Thunor Web Manual

docs.thunor.net

August 7, 2024

Contents

1 Thunor Web Manual

This manual is available in PDF format or as a website at docs.thunor.net.

1.1 What is Thunor Web?

Thunor Web is a web application for managing, visualizing and analyzing high throughput screen (HTS) data. In brief, an HTS is an experiment whereby drugs are applied to cell lines in a multiplexed fashion, using microtiter plates with many wells (typically, 384). Currently, the system is focused on proliferation (cell count) data, but other assay types may be supported in the future.

With Thunor Web, users can upload cell counts data obtained at one or more time points. Data can be upload pre-annotated (i.e. labelled with cell lines, drugs, and drug concentrations), or unannotated. In the unannotated case, Thunor Web has a graphical plate mapper to add annotations efficiently.

Thunor Web will calculate 72 hour viability and, if the data have multiple time points, the drug-induced proliferation rate (DIP rate). In both cases, Thunor Web will fit dose response curves and calculate derivative metrics, such as IC50 and EC50. All these data can be visualized using the plot system.

Thunor Web allows labelling of groups of cell lines or drugs with "tags" using its tag system. Examples include cell line mutations, cell line tissues of origin, drug molecular targets, or drug classifications. These groups can be used for grouping within the plot system.

1.2 Getting Started

- To try out Thunor Web with example data, see the tutorial.
- If you're interested in installing Thunor Web, see installation options.
- If you're a Thunor Web user, this documentation contains a complete user manual, starting with the Thunor web home page.
- For more information, see the frequently asked questions.

2 Citing Thunor Web

Thank you for using Thunor Web and citing our work. Please cite the following publication:

Lubbock A.L.R., Harris L.A., Quaranta V., Tyson D.R., Lopez C.F. Thunor: visualization and analysis of high-throughput dose–response datasets, Nucleic Acids Research (2021), gkab424.

And in bibtex format:

```
@article{lubbock_thunor_2021,
    title = {Thunor: visualization and analysis of high-throughput dose-response datasets},
    issn = {0305-1048},
    shorttitle = {Thunor},
    url = {https://doi.org/10.1093/nar/gkab424},
    doi = {10.1093/nar/gkab424},
    number = {gkab424},
    urldate = {2021-05-26},
    journal = {Nucleic Acids Research},
    author = {Lubbock, Alexander L R and Harris, Leonard A and Quaranta, Vito and Tyson, Darren R and L
    month = may,
    year = {2021},
}
```

3 Frequently asked questions

3.1 General

3.1.1 What is high throughput screening (HTS)?

High throughput screening is a method for rapidly quantifying cellular response to perturbation (typically, the application of one or more drugs). Microtiter plates with multiple wells can have different combinations of drugs, drug doses, and cell lines in each well, thus having the potential to generate large amounts of data.

What is the drug-induced proliferation rate (DIP rate)?

The DIP rate is defined as the steady-state rate of proliferation of a cell population in the presence of a given concentration of drug. It is easily quantified as the slope of the line on a plot of the doubling of cell populations versus time. For further information, see Harris et al. Nature Methods 2017.

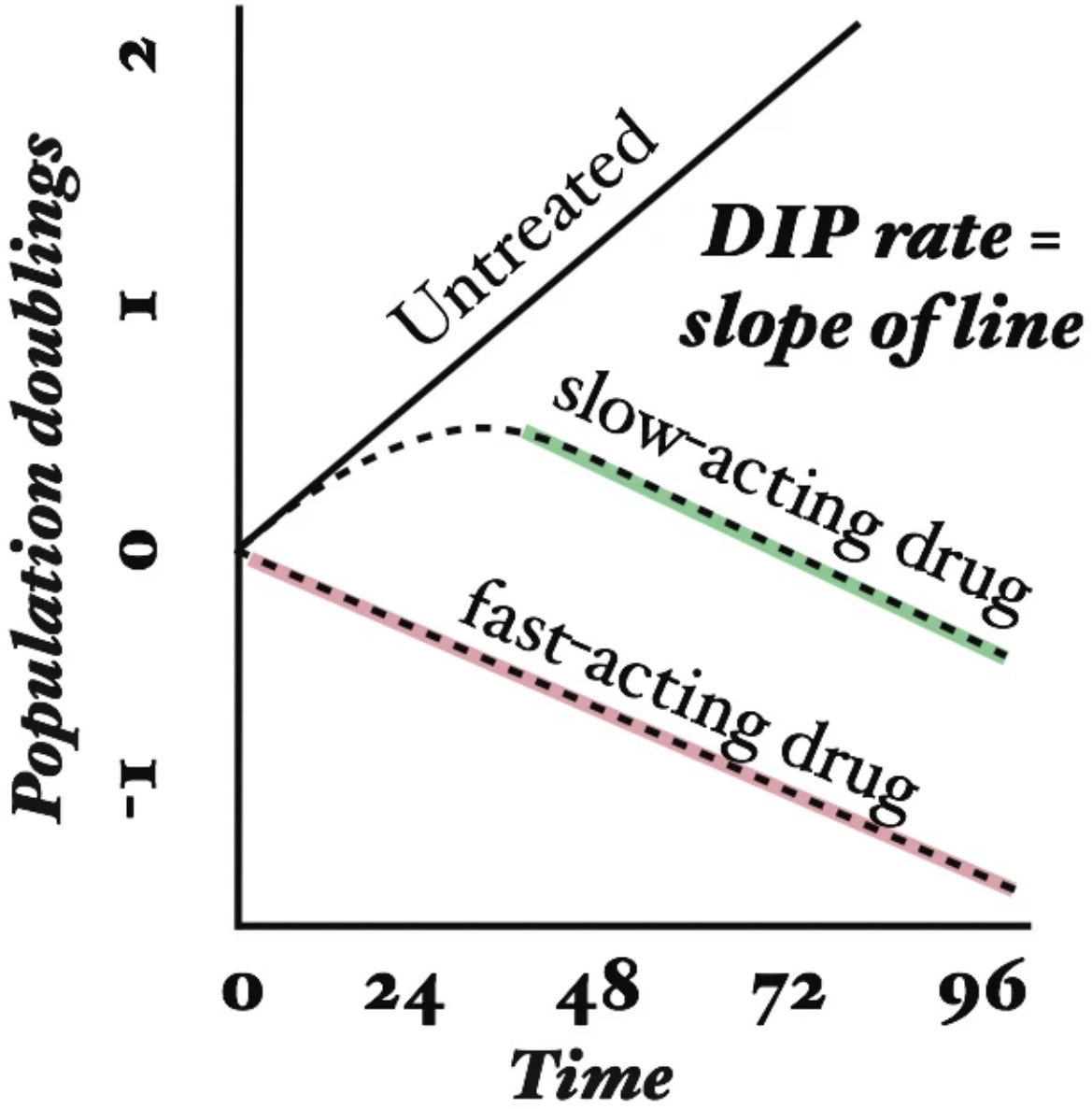

Image: Hypothetical growth curves (in log scale) for a cell line untreated and treated with two different drugs. Also shown is drug-induced proliferation (DIP) rate, defined as the slope of the line after the drug effect has stabilized. Figure from Harris et al. Nature Methods 2017.

3.1.2 What are the advantages of the DIP rate over end-point viability?

Traditionally, dose response curves were constructed by measuring cell counts at a single time point after drug application (e.g. 72 hours). Metrics such as IC50 were then calculated against this curve.

Dose response curves using traditional metrics of drug effect can result in erroneous and misleading values of drug activity parameters, skewing data interpretation. This is because these metrics suffer from time-dependent bias (the metric value varies with the time point chosen for experimental measurement), arising from (i) exponential growth and (ii) delays in drug effect stabilization. For more information, see Harris et al. Nature Methods 2017.

3.1.3 My question isn't answered here. Where can I get help?

If the answer to your question isn't available in this FAQ or elsewhere in this manual, please contact us via our chat room.

3.2 Installation

3.2.1 Why am I seeing "Bad Request (400)" when I try to access Thunor Web after installation?

Please check that the value for `DJANGO_HOSTNAME` set in `thunor-app.env` matches the hostname used in your browser. After changing the value, you'll need to restart Thunor Web: `python thunorctl.py restart`.

3.2.2 How do I log in?

Use the account you created during installation. If you didn't create an account, run `python thunorctl.py createsuperuser`.

3.2.3 How do I customize my Thunor Web installation?

See the list of configuration options. Remember to restart Thunor Web after making changes, by running `python thunorctl.py restart`.

3.2.4 How do I use an external Postgres database server?

Set the `POSTGRES_HOST`, `POSTGRES_USER` and `POSTGRES_PASSWORD` environment variables with the connection details of your Postgres server. Initialize the database with `python thunorctl.py migrate`.

