## Code demonstration

# Title: 3D printed biomimetic cochleae and machine learning co-modelling provides clinical informatics for cochlear implant patients

## Authors

Iek Man Lei[1,2], Chen Jiang[3,1], Chon Lok Lei[4,5], Simone Rosalie de Rijk[3], Yu Chuen Tam[6], Chloe Swords[7], Michael P.F. Sutcliffe[1], George G. Malliaras[1], Manohar Bance[3,*], Yan Yan Shery Huang[1,2,*]

## Affiliations

*[1]Department of Engineering, University of Cambridge, United Kingdom*

*[2]The Nanoscience Centre, University of Cambridge, United Kingdom*

*[3]Department of Clinical Neurosciences, University of Cambridge, United Kingdom*

*[4]Institute of Translational Medicine, Faculty of Health Sciences, University of Macau, Macau*

*[5]Department of Computer Science, University of Oxford, United Kingdom*

*[6]Emmeline Centre for Hearing Implants, Addenbrookes Hospital, Cambridge, United Kingdom*

*[7]Department of Physiology, Development and Neurosciences, Cambridge, United Kingdom*

* Corresponding authors: yysh2@cam.ac.uk and mlb59@cam.ac.uk. These authors jointly supervised this work.

## 1. Installation

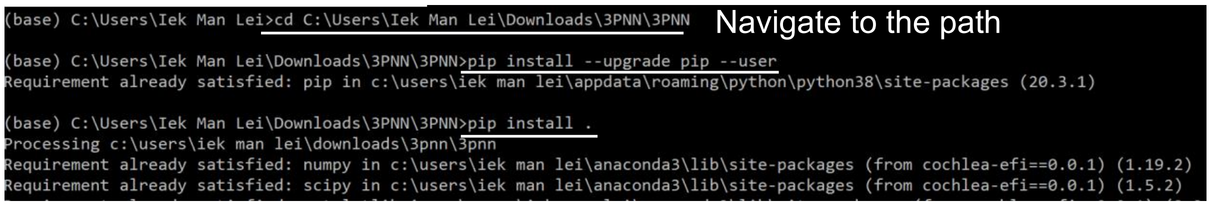
This document provides instructions to use the code with windows 10. It contains instructions to install the code, train a neural network model, and perform forward and inverse predictions. The command could be slightly different on Linux or Mac or on a different python IDE. If python and git are not installed on your device, install anaconda (Python 3.7.6 -64bit) and git. Microsoft Visual C++ Redistributable for Visual Studio 2015, 2017 and 2019 is also required for running tensorflow.

Other versions of python might have compatibility issue with tensorflow. Run the following to change the python version to 3.7.6 on Anaconda prompt if other version was installed.

```
conda install python=3.7.6
```

The code requires Python (3.7.6) and the following dependencies: PINTS, scikit-learn, joblib, tensorflow (2.2). It also needs seaborn for plotting. To install the code and the relevant dependencies, unzip the folder, launch anaconda prompt, navigate to the path of the folder, and run the following:

```
pip install --upgrade pip --user
pip install .
```



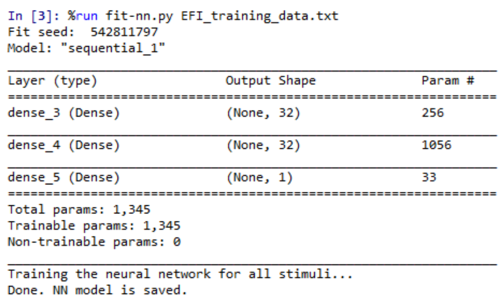
```
(base) C:\Users\Iek Man Lei>cd C:\Users\Iek Man Lei\Downloads\3PNN\3PNN

(base) C:\Users\Iek Man Lei\Downloads\3PNN\3PNN>pip install --upgrade pip --user
Requirement already satisfied: pip in c:\users\iek man lei\appdata\roaming\python\python38\site-packages (20.3.1)

(base) C:\Users\Iek Man Lei\Downloads\3PNN\3PNN>pip install .
Processing c:\users\iek man lei\downloads\3pnn\3pnn
Requirement already satisfied: numpy in c:\users\iek man lei\anaconda3\lib\site-packages (from cochlea-efi==0.0.1) (1.19.2)
Requirement already satisfied: scipy in c:\users\iek man lei\anaconda3\lib\site-packages (from cochlea-efi==0.0.1) (1.5.2)
```

'Successfully installed….' will be printed when it is done. The total install time is around 20min on a normal computer. All the expected output in this demo can be found in `'demo_expected_output'` folder.

