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# Guideline for Lyophilization Model

## Purpose:

This guideline goes over how to implement the lyophilization model using Jupyter Notebooks. In order to implement this code, make sure that you have Anaconda and Jupyter Notebooks installed. You can find a detailed guideline for installation here:

https://nickmccullum.com/python-course/how-to-install-anaconda/

## Code Implementation:

To access the code files, use this GitHub link:

https://github.com/sbadih/LyoModel/tree/main

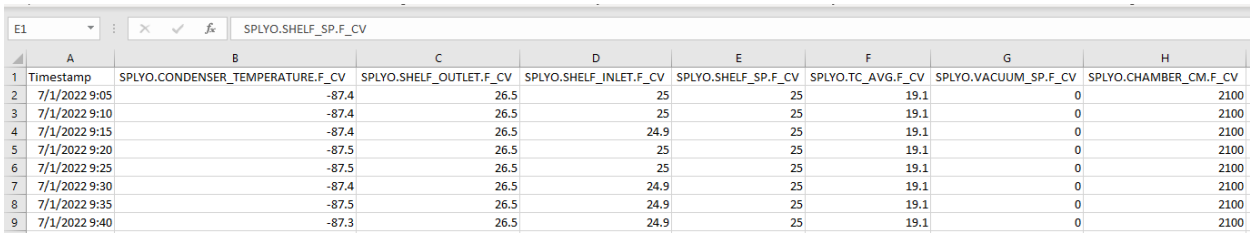
### Section 1:

If you're using this code to find new resistance parameters from experimental data start at **step 1 in this section**. If you only want to use the design space for the F2 formulation start at section 2.

1. **Open the Tchessalov Model-2.0.ipynb file.**
2. **Run the first cell to import all libraries**
   - This cell starts with #Libraries
3. **Run the cell under inputs, Data Loading**
   - You should see a black box asking to input the surface area. Enter a numerical value for the surface area of the vial you're using. Make sure the units are correct. The program will ask for a series of input values. At the end the initial dry cake height will be printed on the screen. Make sure this value makes intuitive sense before moving forward.
   - If you enter a value incorrectly and wish to change it, run the cell again.
4. **Change file path in the Initial Data (SV file) cell.**
   - In order to load the SV file from the lyo cycle run, you need to change the line that says:

     file_location = r'C:\Users\sbadih\OneDrive - Gilead Sciences\Trodelvy 2.0 Modelling Data\GS-0132_F2_LL_SV_mins.xlsx'

   - Insert the correct path to your file in place of the path shown above. Make sure to keep the r'Path' format**. Make sure the SV file has data collected every 5 minutes. Also make sure the file is saved as an excel workbook (.xlsx) and not (.csv). Delete any unnessacry information from the first few rows of the excel sheet and make sure the headers look like this:**



E1 | SPLYO.SHELF_SP.F_CV

| | A | B | C | D | E | F | G | H |
|---|---|---|---|---|---|---|---|---|
| 1 | Timestamp | SPLYO.CONDENSER_TEMPERATURE.F_CV | SPLYO.SHELF_OUTLET.F_CV | SPLYO.SHELF_INLET.F_CV | SPLYO.SHELF_SP.F_CV | SPLYO.TC_AVG.F_CV | SPLYO.VACUUM_SP.F_CV | SPLYO.CHAMBER_CM.F_CV |
| 2 | 7/1/2022 9:05 | -87.4 | 26.5 | 25 | 25 | 19.1 | 0 | 2100 |
| 3 | 7/1/2022 9:10 | -87.4 | 26.5 | 25 | 25 | 19.1 | 0 | 2100 |
| 4 | 7/1/2022 9:15 | -87.4 | 26.5 | 24.9 | 25 | 19.1 | 0 | 2100 |
| 5 | 7/1/2022 9:20 | -87.5 | 26.5 | 25 | 25 | 19.1 | 0 | 2100 |
| 6 | 7/1/2022 9:25 | -87.5 | 26.5 | 25 | 25 | 19.1 | 0 | 2100 |
| 7 | 7/1/2022 9:30 | -87.4 | 26.5 | 24.9 | 25 | 19.1 | 0 | 2100 |
| 8 | 7/1/2022 9:35 | -87.5 | 26.5 | 24.9 | 25 | 19.1 | 0 | 2100 |
| 9 | 7/1/2022 9:40 | -87.3 | 26.5 | 24.9 | 25 | 19.1 | 0 | 2100 |