4 Tutorial

4.1 What is Thunor Web?

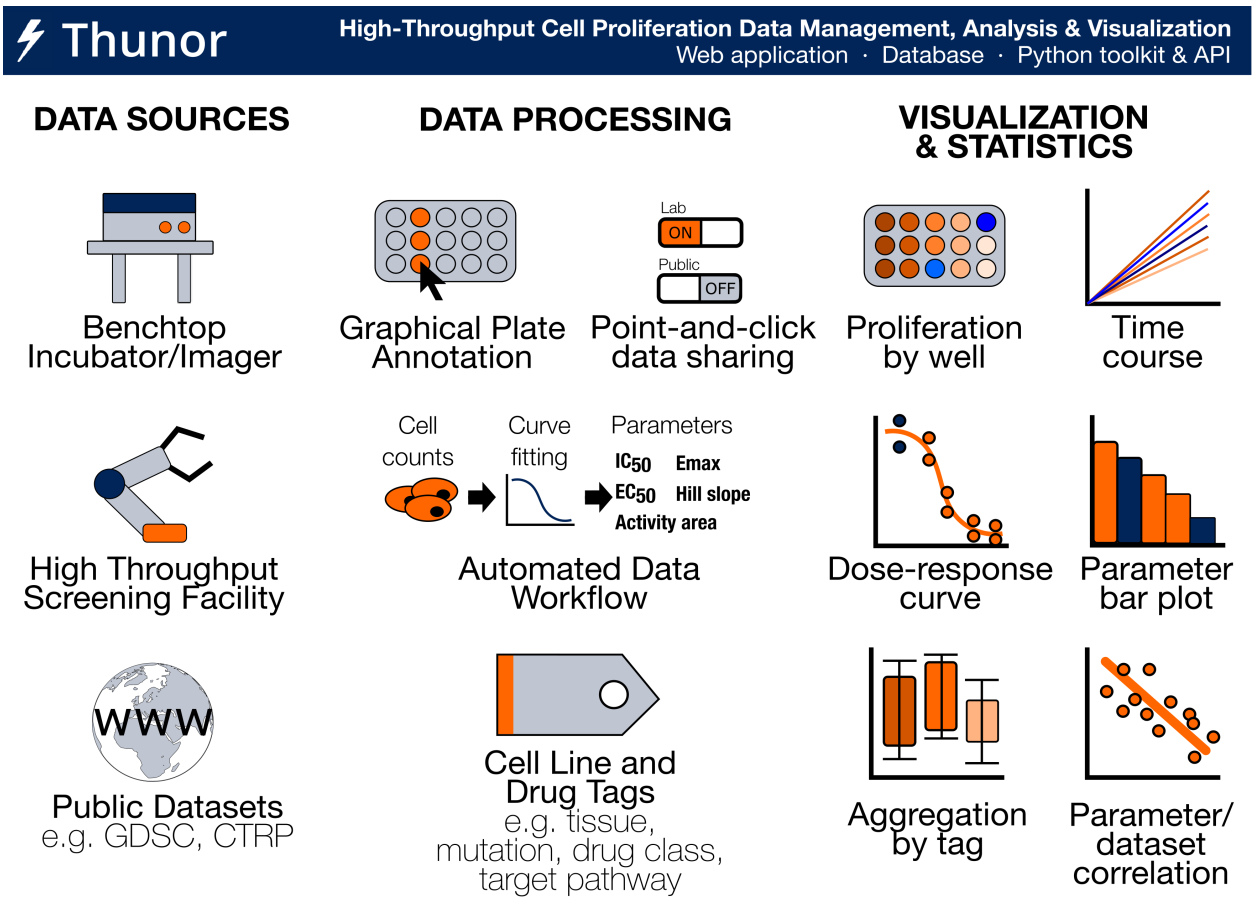

Image: Thunor Web - Overview of Features

Thunor Web is a web application for managing, visualizing and analyzing high throughput screen (HTS) data. It works with both end-point and time-series dose-response cell proliferation data, where it calculates viability scores and the DIP rate respectively. Key features include data management and sharing, automated DIP rate calculation, a plate mapper to label multi-well plates with cell lines, drugs, and drug concentrations, dose-response curve fitting, derived parameter calculation and comparison (e.g. IC50, Emax, activity area; see parameters), and, a tag system for annotating drugs and cell lines for aggregation and categorical analysis/visualization.

Many of these features are also available for programmers in a Python library with Jupyter Notebook compatibility called Thunor Core, which can be used separately or together with Thunor Web. See Thunor Core documentation for more information.

Thunor Web is a modular application written in Python and deployed using Docker Compose. For further details on the software and technology stack, see design and components.

4.2 Can I try Thunor Web without installing it?

Absolutely. See our online demo, which has been pre-loaded with example data. You can view example plots, example cell line tags, and an example plate map.

4.3 System Requirements

Thunor utilizes Docker containers built for computers with Intel or AMD CPUs (x86-64) and ARM CPUs (arm64) - the majority of laptops, desktops, and servers. Windows, MacOS, and Linux are all supported.

- **Docker** and **Docker Compose v2** (i.e. `docker compose` should work, without a dash). Follow instructions for your platform:
  - Docker for Windows
  - Docker for Mac
  - Docker for Linux
  - Other platforms: Docker installation instructions
- A **Python** installation*. Python 3.6 or later is recommended, but other versions will probably work - it is only used for the configuration script.
- **Git***

*If you use MacOS or Linux, you probably already have Python and git installed. If you use Windows, we recommend installing Anaconda, a Python distribution which includes lots of useful software.

4.4 Installation steps

These steps cover a local-only (single machine) installation. For a network-accessible installation, see the full installation instructions.

1. **Retrieve the Thunor Web quick start tool**

   ```
   git clone https://github.com/alubbock/thunor-web-quickstart thunor-web
   cd thunor-web
   ```

2. **Run the Thunor Web deploy script**

   ```
   python thunorctl.py deploy --hostname=localhost
   ```

3. **Create an admin account**

   ```
   python thunorctl.py createsuperuser
   ```

That's it! Thunor Web is now ready to start. If you encounter any issues, please see the installation FAQs for further guidance.

4.5 Load the site in a browser

Open a web browser to http://localhost and you should see the Thunor Web login page.

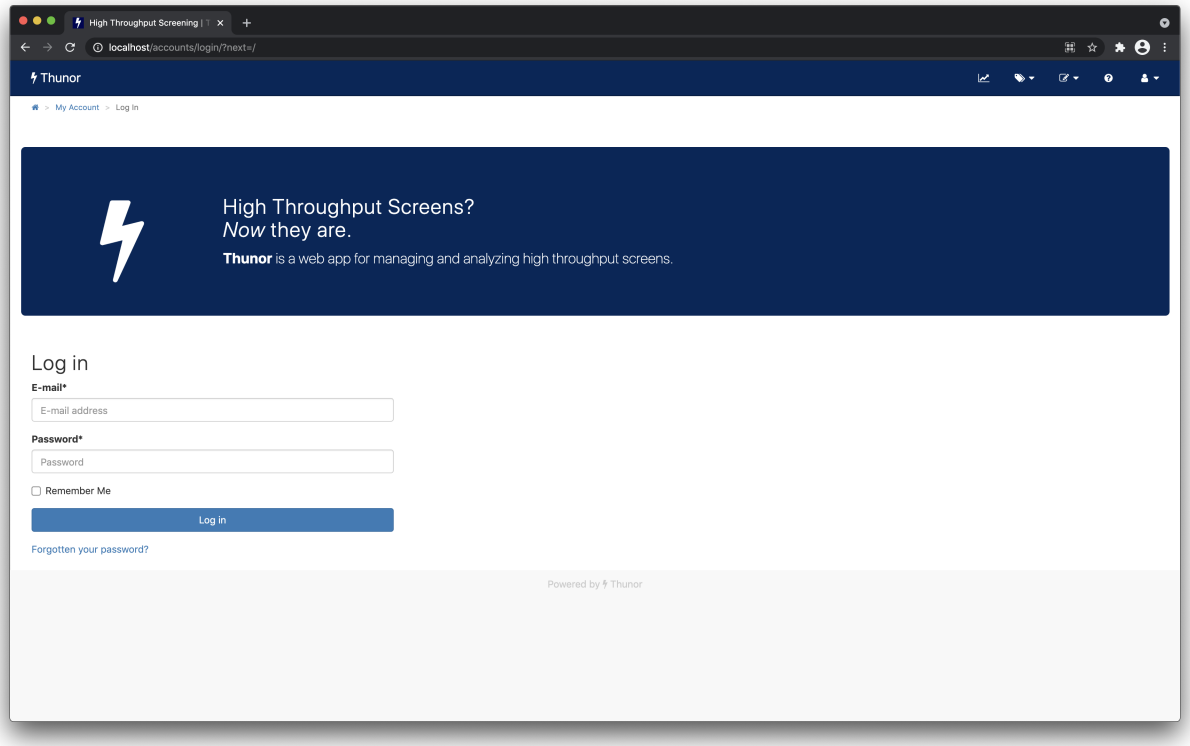

Image: Thunor Web login page

If you cannot load the page, check that Thunor Web has started - run:

```
python thunorctl.py start
```

Check the installation FAQs if you encounter any issues.