## 2. Create NN model using experimental EFI data

Demo To generate the NN model using the experimental EFI data obtained in this study, launch Spyder (Spyder IDE is installed by default with the Anaconda package) or any python IDE, navigate to the path of the main folder, and run the following line.

```
%run fit-nn.py EFI_training_data.txt
```



```
In [3]: %run fit-nn.py EFI_training_data.txt
Fit seed:  542811797
Model: "sequential_1"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
dense_3 (Dense)              (None, 32)                256
_________________________________________________________________
dense_4 (Dense)              (None, 32)                1056
_________________________________________________________________
dense_5 (Dense)              (None, 1)                 33
=================================================================
Total params: 1,345
Trainable params: 1,345
Non-trainable params: 0
_________________________________________________________________
Training the neural network for all stimuli...
Done. NN model is saved.
```

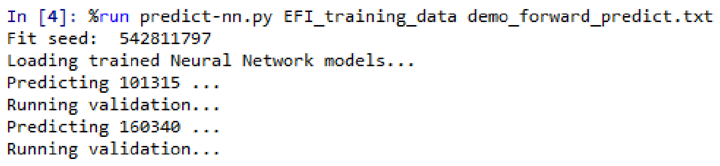
The run time is around 30min. A NN model file ‘`nn-EFI_training_data-stim_all.h5`’ will be saved in ‘`out-nn`’ folder after running.

Details Run `fit-nn.py` with argument `[str:input_file.txt]`. `input_file.txt` containing a list of file IDs as training data. The file IDs of our training dataset are listed in `EFI_training_data.txt`, which contains 82 experimental file IDs of our 3D printed biomimetic cochleae. All experimental EFI data are stored in ‘`data`’ folder, and the input parameters (model descriptors) of each experimental EFI data are stored in ‘`input`’ folder with the same file ID as the EFI data. The format of the inputs should be listed in a column format [p0; p1; p2; p3; p4], where p0 = basal lumen diameter (mm), p1 = infill density (%), p2 = taper ratio, p3 = cochlear width (mm) and p4 = cochlear height (mm). For more instructions, see ‘`README.txt`’ in ‘`input`’ folder. ‘`available-electrodes.csv`’ in ‘`data`’ folder specifies the available electrodes in each EFI measurement, with ‘1’=available and ‘0’=unavailable. By default, position information of Advanced Bionics 1J electrode array is used here. Electrode position can be specified in line 71 in `fit-nn.py` if other cochlear implant is used;

## 3. Perform forward predictions with the trained NN model

Demo `predict-nn.py` performs predictions of EFI based on input parameters. The trained NN model created in the above step with the name ‘`EFI_training_data`’ is used in this demo. A txt file ‘`demo_forward_predict.txt`’ can be found in the main folder, which contains two `predict_ids` (101315 & 160340) for EFI predictions. Run the following line:

```
%run predict-nn.py EFI_training_data demo_forward_predict.txt
```



```
In [4]: %run predict-nn.py EFI_training_data demo_forward_predict.txt
Fit seed:  542811797
Loading trained Neural Network models...
Predicting 101315 ...
Running validation...
Predicting 160340 ...
Running validation...
```

The run time is around 2 s for each prediction. Predicted EFIs with the file name (‘`id_101315-efi.csv`’ and ‘`id_160340-efi.csv`’) can be found in ‘`./out-nn/EFI-training_data-predict`’ folder. ‘`id_101315-simple-plot.png`’ and ‘`id_160340-simple-plot.png`’ compare the predicted EFI and the experimental EFI.