- Run the cell after the path is adjusted and the headers are in the correct format and you should see the headers of your data pop up as follows:

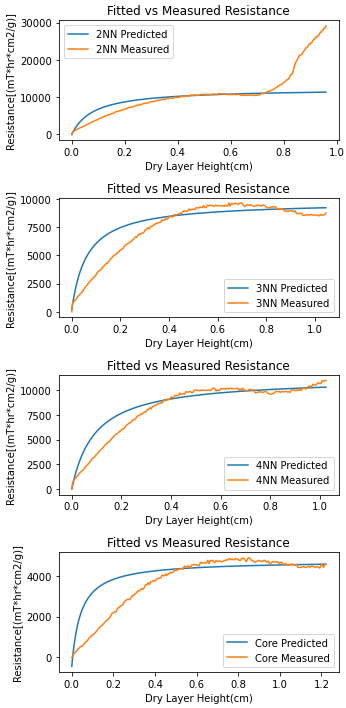
```
['Timestamp', ' SPLYO.CONDENSER_TEMPERATURE.F_CV', ' SPLYO.SHELF_
OUTLET.F_CV', ' SPLYO.SHELF_INLET.F_CV', ' SPLYO.SHELF_SP.F_CV',
' SPLYO.TC_AVG.F_CV', ' SPLYO.VACUUM_SP.F_CV', ' SPLYO.CHAMBER_CM
.F_CV', ' SPLYO.ROUGH_VACUUM.F_CV', ' SPLYO.CHAMBER_PIRANI.F_CV',
' SPLYO.CONDENSER_VACUUM.F_CV']
```

5. **Follow the same steps as step 4 but for the PP file**
   - You should adjust the path where it says file_location1.
   - You should see the following headers pop up:
   -

```
['Timestamp', ' SPLYO.TC01.F_CV', ' SPLYO.TC02.F_CV', ' SPLYO.TC03.F
_CV', ' SPLYO.TC04.F_CV', ' SPLYO.TC05.F_CV', ' SPLYO.TC06.F_CV', '
SPLYO.TC07.F_CV', ' SPLYO.TC08.F_CV', ' SPLYO.TC09.F_CV', ' SPLYO.TC
10.F_CV', ' SPLYO.TC11.F_CV', ' SPLYO.TC12.F_CV', ' SPLYO.TC13.F_CV'
, ' SPLYO.TC14.F_CV', ' SPLYO.TC15.F_CV', ' SPLYO.TC16.F_CV', ' SPLY
O.TC_AVG.F_CV']
```

6. **Click on the Sublimation Pressure text and run all cells below it**
   - To run cells below a cell, click on the Cell icon at the top left then click Run All Below
7. **Enter Kv Value when prompted to.**
8. **Scroll Down to the Very Bottom of the notebook. You should see an output like this:**

```
0
Current Vial Case: 2NN
Parameters for 2NN : [1.16346289e+01 1.50000096e+05 1.21896835e+01]
1
Current Vial Case: 3NN
Parameters for 3NN : [2.18050145e+02 1.50001103e+05 1.56730158e+01]
2
Current Vial Case: 4NN
Parameters for 4NN : [1.79561470e-01 1.20100004e+05 1.07020467e+01]
3
Current Vial Case: core
Parameters for core : [-4.42872347e+02  1.20078699e+05  2.31393004e
+01]
```




At this step you have extracted the resistance parameters to your model.

9. **Open the DryingTime_ProductTemp_Model-2.0.ipynb notebook.**
10. **Run the Libraries cell.**
11. **Copy and Paste your resistance parameters from the previous notebook into the Markdown (text) cell in this notebook under the Resistance Parameters from Resistance Fitting Model header.**
    - This step is only for your reference, it's not necessary.
12. **Under Load Excel Sheet, edit the file_location and file_location2 paths to load the SV and PP files**
    -Make sure your files have data recorded **every hour**
    -Make sure the first row in the excel sheet only has the headers of the file.
    -You should see the headers pop up as the data is loaded.
13. Click on the **Load Parameters** header and run all cells below it.
14. **You will be promoted to enter Surface Area as the first input.**
    -Enter all Inputs until the Dry Cake Initial Height.