4.6 Log in and home page

Enter the email address and password that you created during the installation process into the form in your browser, and click the **Log In** button. You should now see the home page.

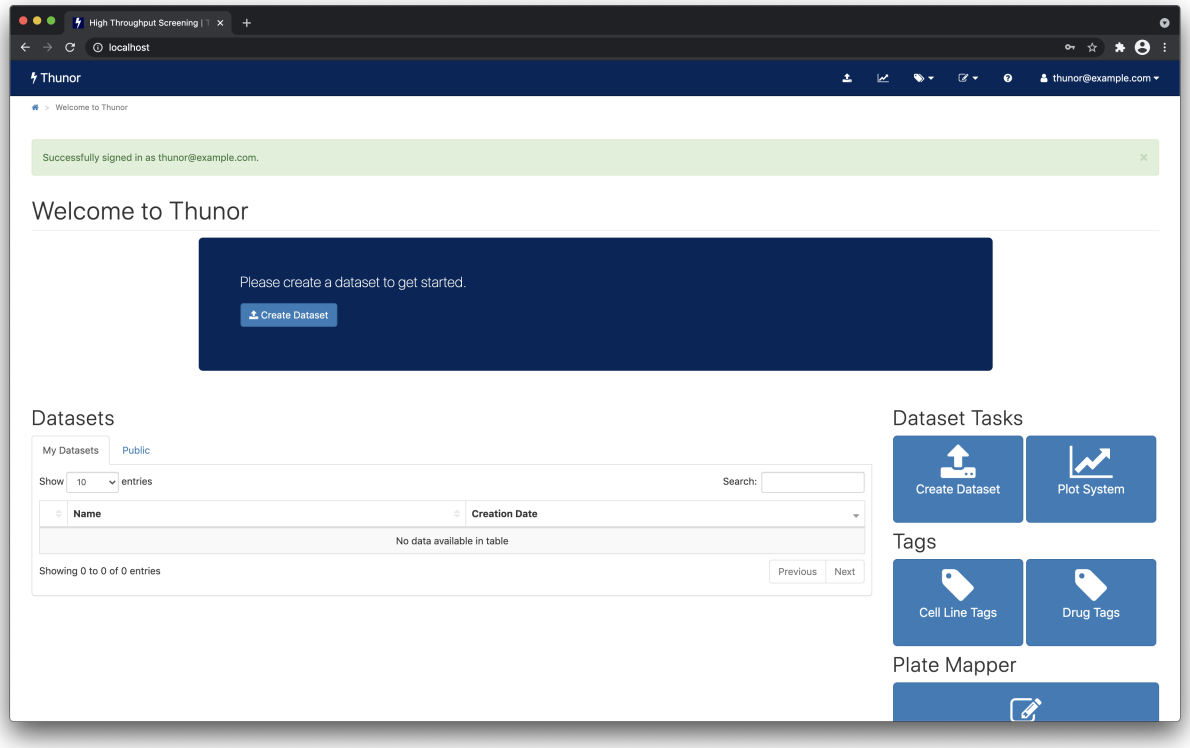

Image: Thunor Web home page

4.7 Upload a dataset

First, you'll need some data. Download the example HTS007 dataset, which is a comma-separated value (CSV) file containing 8 cell lines and 27 drugs quantified as cell proliferation time course data (i.e., the number of cells at each time point in each condition). See our documentation on the dataset page for information on the file format (or open the CSV file in a spreadsheet program like Microsoft Excel).

Next, from the home page, click the **Create dataset** button. Give the dataset a name (**HTS007** seems appropriate), like the screenshot below, and click **Next**.

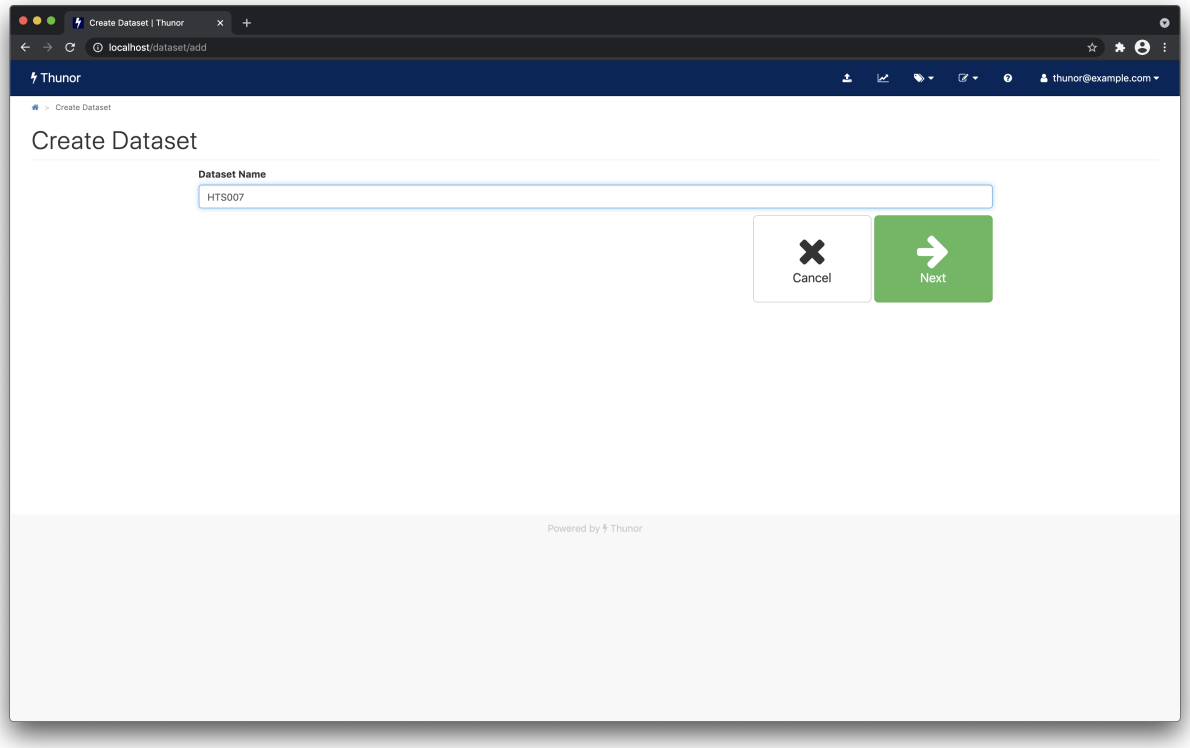

Image: Thunor Web - create a dataset

On the next screen, you'll see an area where you can upload files. You can either:

- Drag-and-drop the hts007.csv file you downloaded earlier (from Windows Explorer, Finder on a Mac, etc.) into the dotted area; or
- Click within the dotted area and browse for the hts007.csv file

The file should start uploading and processing, as per the screenshot below. Thunor Web loads the file into its database, calculates viability and DIP rate scores, and fits dose-response curves. **This may take several minutes.**

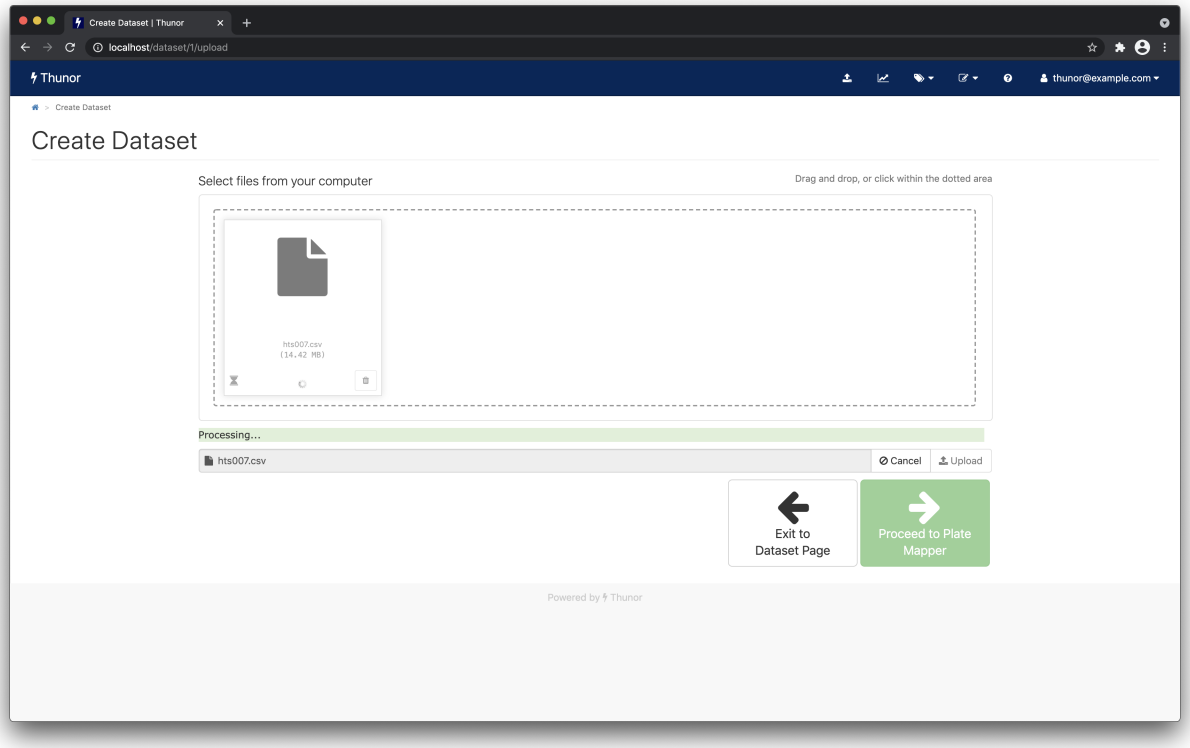

Image: Thunor Web - proecssing a dataset

When complete, you'll see a screen like the one below. Click **Proceed to Plate Mapper** to move onto data annotation.