Details Run `predict-nn.py`, with argument `[str:nn_name]` and `[str:predict_ids.txt]`. `'nn_name'` is the name of the trained NN model, which is `EFI_training_data` in this demo. `‘predict_ids.txt'` contains a list of file IDs (`predict_ids`) for prediction. The input parameters of the prediction file IDs should be stored in the `‘input’` folder. Again, by default, position information of 1J electrode array is used here. Electrode position can be specified in line 77-80 in `predict-nn.py` if other cochlear implant is used. `‘id_predict_id-efi.csv’`, which contains the EFI profile, will be saved in `‘./out-nn/nn_name-predict’`

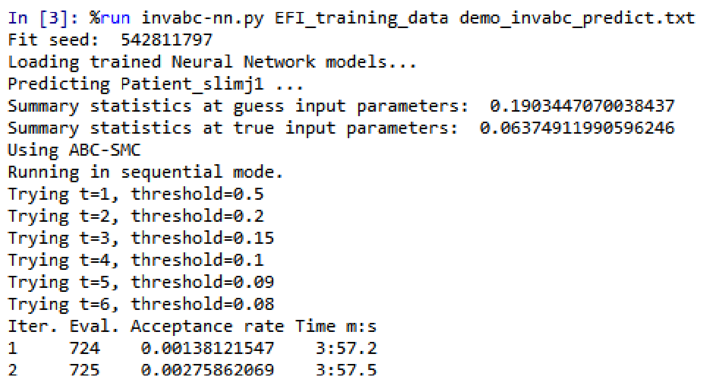
## 4. Perform inverse predictions with the trained NN model

Demo `invabc-nn.py` predicts a posterior distribution of the input parameters (model descriptors) that satisfies a threshold defined by the user best-fitting the EFI data. It allows predictions when all input parameters are unknown (4.1) or when some of the input parameters are known (4.2). Again, the trained NN model `‘EFI_training_data’` is used here. `demo_forward_predict.txt` contains a slimJ patient file ID `(patient_slimj1)` for this inverse prediction demonstration.

### *4.1 Prediction of input parameters with unknown cochlear geometrical features and resistivity*

Demo Run the following line. A final MAPE of 8% is used here (the MAPE threshold can be defined in line 254.

```
%run invabc-nn.py EFI_training_data demo_invabc_predict.txt
```

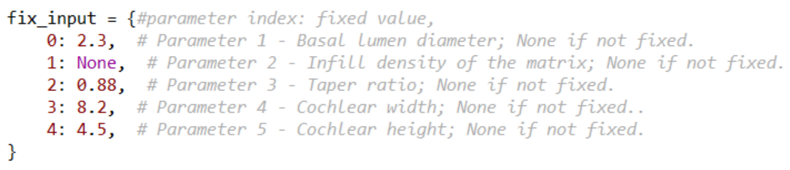


```
In [3]: %run invabc-nn.py EFI_training_data demo_invabc_predict.txt
Fit seed:  542811797
Loading trained Neural Network models...
Predicting Patient_slimj1 ...
Summary statistics at guess input parameters:  0.1903447070038437
Summary statistics at true input parameters:  0.06374911990596246
Using ABC-SMC
Running in sequential mode.
Trying t=1, threshold=0.5
Trying t=2, threshold=0.2
Trying t=3, threshold=0.15
Trying t=4, threshold=0.1
Trying t=5, threshold=0.09
Trying t=6, threshold=0.08
Iter. Eval. Acceptance rate Time m:s
1     724    0.00138121547    3:57.2
2     725    0.00275862069    3:57.5
```

‘Done’ will be printed to the console when it is finished. The outputs are saved in `'./out-nn/EFI_training_data-inv-predict'` folder. The 1000 combinations of the predicted input parameters are listed in `‘id_Patient_slimj1-samples.csv’`, with p1 (infill density) converted to resistivity.

