Enabling Reproducible NGS Analysis Through Automated Jupyter Pipelines

Amanda Birmingham

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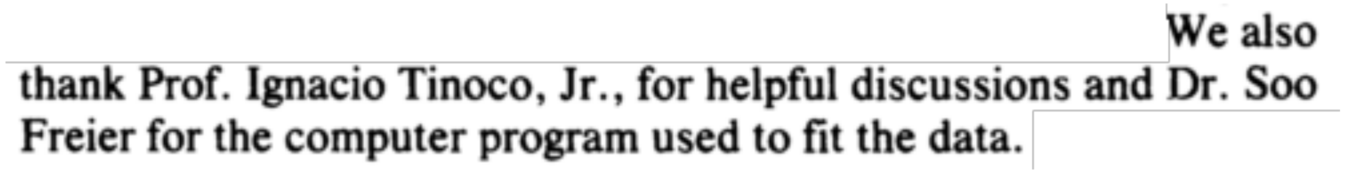
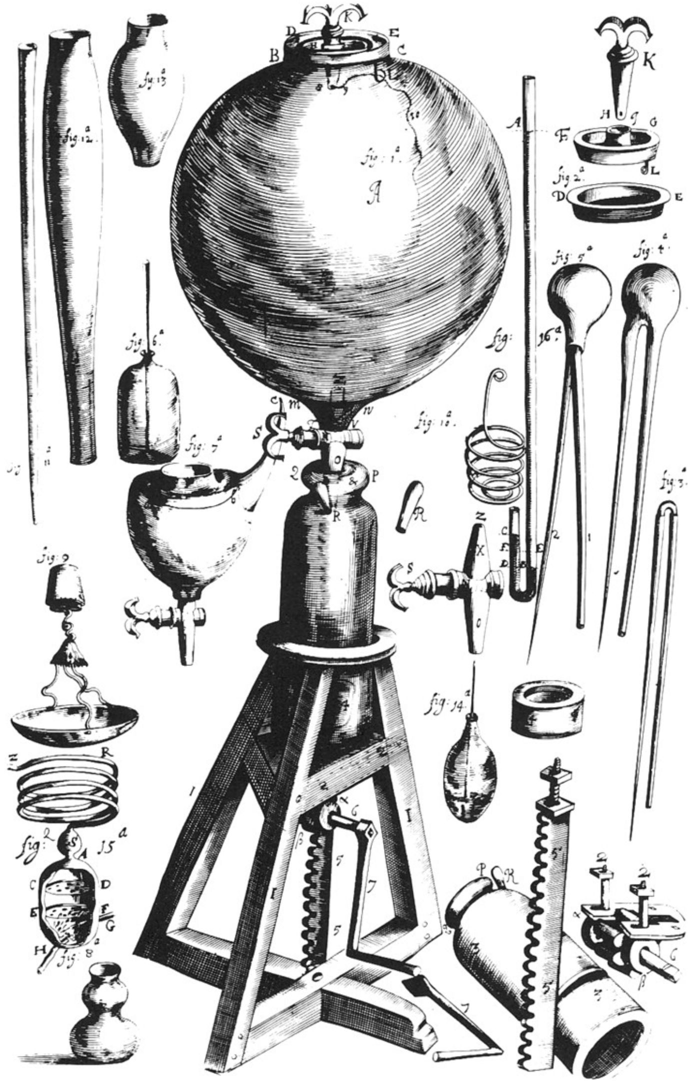
Center for Computational Biology & Bioinformatics, UCSD

Reproducible Research

- Repeatability & reproducibility are key to the scientific method
  - In 1663, only Robert Boyle and Christiaan Huygens could produce a vacuum—and their findings didn't agree
- Informatics *should* be at the forefront of reproducible research
  - Doing the same thing over and over is what computers do best!
  - But has taken a long time for methods reports for computational work to become as good as those for wet lab work
  - Ex: Proc Natl Acad Sci USA. 1986 Jun;83(11):3746-50


We also thank Prof. Ignacio Tinoco, Jr., for helpful discussions and Dr. Soo Freier for the computer program used to fit the data.



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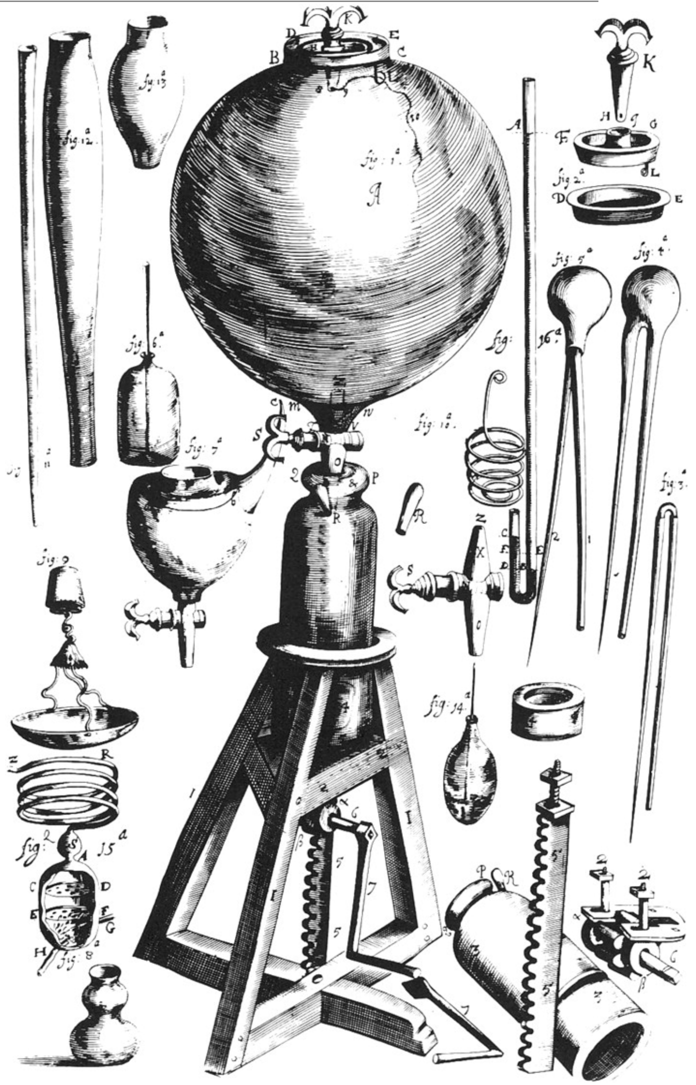
  - But has taken a long time for methods reports for computational work to become as good as those for wet lab work
  - Ex: Proc Natl Acad Sci USA. 1986 Jun;83(11):3746-50
  - Progress:
    - "Alignments were run"
    - "Alignments were run with BLAST"
    - "Alignments were run with BLASTN version 2.2.6 against human"
    - "Alignments were run with NCBI BLASTN v.2.2.9 using the command `blastn -W 7 -q -1 -F F` against the NCBI RefSeq release 80 human transcriptome"
- Parity with wet-lab methods shouldn't be the end of the road!