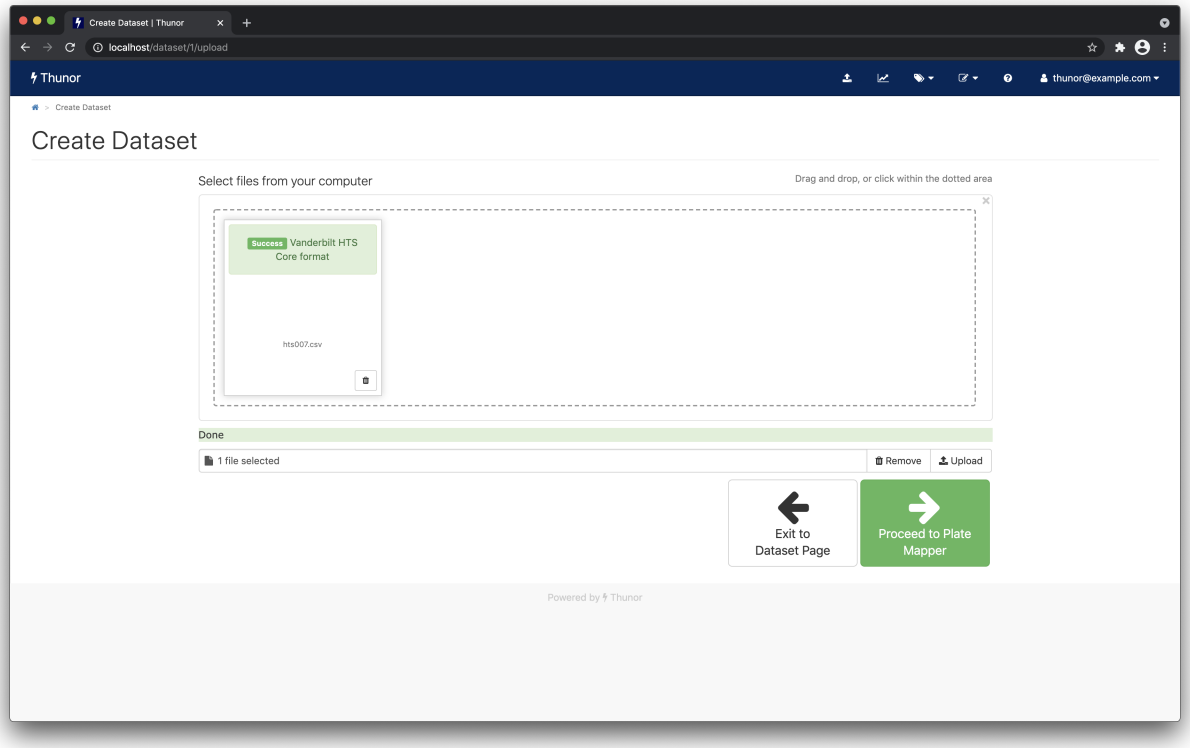

Image: Thunor Web - upload complete

4.8 View the plate maps

You should now be looking at the plate mapper, as shown below.

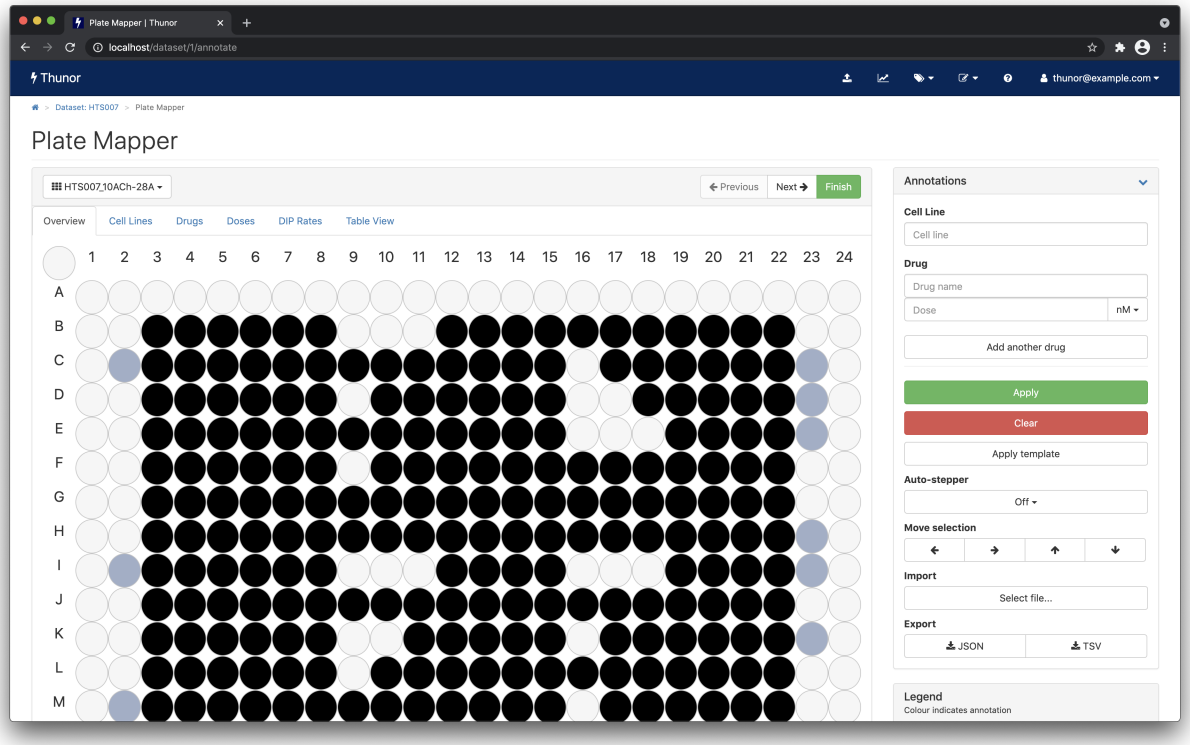

Image: Thunor Web - plate mapper

This view shows you the annotations of each multi-well plate in the dataset. In this case, the data are already pre-annotated, so there's no need to edit the data. But you can view and browse through the dataset:

- Change the plate using the drop-down box in the top left, or the next/previous buttons
- Change the view using the tabs - Overview, Cell Lines, Drugs, etc.
- Hover over a well to view its annotations

There are many other features which are useful for annotating large datasets efficiently, including templates to annotate multiple plates and once, and an "auto-stepper" for dosing concentration series. See the plate mapper documentation for further details.

When ready, move on to the dataset page by clicking **Finish**.

4.9 Dataset page

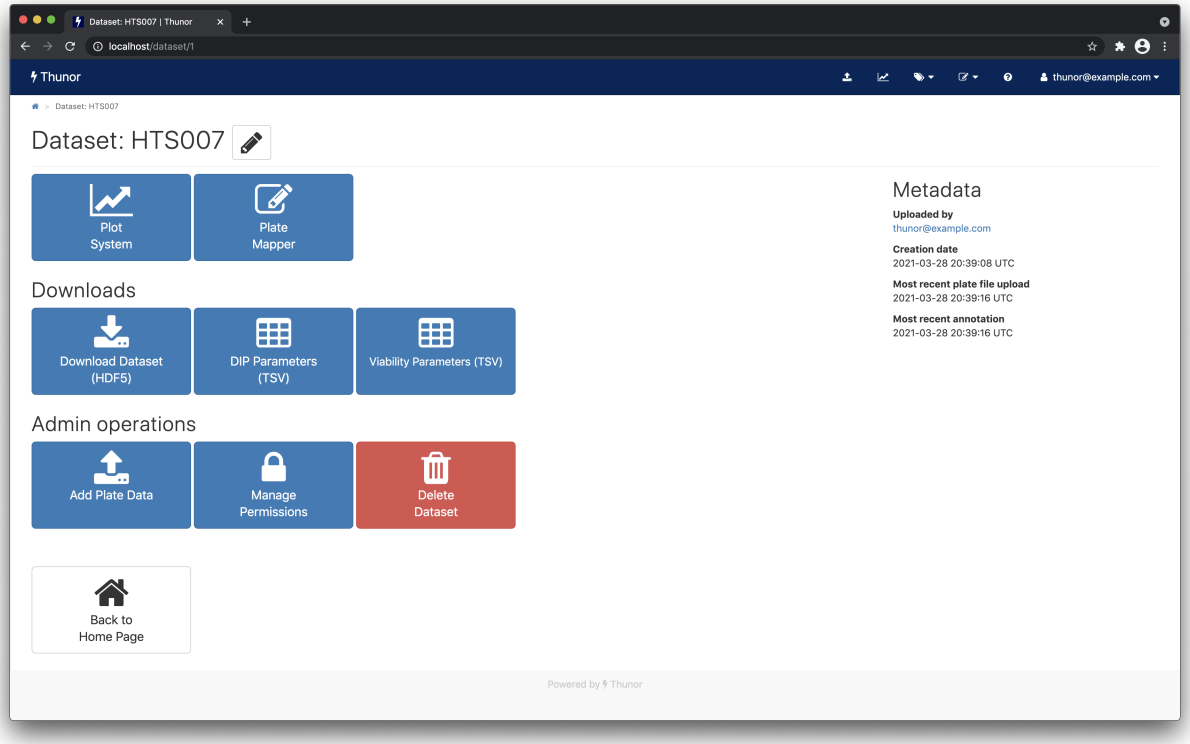

Image: Thunor Web - dataset page

The dataset page shows various tasks you can do with the dataset, including:

- The plot system, which allows interactive visualization of the dataset
- The plate mapper, covered above
- Dataset downloads, which allows datasets and derived parameters to be exported for further analysis using other tools
- Dataset permissions, to share the dataset with other user groups

Various metadata such as upload date are shown on the right.

To share a dataset with other users on the system (if this were a multi-user, networked installation), we click on **Dataset Permissions**, then on the new page we can toggle on and off various permissions for different user groups. For example, we could allow anyone to view plots from this dataset (screenshot below). Additional users and user groups are created in the admin interface.

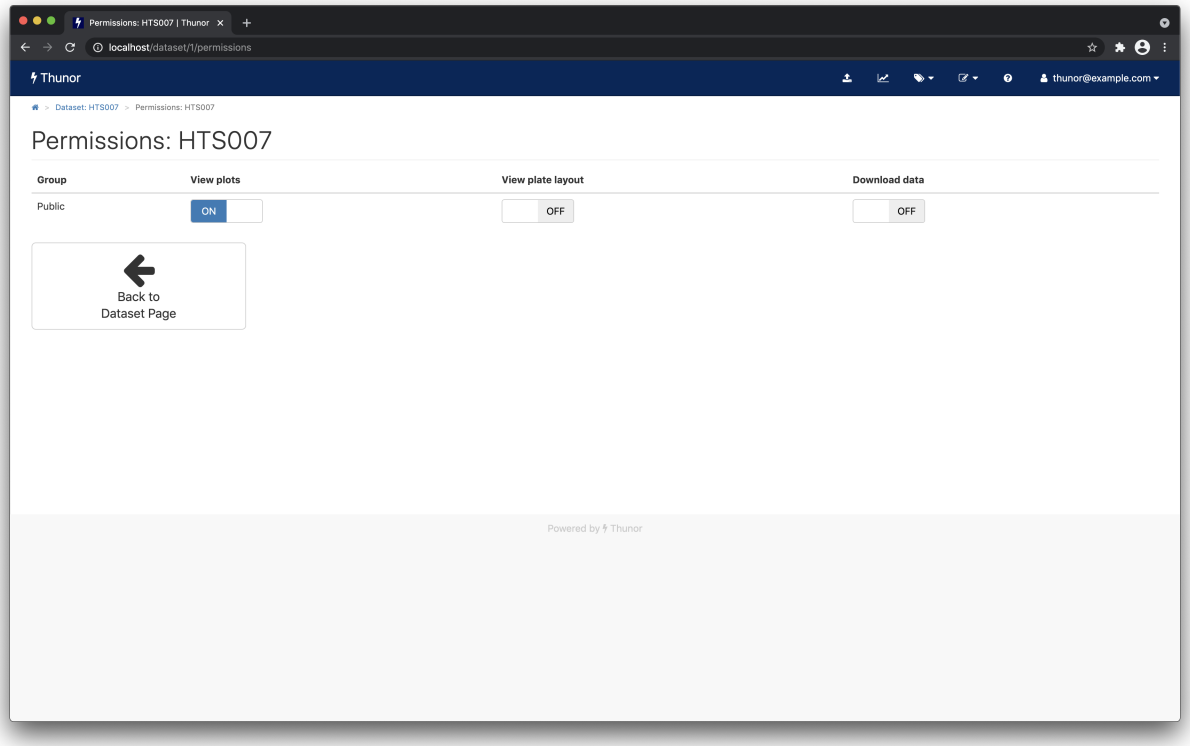

Image: Thunor Web - dataset permissions page

From the permissions page, click **Back to Dataset Page**.

From the dataset page, click the **Plot System** button.