15. **Under the Kv and Resistance header, enter the model's parameters**
    - Note: The resistance parameters are the same one's you pasted in **step 11**.
16. Click on the **Iterative OLS …** header, and run all cells below.
17. **Scroll all the way to the end of the notebook, and you should see an output that gives you a prediction of the Drying Time.**
    - Scroll through the code and you should see multiple graph outputs including a graph that has the predicted temperature.
18. Open the **LyoCycle Design Space.ipynb** notebook
19. **Run the libraries cell**

20. Run the cell below the **Model Constant Inputs** header.
21. **When prompted, enter all the inputs requested.**
    -The final output printed on the screen should be the dry cake initial height.

22. Run the cell below **the Iterative Code to Create Design Space** header.
23. **When prompted enter the pressure and temperature ranges of interest along with the sampling rate.**
24. Run the cell below the **Cake Resistance Parameters** header.
25. **When prompted enter the A,B,C parameters for resistance.**
26. **Run the cell under Start Iterations**
    - You should see what pressure/temperature combo the program is currently at and what iteration it's on.
    - This will take a long time to run, just make sure the computer never sleeps to prevent interruptions in the code.
27. **When the iterations are completed, go to the cell under the Save the Output in an Excel Sheet header:**
    - Change the path and file name in the following line:
      df_out.to_csv(r'C:\Users\sbadih\OneDrive - Gilead Sciences\Trodelvy 2.0 Modelling Data\Outputs\Design Space\data_log(Edge)_F4.csv')

28. **Run the cell and you should see an excel sheet saved to the location you specified above. This excel sheet will look like this:**

| | A | B | C | D | E | F |
|---|---|---|---|---|---|---|
| 1 | | Shelf Temperature(C) | Chamber Pressure(mTorr) | Drying Time(Hrs) | Product Temperature(C) | |
| 2 | 0 | -30 | 50 | 76 | -33.57960273 | |
| 3 | 1 | -30 | 55 | 76 | -33.50999198 | |
| 4 | 2 | -30 | 60 | 76 | -33.44038498 | |
| 5 | 3 | -30 | 65 | 76 | -33.37078073 | |
| 6 | 4 | -30 | 70 | 76 | -33.30117741 | |
| 7 | 5 | -30 | 75 | 76 | -33.23157184 | |
| 8 | 6 | -30 | 80 | 76 | -33.16196025 | |
| 9 | 7 | -30 | 85 | 76 | -33.09233814 | |
| 10 | 8 | -30 | 90 | 76 | -33.02270029 | |
| 11 | 9 | -30 | 95 | 76 | -32.95304079 | |

29. **Open the Design Space Fitting and Predictions notebook.**

30. **Under the Load Data section, edit the file_location path to read in the excel sheet you saved in step 28.**

    - You can load data for edge and core cases as needed.
31. **Under surface fitting, run the Edge or Core case and you should see graphs of the design space along with the parameters of the fitted plane and the covariance matrix.**
32. Under the **Predict** header, run either the **Core** or **Edge** cell, and then run either the **Predict Core** or the **Predict Edge** cell.

33. **You should be asked to input a temperature/pressure combination.**
    - The program will print out predicted drying times and product temperatures for either the edge or core cases or both depending on which cells you choose to run.

## Section 2:

**This section is intended for using the design space that was created for the F2 formulation.**

1. Open the Design Space Fitting and Predictions(F2).ipynb notebook
2. Download the following excel sheets from the GitHub page:
    - data_log(Edge)_incr.xlsx
    - data_log(Core)_incr.xlsx
3. Modify the file paths under the **Load Data** section.
4. Under the Cell tab, click Run All
5. Enter the Shelf Temperature and Chamber Pressure of interest when prompted to
6. All outputs should be printed in the Notebook including the design space plots, the design space parameters, and the drying time/product temperature predictions.