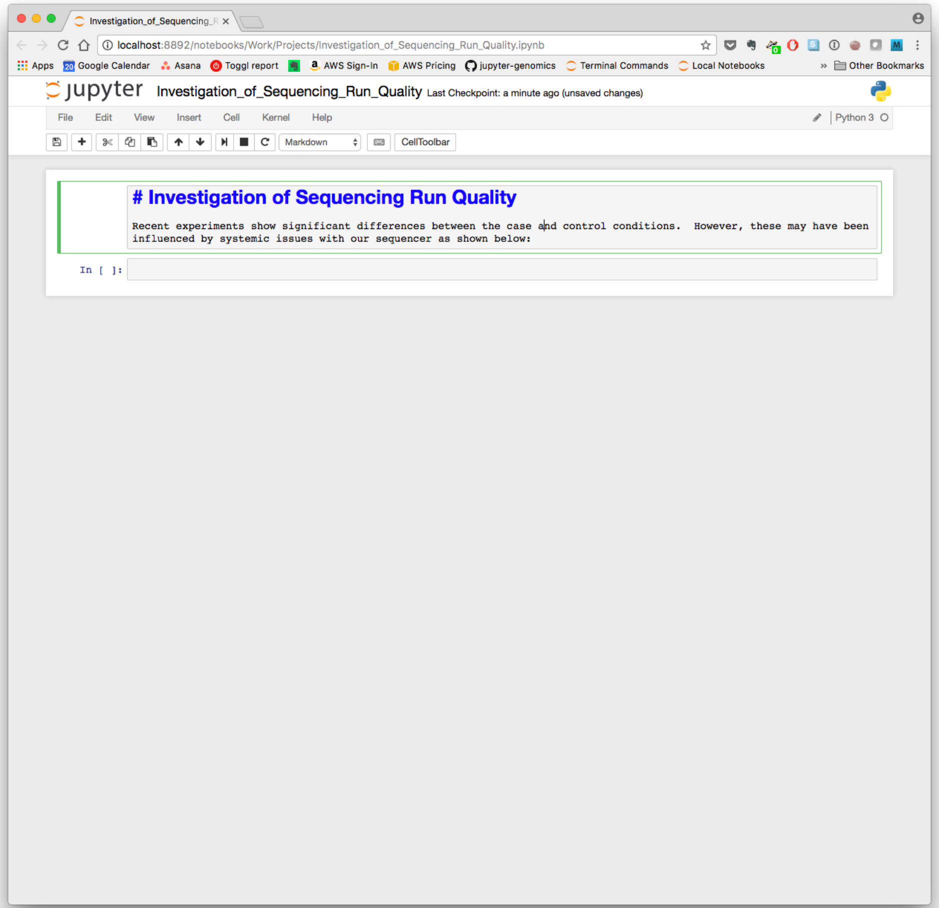


What Is Jupyter?

- What Is Jupyter?
  - "Open source, interactive data science and scientific computing across over 40 programming languages"
    - Grew out of the IPython project, which started in 2001 when Dr. Fernando Perez was procrastinating on his Physics PhD :)
  - A "literate computing" environment, "weaving of a narrative directly into a live computation, interleaving text with code and results to construct a complete piece" --Fernando Perez
- Computing platform is named "jupyter" because early languages were julia, python, and R
  - Community-maintained kernels for other languages: Bash, C, C++, C#, Fortran, Go, Haskell, Javascript, Lisp, Mathematica, Matlab, Perl, PHP, Powershell, Ruby, SAS, Scala, Scheme, and many more
- Most well-known for a web-based "notebook" system
  - Allows writing & running of code from browser environment
  - Can mix in HTML, links, images, interactive controls, extensions