4.10 Plot system

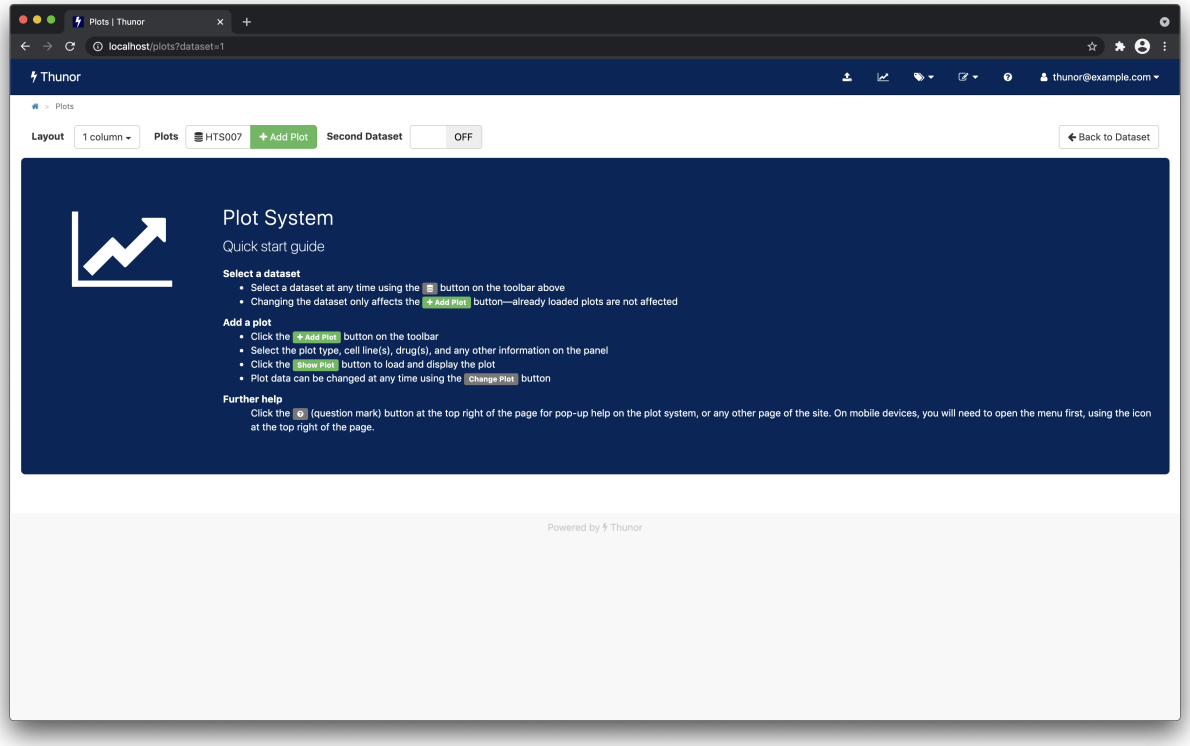

Image: Thunor Web - plot system

From the Plot System page, click **Add Plot**

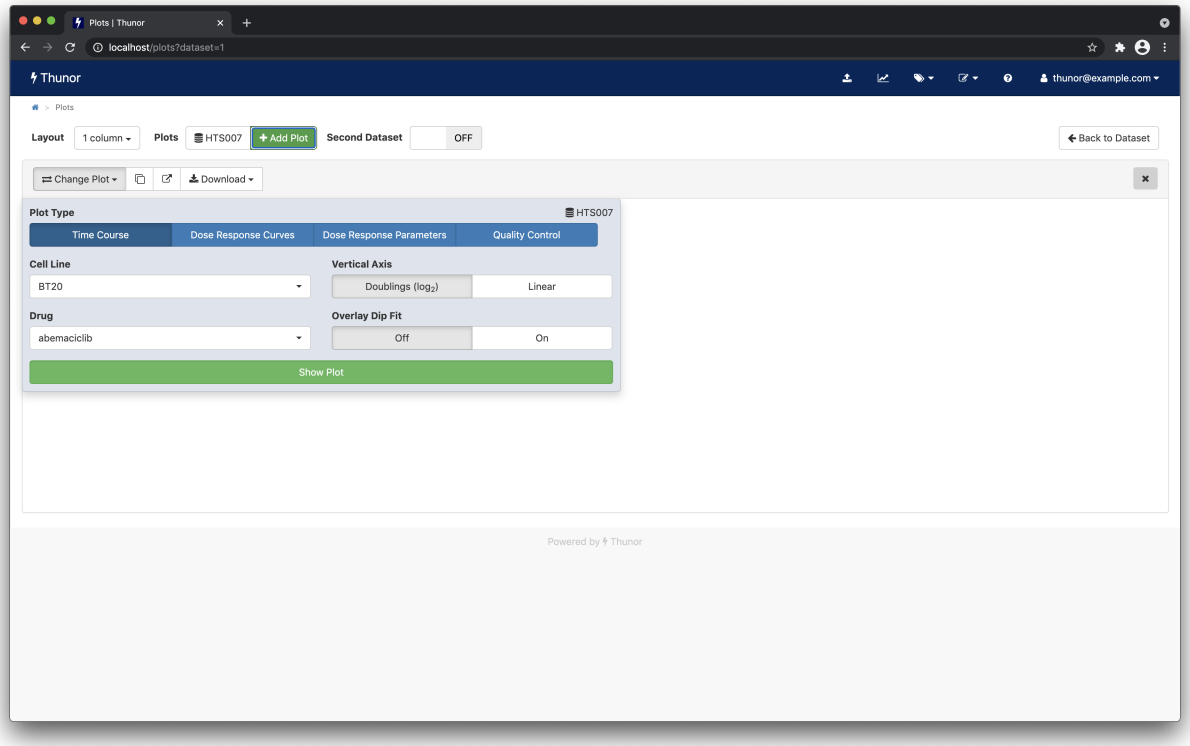

Image: Thunor Web - add plot

From this plot system, you can change the plot type and plot options. Leave these as default, and click **Show Plot**.

Next, change the layout to **2 column** using the dropdown box in the top left. Notice how the plot resizes.

Each plot is interactive - you can hover over it to view the underlying data. A toolbar also appears on hover with options to resize the plot, zoom, pan etc. If you move over the main plot data area (cursor turns to crosshairs), and double click, you should find it auto-resizes the plot (you can also use the "Autoscale" button in the plot toolbar), giving a result similar to the screenshot below.

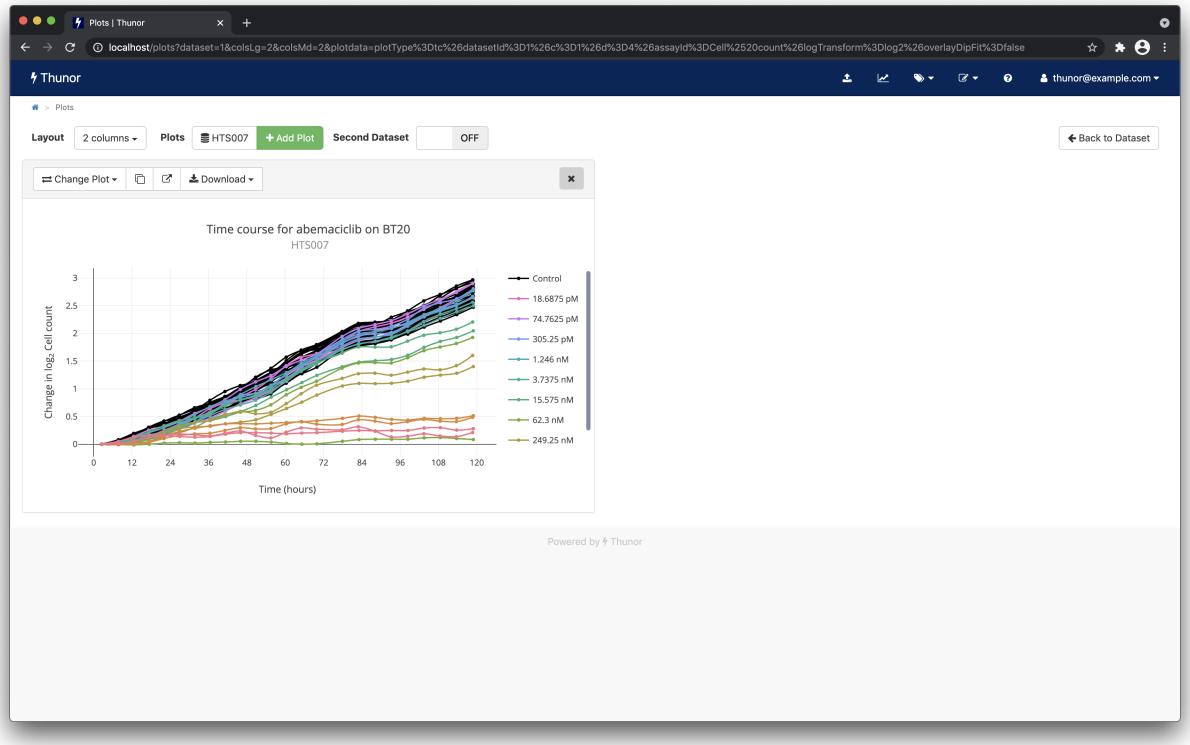

Image: Thunor Web - time course plot

To add a second plot, click **Add Plot** again. This time, click the **Dose-response curves** option, then click **Show Plot**. This shows a dose-response curve, with the underlying DIP rate values shown as individual data points. You can also drag and drop plots to rearrange them, by clicking on the grey header bars for each plot (outside of the buttons and "X"). We note there is one data point which looks like a possible outlier, highlighted in the screenshot below.

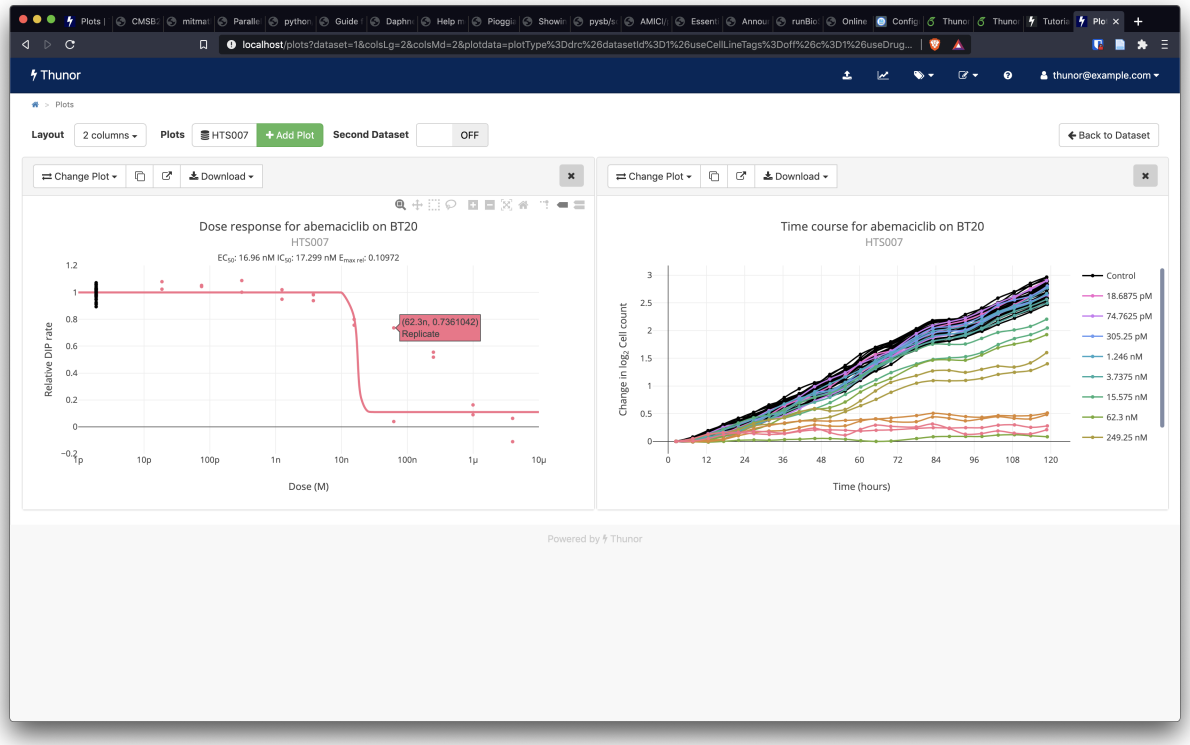

Image: Thunor Web - dose-response curve plot (left) with outlier data point highlighted

One of Thunor Web's strengths is the ability to interactively alter plots to quickly ask follow-up questions of the data. On the time-course plot, click **Change Plot**. In the **Overlay DIP fit** area, click the **On** button, then press **Show Plot**. The plot has now updated to show the fitted DIP rate values (solid, straight lines) over the raw data (dotted lines with data points). Double click the plot area to auto-resize it. In the list of concentrations on the right-hand side of the plot, click **62.3nM**. This isolates the trace (shows only that concentration), as shown in the screenshot below.