## *4.2 Prediction of resistivity (infill density) with known cochlear geometrical features*

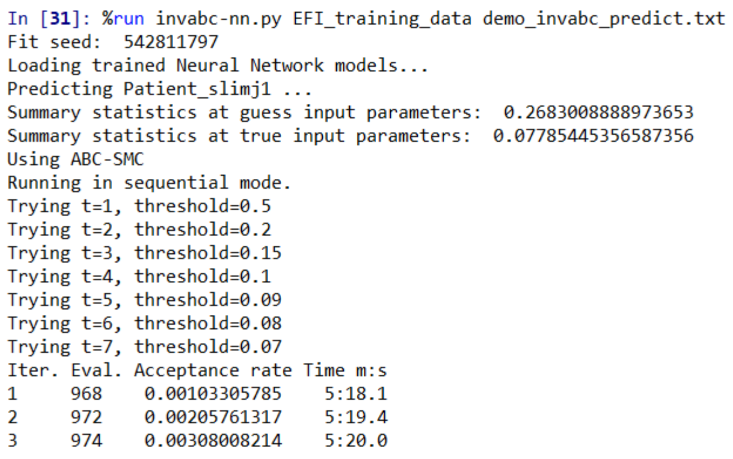
Demo Specify the fixed parameters in ‘`fix_param.py`’. For instance, `patient_slimj1` has cochlear geometric features of basal lumen diameter (p0) = 2.3 mm, taper ratio (p2) = 0.88, cochlear width (p3) = 8.2 mm and cochlear height (p4) = 4.5 mm. The fixed values are specified as below in ‘`fix_param.py`’ with `None` in p1 because infill density (resistivity) is unknown.



```
fix_input = {#parameter index: fixed value,
    0: 2.3,  # Parameter 1 - Basal lumen diameter; None if not fixed.
    1: None,  # Parameter 2 - Infill density of the matrix; None if not fixed.
    2: 0.88,  # Parameter 3 - Taper ratio; None if not fixed.
    3: 8.2,  # Parameter 4 - Cochlear width; None if not fixed..
    4: 4.5,  # Parameter 5 - Cochlear height; None if not fixed.
}
```

A MAPE of 7% is used here (by changing line 254) and run the following line:

```
%run invabc-nn.py EFI_training_data demo_invabc_predict.txt
```



```
In [31]: %run invabc-nn.py EFI_training_data demo_invabc_predict.txt
Fit seed:  542811797
Loading trained Neural Network models...
Predicting Patient_slimj1 ...
Summary statistics at guess input parameters:  0.2683008888973653
Summary statistics at true input parameters:  0.07785445356587356
Using ABC-SMC
Running in sequential mode.
Trying t=1, threshold=0.5
Trying t=2, threshold=0.2
Trying t=3, threshold=0.15
Trying t=4, threshold=0.1
Trying t=5, threshold=0.09
Trying t=6, threshold=0.08
Trying t=7, threshold=0.07
Iter. Eval. Acceptance rate Time m:s
1      968     0.00103305785     5:18.1
2      972     0.00205761317     5:19.4
3      974     0.00308008214     5:20.0
```

‘Done’ will be printed when it is finished. The run time is around 1 hr for this prediction. Again, the outputs are saved in `'./out-nn/EFI_training_data-inv-predict'` folder. The 1000 predicted values of p1 (infill density) and the converted resistivity can be found in ‘`id_Patient_slimj1-samples.csv`’.

Details Run `invabc-nn.py`, with argument `[str:nn_name]` and `[str:predict_ids.txt]`. `'nn_name'` is the name of the trained NN model, which is `EFI_training_data` in this demo, and ‘`predict_ids.txt`' contains a list of file IDs for prediction. The EFI profiles of the `predict_ids` are stored in the ‘`data`’ folder. MAPE (median absolute percentage error) threshold is defined in line 254 in `invabc-nn.py`, and 1000 samples are drawn from the final posterior distribution to approximate the distribution.