Jupyter logo courtesy of http://jupyter.org/

What *Is* Jupyter, Really?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In [ ]:

```
# Investigation of Sequencing Run Quality

Recent experiments show significant differences between the case and control conditions.  However, these may have been
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```

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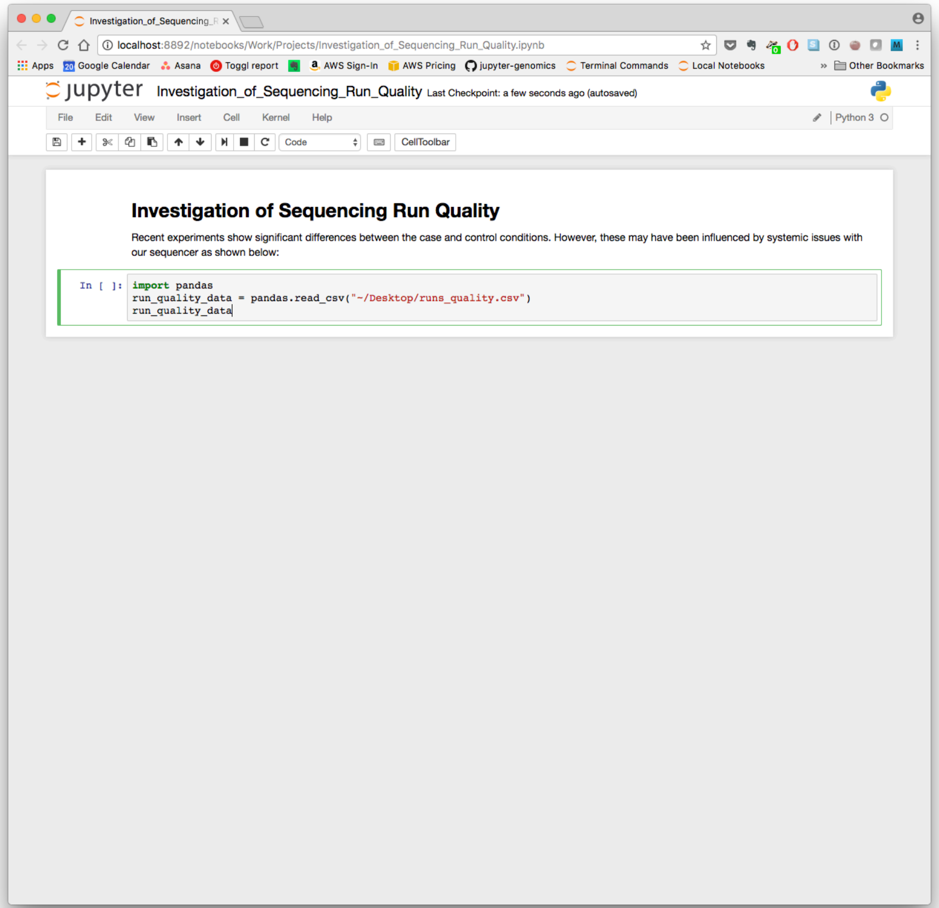
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UC San Diego
SCHOOL OF MEDICINE

CCBB CENTER FOR COMPUTATIONAL BIOLOGY & BIOINFORMATICS

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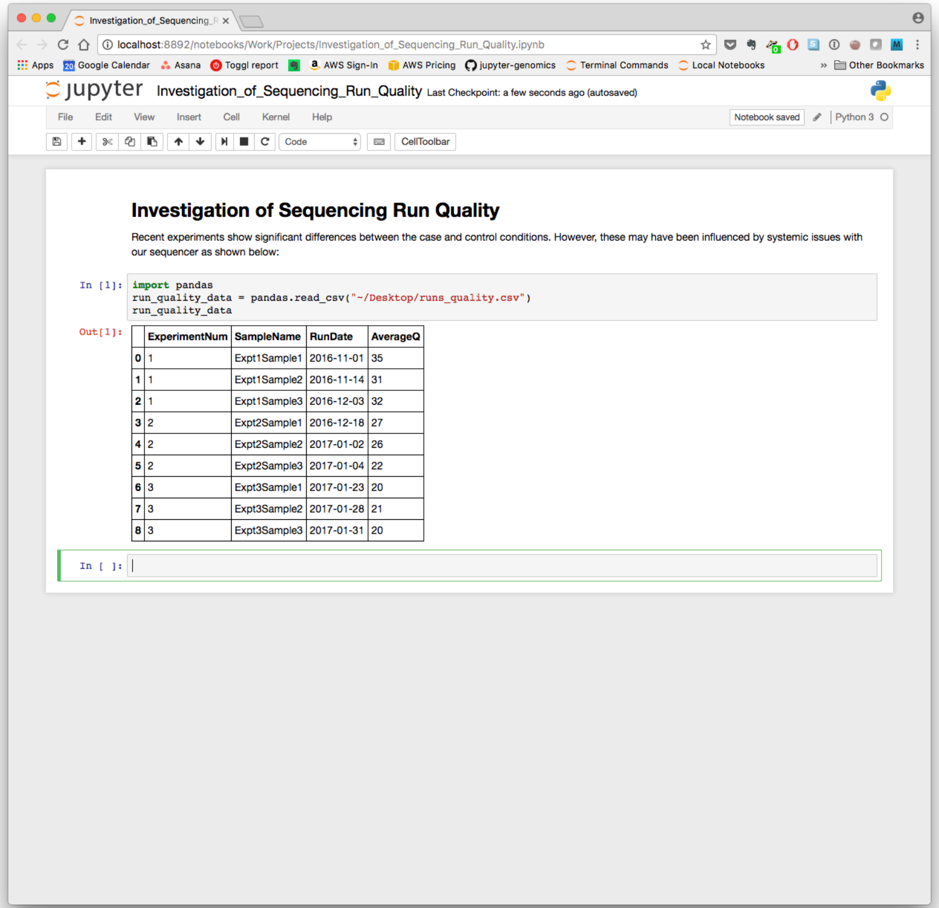
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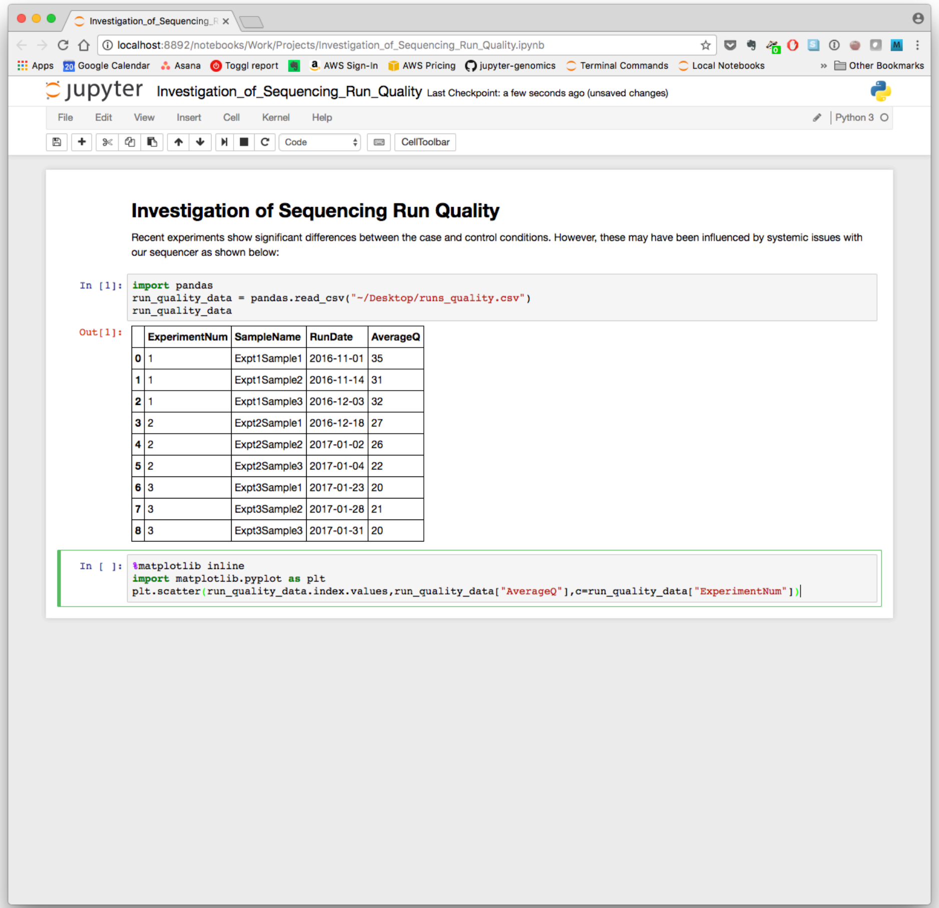
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In [ ]: %matplotlib inline
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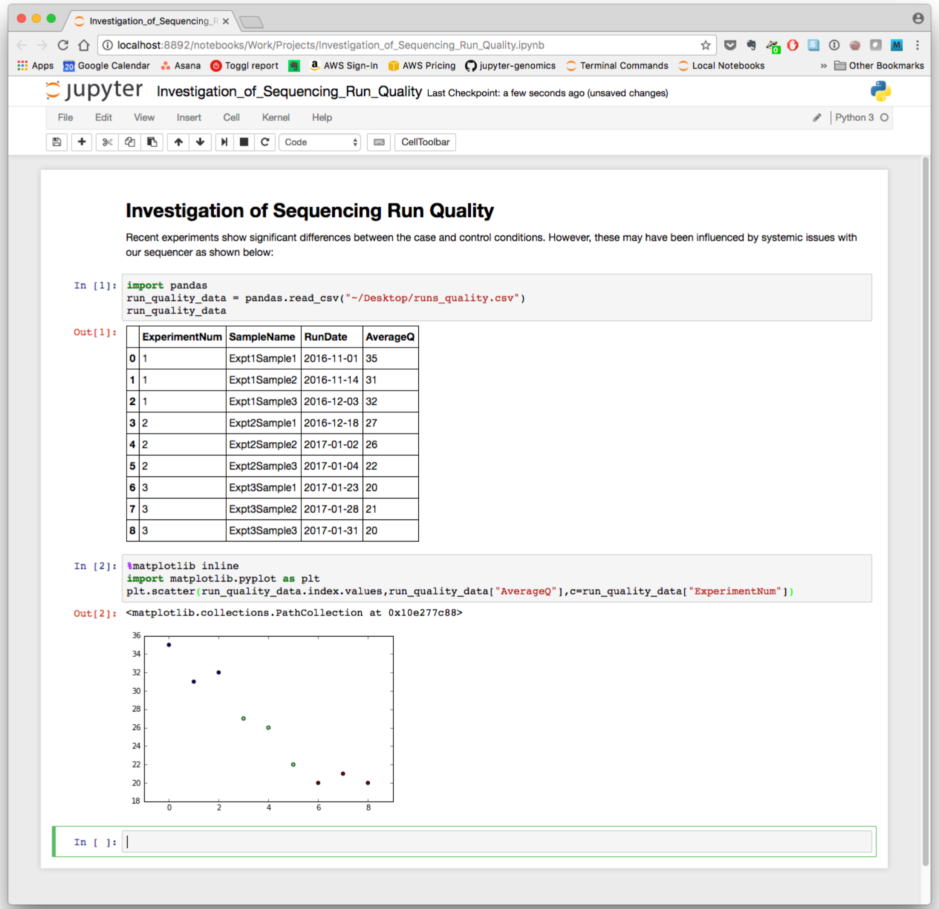
