

Hands-on Analysis Session

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Measure the dose-response curve of an anti-proliferative drug candidate

In your lab, you are studying the effects of a novel drug that apparently inhibits cell division; from preliminary experiments, this compound appears to be a potential treatment against metastasis in cancer patients. In an experiment, you seeded a constant number of cells (in four replicates) across consecutive wells in a plate and let them proliferate over 48h. In the lab automation facility, you calculated that the **final** cell density after 48h of culture should correspond to **10,240** cells per well (well area is 0.32 cm^2) if the proliferation is **not** hampered by the drug.

At the onset of the experiment, you applied increasing concentrations of the drug and let the cells proliferate in the presence of the compound. Following table shows the drug application protocol: four rows **A** through **D** with each 10 columns **0** through **9** representing **four replicates**.

C [$\mu\text{g}/\mu\text{l}$]	0	1	2	3	4	5	6	7	8	9
A	0	1	2	3	4	5	6	7	8	9
B	0	1	2	3	4	5	6	7	8	9
C	0	1	2	3	4	5	6	7	8	9
D	0	1	2	3	4	5	6	7	8	9

You collected the data on a Nikon Widefield microscope that stored all 40 images for one plate into an individual ND2 file. Please note that the sequential acquisition performed by the microscope followed a snake pattern with **odd rows being scanned left to right and even rows being scanned right to left**. Also, notice that the field of view of your microscope **does not cover the whole well**.

Now that the experimental part is concluded and you have your data, you want to **measure the dose-response curve of your anti-proliferative drug candidate**.

Based on preliminary results from biochemical experiments, you expect to obtain the following relationship between drug concentration and final cell number **per well**:

C [$\mu\text{g}/\mu\text{l}$]	0	1	2	3	4	5	6	7	8	9
Cell count	10240	5120	2560	1280	640	320	160	80	40	20

You can find the dataset on <https://ia-res.ethz.ch/courses/iaf/plate01.zip> → data/hands_on/plate01.zip [2.1 GB].

The dataset is in the Nikon ND2 file format. To read it in your python code, you can use the `NikonND2Reader` class from `iaf.io.readers`.

Your tasks

Day 1

- In a **Jupyter notebook**, write Python code to process all images (wells) in the provided file and export a cell count per series (well).
- Are you getting close to the expected number of cells? If not, why?

Day 2

- In a **Jupyter notebook**, write Python code to import the CSV file and format the data into a matrix Y with 10 columns (one for each concentration of cells) and as many rows as replicates.
- The model that fits the data in the table above should also be valid to describe the cell counts from your data:
 - Use the data in the table above to test your model and get a proper fit.
 - Use the same model **type** (not its parameters!) to fit the data you extracted from your images.
- Is the model from the expected data compatible with the model for the actual image data?
- Try using the standard error of your measurements to weigh the fit.
- Explain any discrepancies of the models fitted to the data in the table above and to your data.