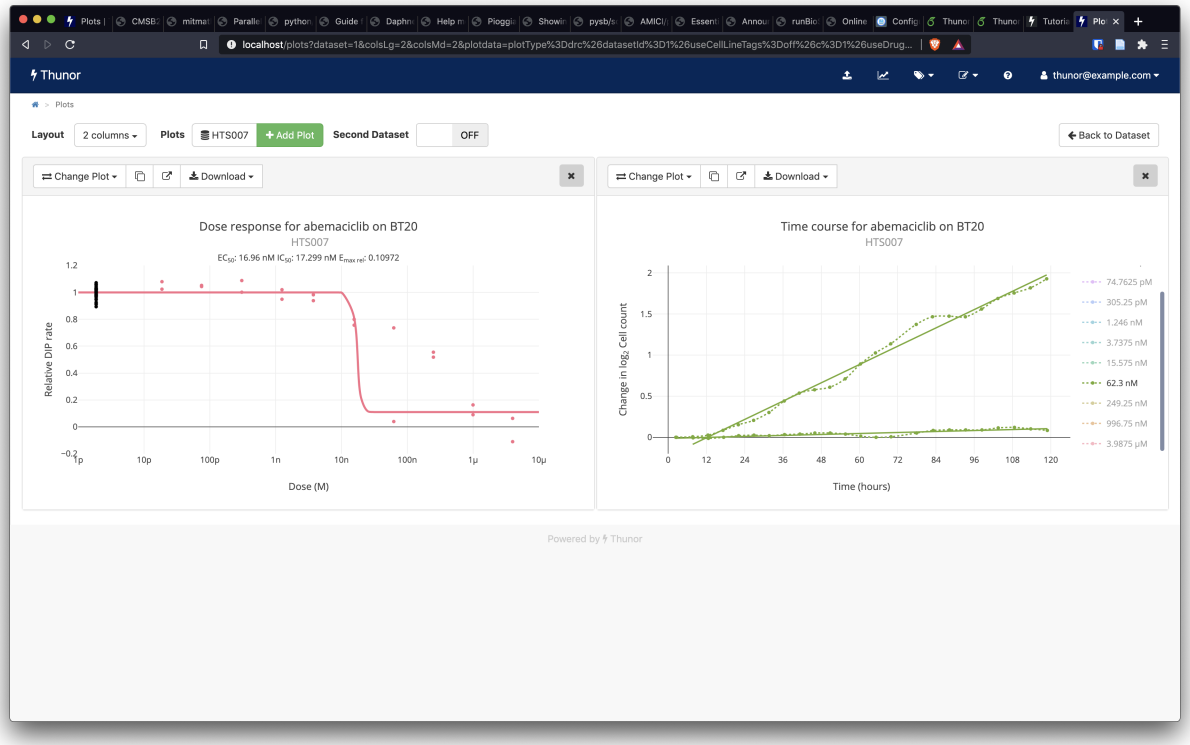

Image: Thunor Web - time-course plot with DIP rate overlay (right)

We can see that the DIP rates fit the underlying data well, but they have markedly different drug-induced proliferation rates, pointing to a possible experimental or image quantification issue with one of the wells. This is one example of how Thunor Web can be used to quickly interrogate a dataset.

There are many other plot types available and lots of options in the plot interface. We recommend reading the plot system documentation, which gives a comprehensive overview of its features.

4.11 Tag System

The tag system allows cell lines and drugs to be annotated with categorical labels, which can be used to group them in plots and for statistical analysis. This is most useful on larger datasets, so we recommend viewing our demo site, which has been preloaded with the Genomics of Drug Sensitivity in Cancer (GDSC) dataset and some related cell line tags and drug tags.

Here, we'll briefly show how to create some tags in Thunor Web. You can download some example cell line tags (CSV format) from this site. The format is covered in the tag system documentation.

From the home page, click the **Cell line tags** button.

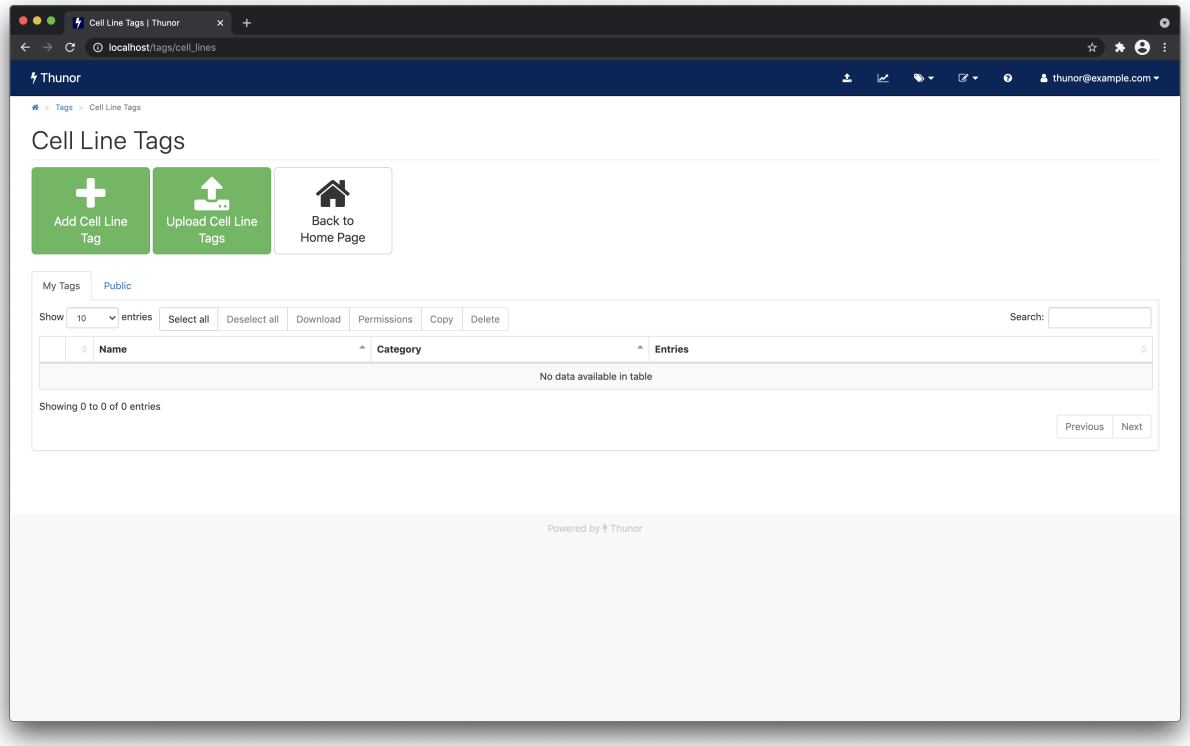

Image: Thunor Web - cell line tags page

Next, click **Upload Cell Line Tags**. Toggle the **Create cell lines if required** switch to **on** by clicking it. Then, drag and drop or browse for the exmaple cell line tags CSV file you downloaded. The tags will be created automatically and the page should refresh in few moments to look the one below.

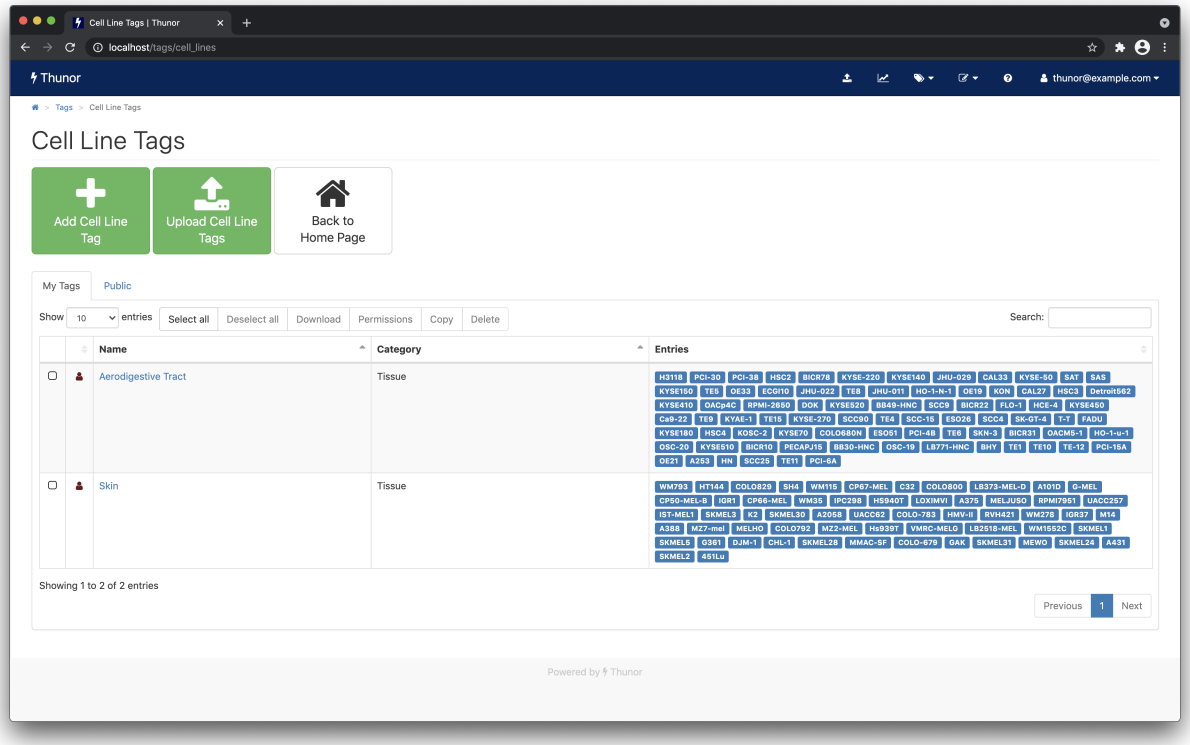

Image: Thunor Web - example cell line tags

Two example tags - “aerodigestive tract” and “skin” have been created, annotating several cell lines that originate from those tissues. Tags can be edited within this interface manually, and composite tags can be created using merge, intersection, and difference operations. Tags can also be shared with other users of the system by setting permissions, and downloaded for use with external tools. These features are all covered in the tag system documentation.