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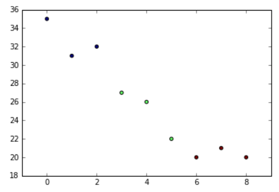

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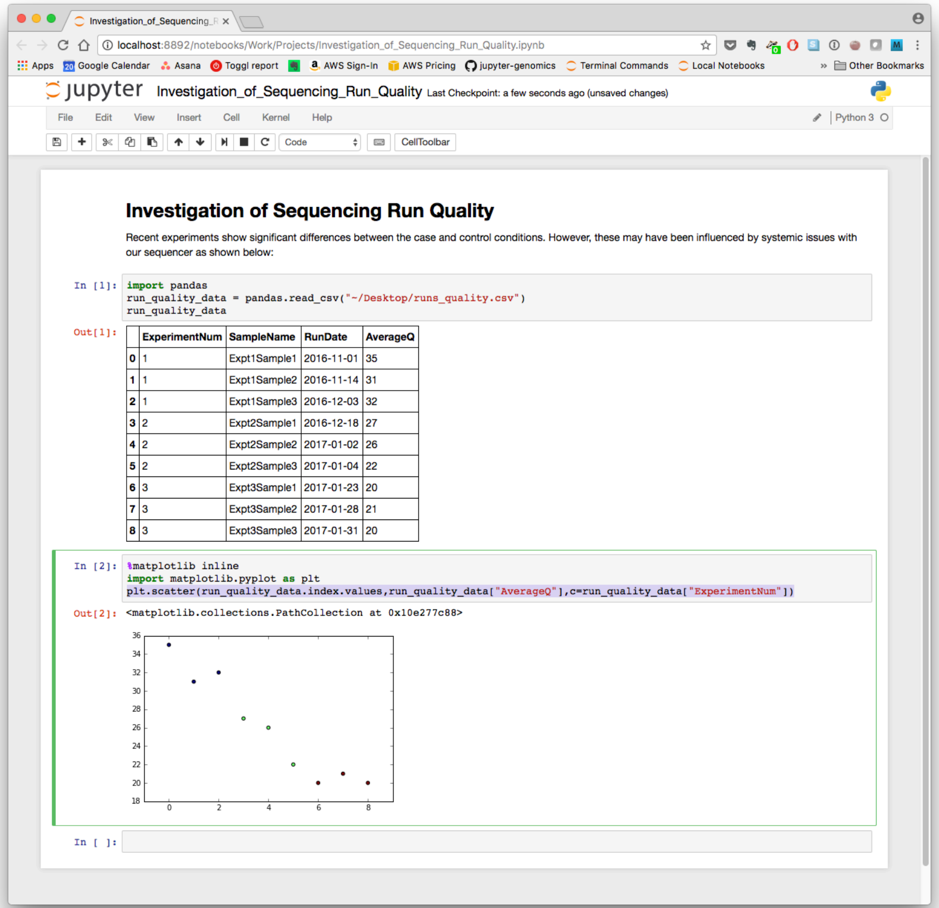

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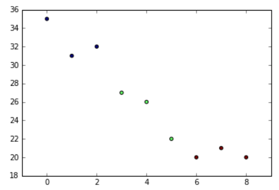

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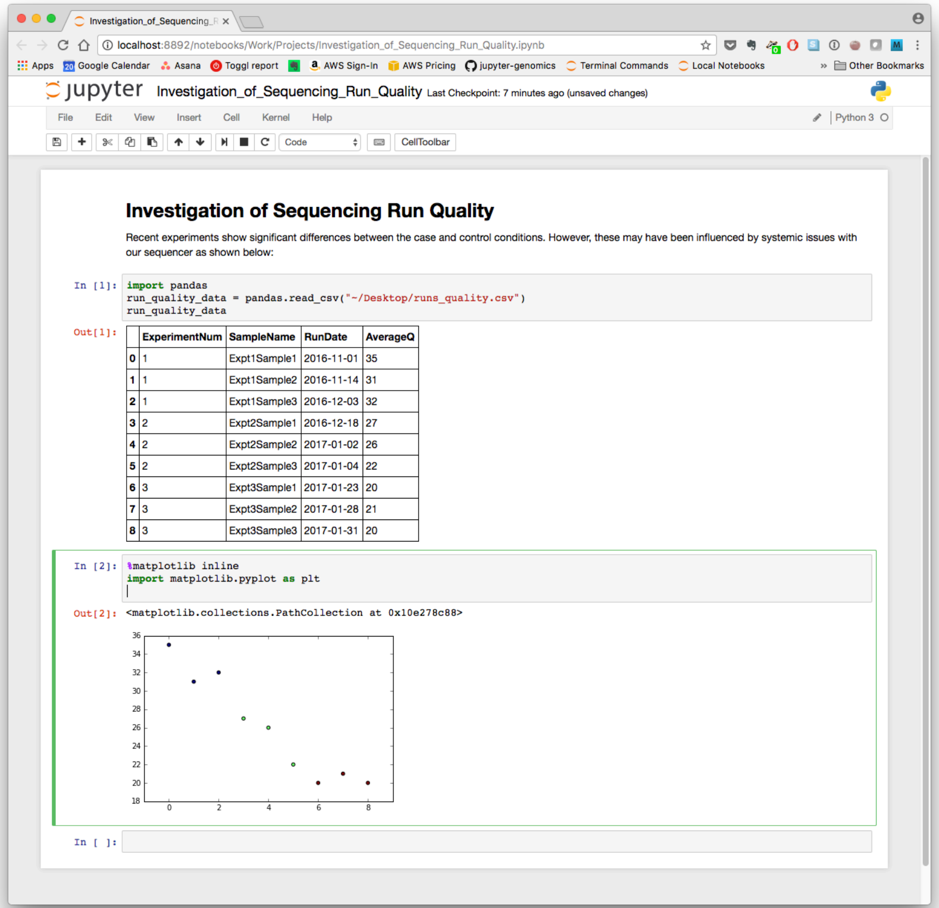
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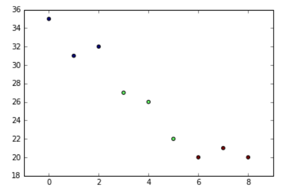

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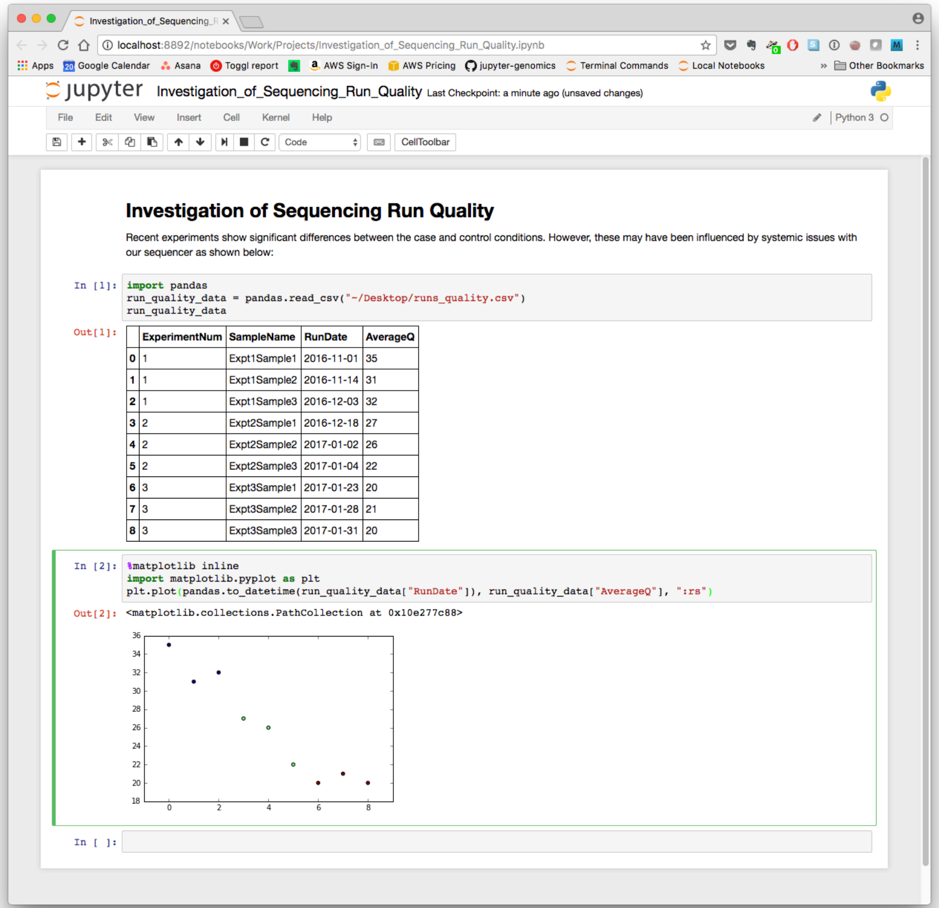
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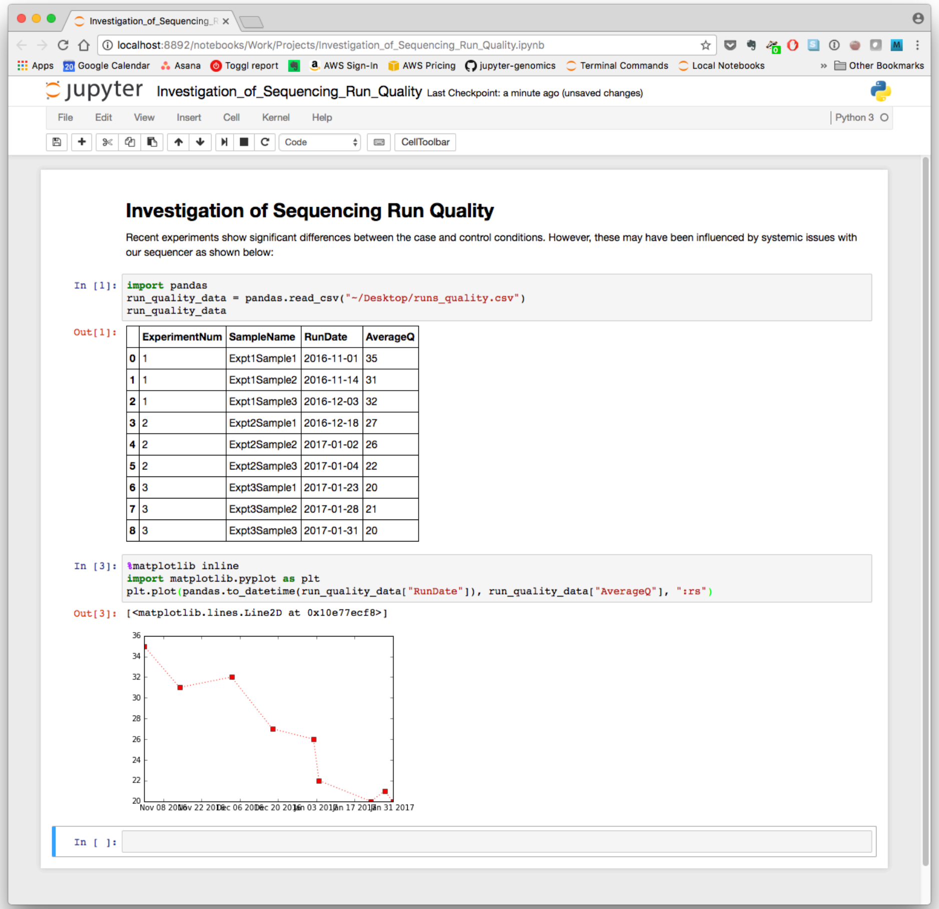
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Out[3]: [<matplotlib.lines.Line2D at 0x10e77ecf8>]
```

```
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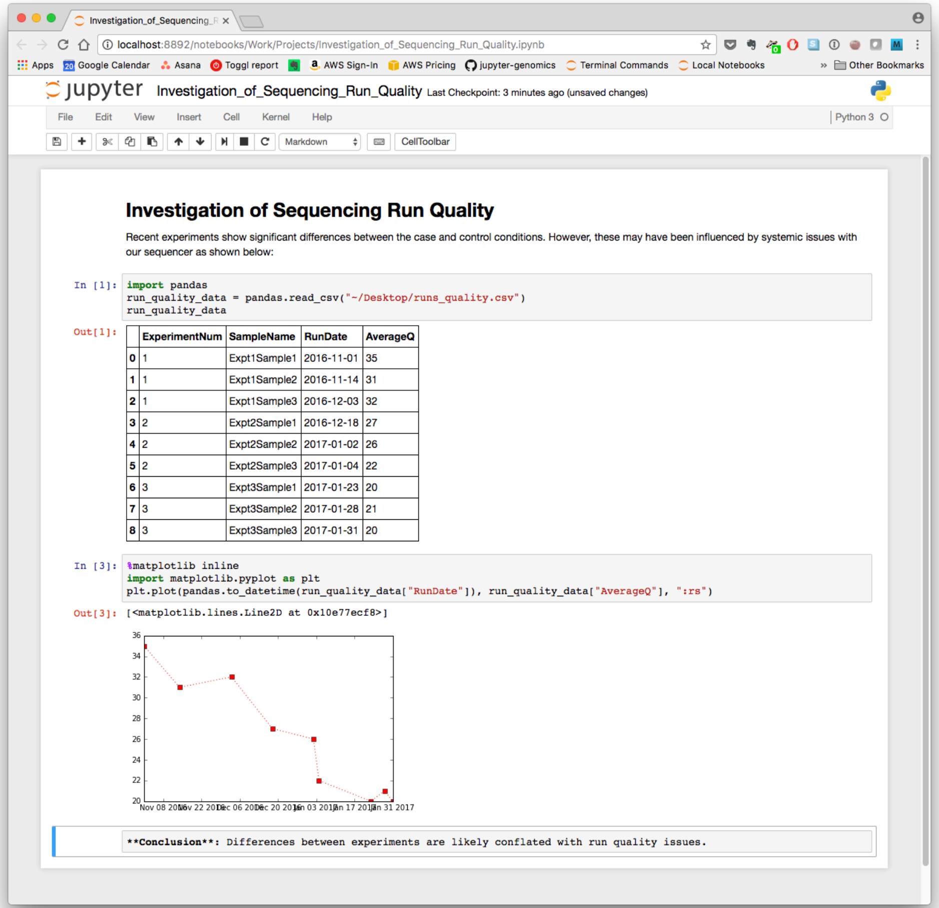

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**Conclusion**: Differences between experiments are likely conflated with run quality issues.
