SVM model when using time windows of 500 ms (with an overlap of 100 ms). Each confusion matrix is the average across the 10 test folds of the Nested Cross-Validation. Values are reported in percentages and are normalized per row (true class).





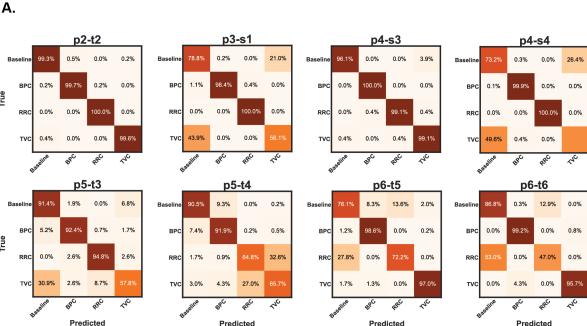
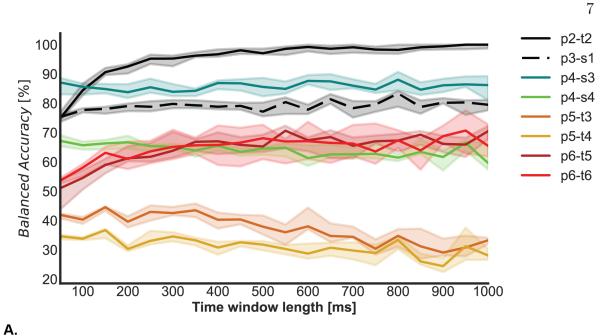


Figure S4: Overall classification results obtained with a MLP classifier. **A:** Balanced Accuracy obtained by the MLP classifier for each animal and for each time window tested. The duration of the time windows extracted from the signals was incremented by 50 ms starting from an initial duration of 50 ms and reaching a final duration of 1 second. A constant overlap of 20% between consecutive time windows was used. Bold lines indicate median performance, while the faded colored area spans the range from the  $1^{st}$  to the  $3^{rd}$  quartiles across the 10 test folds. **B:** Confusion matrices for all 4 classes and for each animal indicating the performance of the MLP model when using time windows of 500 ms (with an overlap of 100 ms). Each confusion matrix is the average across the 10 test folds of the Nested Cross-Validation. Values are reported in percentages and are normalized per row (true class).

В.



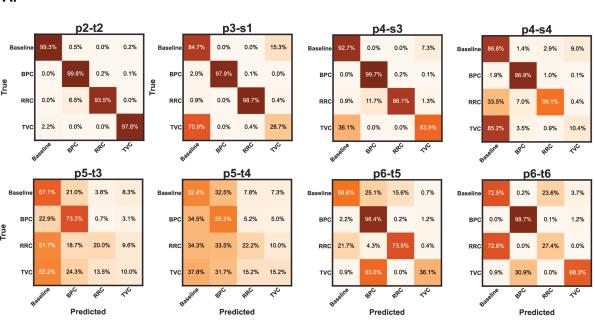


Figure S5: Overall classification results obtained with a KNN classifier. **A:**  $Balanced\ Accuracy$  obtained by the KNN classifier for each animal and for each time window tested. The duration of the time windows extracted from the signals was incremented by 50 ms starting from an initial duration of 50 ms and reaching a final duration of 1 second. A constant overlap of 20% between consecutive time windows was used. Bold lines indicate median performance, while the faded colored area spans the range from the  $1^{st}$  to the  $3^{rd}$  quartiles across the 10 test folds. **B:** Confusion matrices for all 4 classes and for each animal indicating the performance of the KNN model when using time windows of 500 ms (with an overlap of 100 ms). Each confusion matrix is the average across the 10 test folds of the Nested Cross-Validation. Values are reported in percentages and are normalized per row (true class).

В.

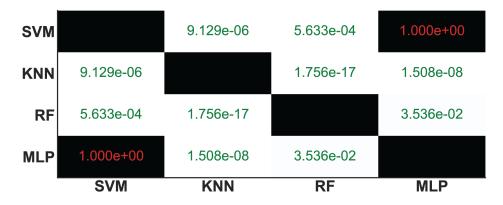


Figure S6: Results from the Dunn's post-hoc tests following the Kruskal-Wallis one-way analysis of variance test. p-values were corrected via the Bonferroni correction. Each group (model) contained 80 measures corresponding to the 10 test folds of the Nested Cross-Validation  $\times$  8 animals. Green values indicate the rejection of the null hypothesis, while red one its acceptance if considering a significant threshold of  $\alpha$ = 0.05.

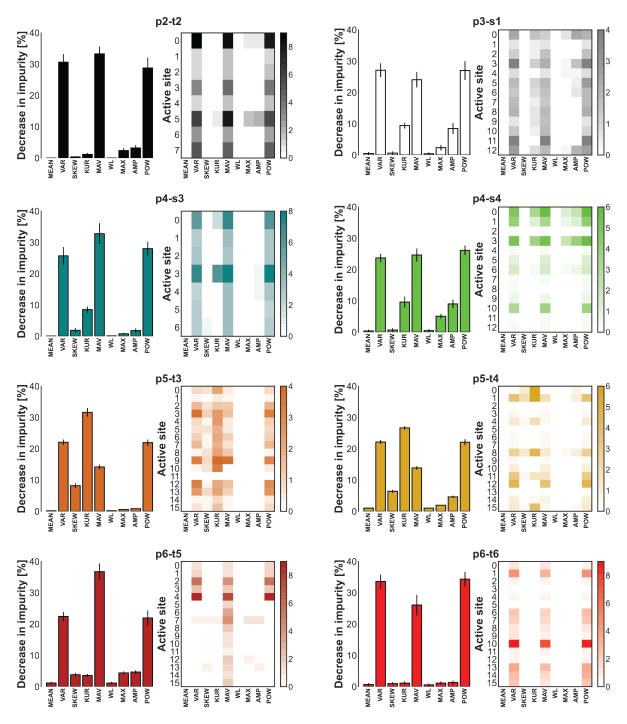


Figure S7: Relative features importance shown for each animal. The bar-plots represent the decrease in impurity of each feature computed as the sum over the active sites then averaged across the 10 test folds. Error-bars indicate standard deviation. The heat maps represent the relative importance of each feature across the different active sites.

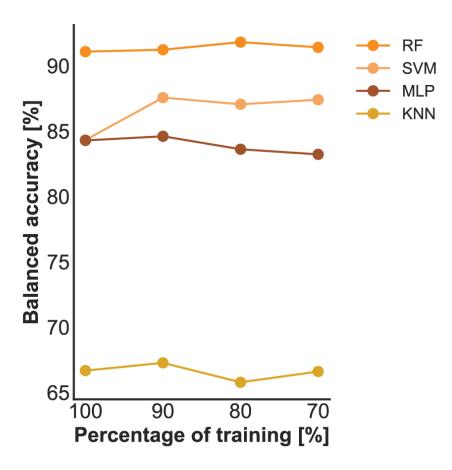


Figure S8: Grand median performance (median of the median performance for each animal across the 10 test folds) of the 4 classification models we investigated versus the amount of time windows we kept in the training set. Time windows were selected randomly in the training set at each fold.