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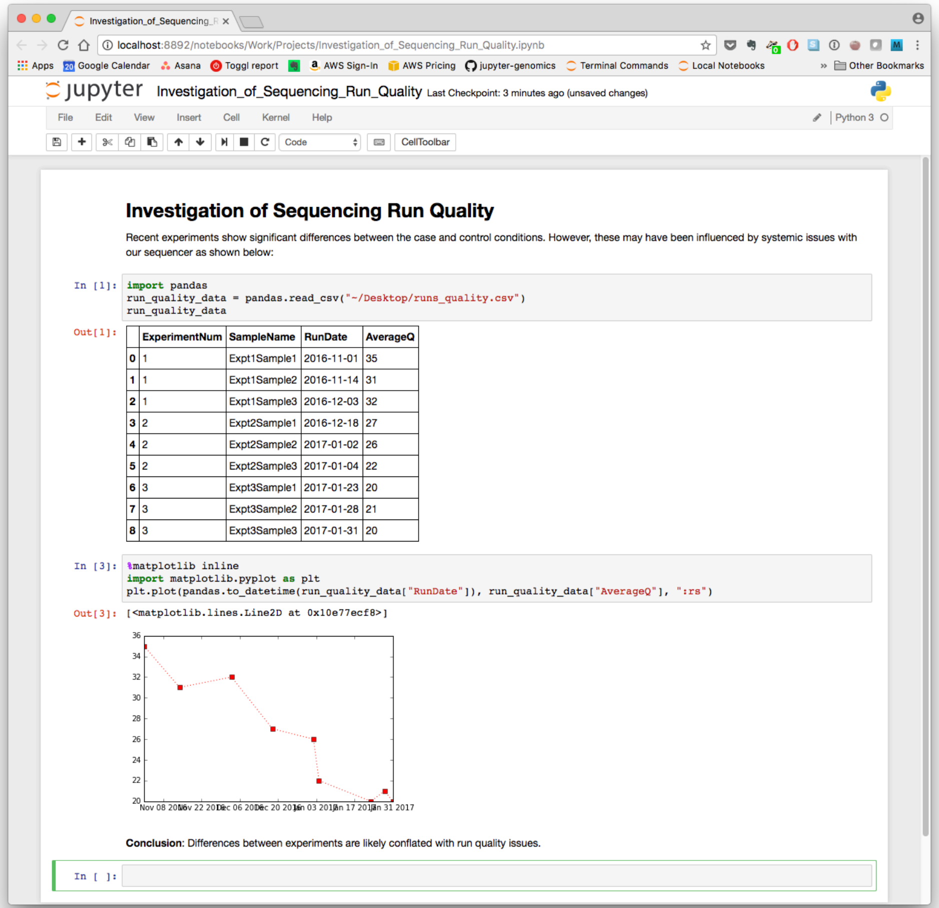
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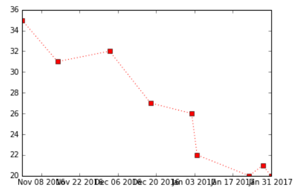

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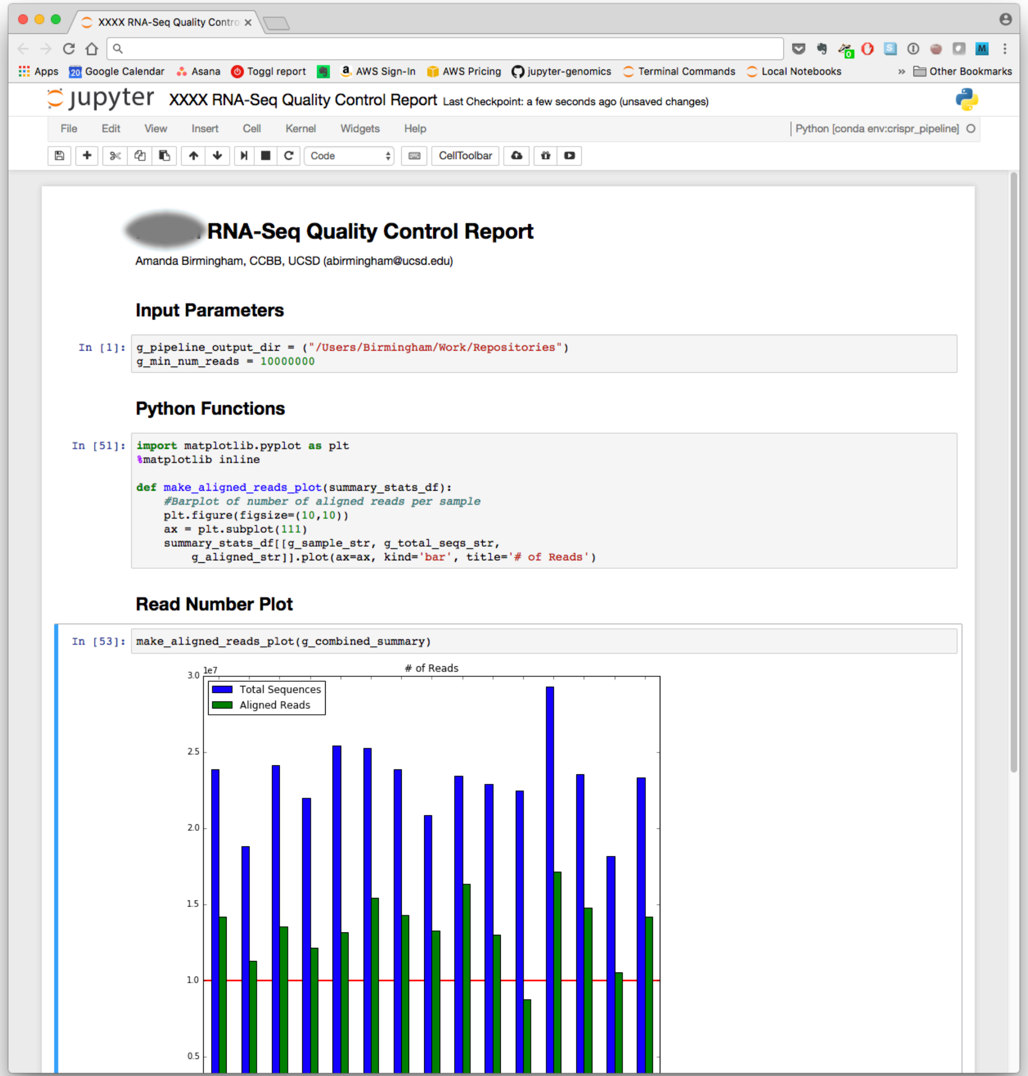
Jupyter Notebooks: Friend or Foe?

- Are notebooks the key to reproducibility?
  - Data Carpentry offers an entire workshop on "Reproducible Research using Jupyter Notebooks”
- Easy to save, modify, and extend
  - Great for rerunning or tweaking previous data analyses
- CCBB delivers analyses as notebooks
  - Report becomes more than a record—it is itself a tool!
- Notebooks’ *greatest strength* is interactivity
  - Between input and output
  - Between (e.g.) Python and R
  - Between narrative and code
  - Between material and reader



[redacted] RNA-Seq Quality Control Report

Amanda Birmingham, CCBB, UCSD (abirmingham@ucsd.edu)

Input Parameters

```
In [1]: g_pipeline_output_dir = ("/Users/Birmingham/Work/Repositories")
        g_min_num_reads = 10000000
```

Python Functions

```
In [51]: import matplotlib.pyplot as plt
         %matplotlib inline

         def make_aligned_reads_plot(summary_stats_df):
             #Barplot of number of aligned reads per sample
             plt.figure(figsize=(10,10))
             ax = plt.subplot(111)
             summary_stats_df[[g_sample_str, g_total_seqs_str,
                 g_aligned_str]].plot(ax=ax, kind='bar', title='# of Reads')
```

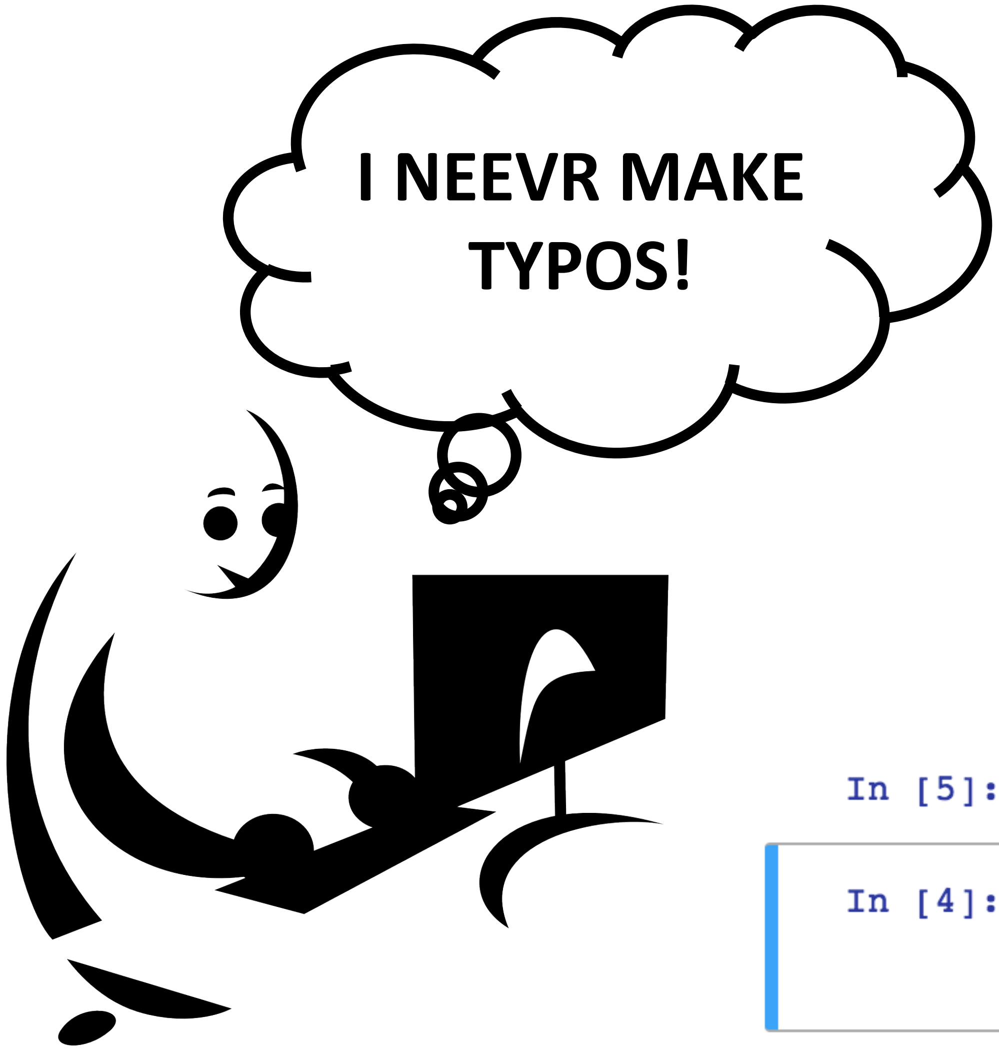
Read Number Plot

```
In [53]: make_aligned_reads_plot(g_combined_summary)
```

(Inter-)Actively Dangerous

- Interactivity can also be a *huge danger* to reproducibility
- Humans are inconsistent
  - We make unpredictable mistakes
  - Thus, “interactive”=“bad” for repetitive tasks
    - Like primary NGS analysis pipelines
- Jupyter Notebooks can be inconsistent, too
  - Changing code/variables in a notebook does NOT rerun cells that depend on that change
  - In fact, doesn’t even clear old outputs!

(Inter-)Actively Dangerous



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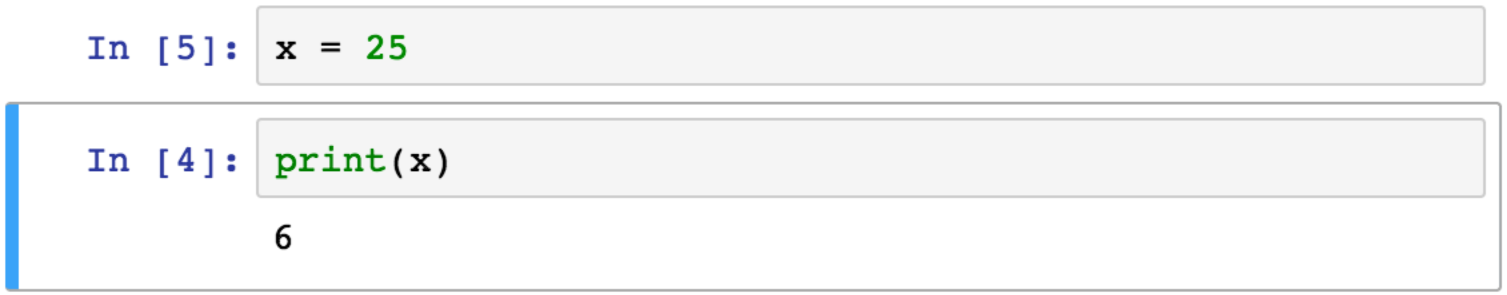

```
In [5]: x = 25

In [4]: print(x)

        6
```

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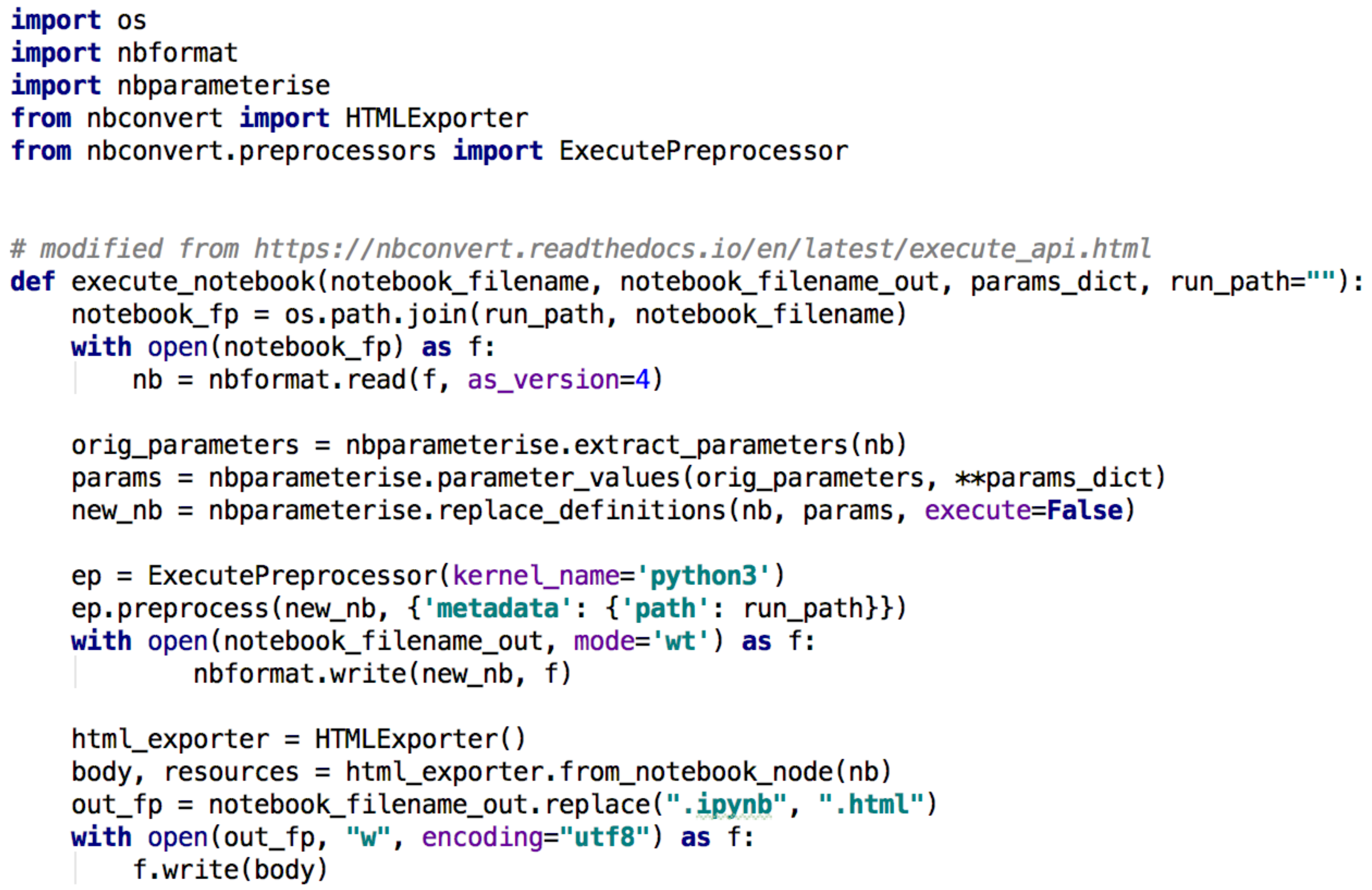
  - In fact, doesn’t even clear old outputs!
  - Thus, “interactive”=“bad” for important records
    - Like experimental records (i.e., methods)
- Do we have to give up other advantages of Jupyter Notebooks when building pipelines and recording methods?

Scripting Jupyter Notebooks

- No! We can have our cake and eat it, too ☺
- Jupyter ships with **nbconvert** package that can read, write, and execute notebooks from Python
- An extension, **nbparameterise** (note British spelling) allows injection of new variable values
- **nbconvert** and **nbformat** (also built-in) can output notebooks and static html, respectively
- With these three pieces, we can script pipelines built from Jupyter Notebooks
  - Notebooks give readability and reusability
  - Script prevents human errors and speeds execution
  - HTML output of notebooks provides read-only record of methods
- Entire approach takes less than one page of code

Scripting Jupyter Notebooks



```python
import os
import nbformat
import nbparameterise
from nbconvert import HTMLExporter
from nbconvert.preprocessors import ExecutePreprocessor


# modified from https://nbconvert.readthedocs.io/en/latest/execute_api.html
def execute_notebook(notebook_filename, notebook_filename_out, params_dict, run_path=""):
    notebook_fp = os.path.join(run_path, notebook_filename)
    with open(notebook_fp) as f:
        nb = nbformat.read(f, as_version=4)

    orig_parameters = nbparameterise.extract_parameters(nb)
    params = nbparameterise.parameter_values(orig_parameters, **params_dict)
    new_nb = nbparameterise.replace_definitions(nb, params, execute=False)

    ep = ExecutePreprocessor(kernel_name='python3')
    ep.preprocess(new_nb, {'metadata': {'path': run_path}})
    with open(notebook_filename_out, mode='wt') as f:
            nbformat.write(new_nb, f)

    html_exporter = HTMLExporter()
    body, resources = html_exporter.from_notebook_node(nb)
    out_fp = notebook_filename_out.replace(".ipynb", ".html")
    with open(out_fp, "w", encoding="utf8") as f:
        f.write(body)
```

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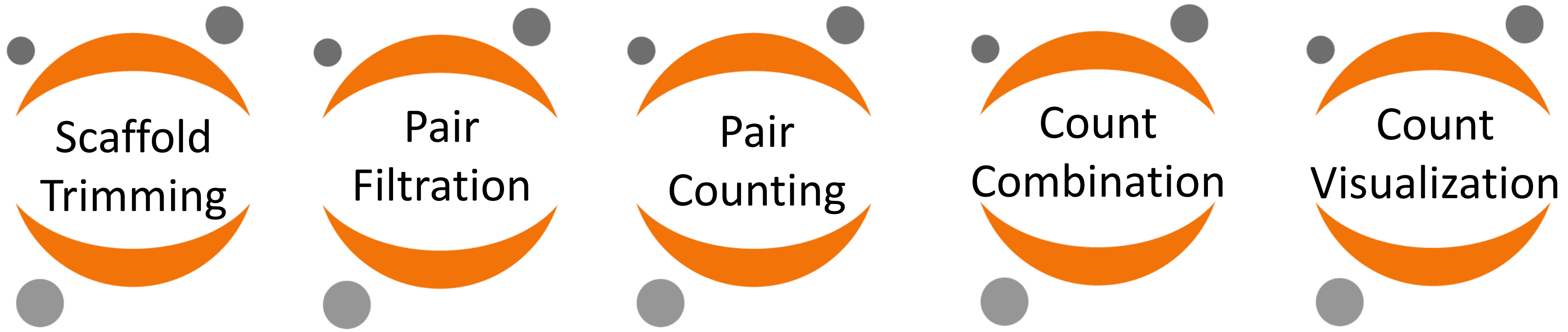
```
execute_notebook("mynotebook.ipynb", "my_new_notebook.ipynb", {"x": 6, "y": "blue"})
```

Notebooks in the Wild

- A sample NGS pipeline using Jupyter Notebooks
  - Goal: identify gene pairs with synergistic survival effects (positive or negative)
  - Experimental system:: Dual-gene knock-outs in human cell lines using CRISPR
  - Read-out: number of instances of each CRISPR guide in final population, assessed by NGS



Jupyter logo courtesy of http://jupyter.org/

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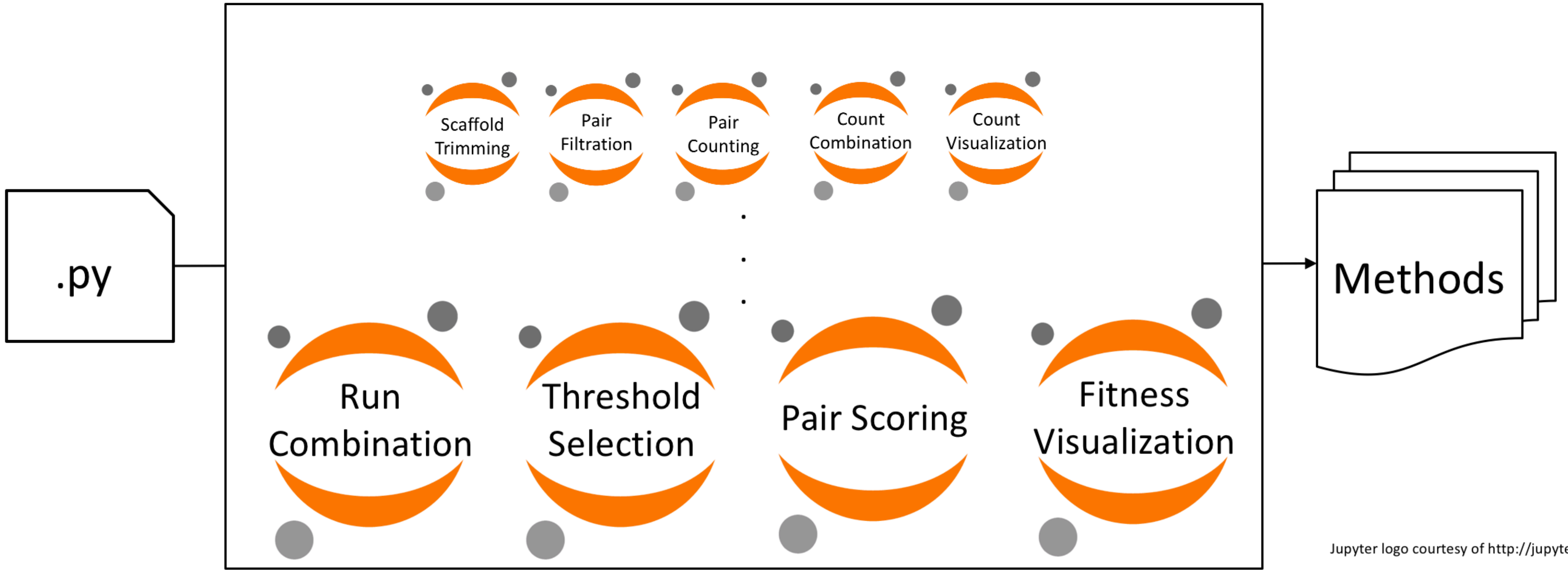

Jupyter logo courtesy of http://jupyter.org/

Conclusions

- Jupyter Notebooks are a fantastic tool for data analysis—*but*:
- Their twin goals of interactivity and reproducibility are often at odds
- Notebooks can be scripted to reduce error potential
  - And notebook-based pipelines self-document nicely!
- CCBB has implemented a sample Jupyter-based pipeline for NGS data from dual CRISPR screens
  - Pipeline is part of work with Dr.s Prashant Mali & Trey Ideker, now in press at Nature Methods
  - Code is available in the "CRISPR" section of CCBB's jupyter-genomics repository on GitHub
    - https://github.com/ucsd-ccbb/jupyter-genomics
- CCBB's Data Science Blog gives a further intro to notebook scripting
  - http://ccbb.bio/outreach/data-science-blog/
- Reproducible data analysis is hard work—but worth the effort!

http://ccbb.bio

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  - Ideker lab
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