We’ve shown cell line tags here, but an analogous system exists for drug tags. Tags can be used to group cell lines and drugs in the plot system, both for visualization and for statistical tests.

4.12 Conclusions and further reading

Here, we’ve covered the basic functionality of Thunor Web, including installation; data upload, annotation, and sharing; the plot system; and the tag system. To explore the features of Thunor further, we recommend reading relevant sections user manual and exploring the online demo, which includes several datasets, including some labeled with tags.

Thunor is also available as a Python library, Thunor Core, which can be used with Jupyter Notebooks or within data analysis pipelines. Thunor Core has its own documentation, including a tutorial and modules reference.

If you’re interested in installing Thunor Web for multi-user, networked use, see the installation instructions. Server admins will also want to read about the admin interface and list of configurable options.

5 Thunor Web home page

The home page consists of a table of datasets on the left hand side of the page, and navigation buttons on the right.

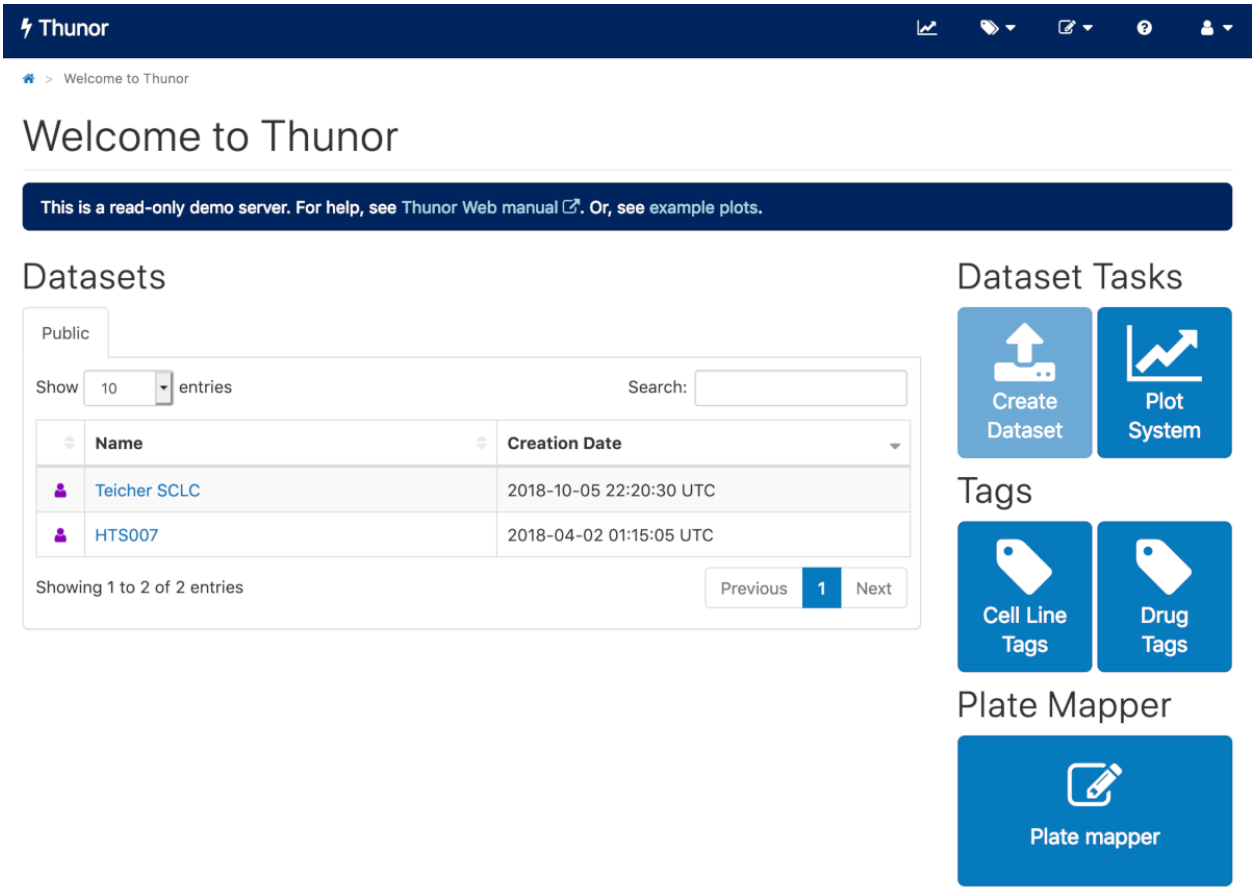

Image: Thunor Web home page

5.1 Dataset table

The dataset table shows the list of available datasets to which you have access. Above the table is a set of tabs, showing the groups to which your user belongs, which should include "Public" - the set of datasets accessible to all users of the Thunor instance. If you're logged in, you'll also see "My datasets", which are datasets you uploaded and own. If you require access to other groups, contact your Thunor administrator.

You can also search for a dataset by name using the search box.

To view a dataset, click on its name in the list. You'll then be on the dataset page. If the list is empty, there are no datasets in that group. If you are logged in, you can create a dataset.

In the first column of the table, a "person" icon shows each dataset owner in a different color. To view the user, hover the cursor over the icon.

5.2 Navigation buttons

On the right hand side (or below, on narrow screens), you will see a set of navigation buttons, which will depend on whether you are logged in and how your Thunor instance is configured by the administrator. These may include:

- Create dataset
- Plot system, for interactive visualization of datasets
- Tag system (cell line and drug tags), for applying custom "tags" for grouping sets of cell lines and tags, e.g. by cancer type, molecular target, or anything else.
- Plate mapper

6 Site navigation

6.1 Anonymous access to public datasets

Depending on how the administrator has set up the Thunor instance, you will either see a list of public datasets when you first visit the site, or be asked to log in. If you are asked to log in, see create an account.

6.2 Logging in and out

1. To log in, move your cursor over the "person" icon in the top right (or tap, on mobile devices), and click *Log in*. Enter your username and password and click the "Log in" button.
2. You will see your email address in the top right of the site when you're logged in.
3. To log out, move your cursor over the "person" icon in the top right (or tap, on mobile devices), and click *Log out*.

6.3 Navigation bar

The navy bar across the top of every page on the site allows navigation.

- Click the site logo in the top left to return to the home page
- Use the icons in the top right to navigate between key features. More your cursor over each icon for a description.

7 Create an account

Note: To create an account on a Thunor instance, the server administrator must have allowed public signups. Contact the server administrator for further information.

1. To create an account, hover the cursor over the "person" icon on the top right (or tap on touch devices), and click on **Create Account**.
2. Enter your e-mail address, password, and type the password again for confirmation. Click **Sign Up**.
3. You'll receive an email at the address you entered, usually within a few minutes. Click on the link in the email to confirm your account.
4. Your account is now ready for use. If you wish to join any groups other than the "Public" group, contact the server administrator.

8 Create a dataset

8.1 File formats

Thunor accepts several file formats containing cell count data from high throughput experiments.

8.1.1 Vanderbilt HTS Core format

Thunor Web can accept annotated (with cell lines, drugs, and concentrations) or unannotated uploads in this format. Annotated files require all the fields in the table below, except those marked as optional. Unannotated files must omit all of cell.line, and "drug" prefixed fields - i.e. the only fields required for unannotated data are upid, well, cell.count and time.

If uploading unannotated data, plates can be annotated with cell lines, drugs and concentrations using Thunor Web's plate mapper.

Tab-delimited format, UTF-8 character encoding. Fields may be in any order. Extra columns may be present but will be ignored. The plate size will be detected based on the highest well number of the plate.

Field	Data type	Description
upid	string	Unique plate ID (only needs to be unique within a dataset)
well	string	Well position on a plate, 1 character and 2 numbers, e.g. `A01`
cell.count	non-negative float	Count of cells in specified well (or a fluorescence proxy for cell count)
time	non-negative float	Time in **hours**
cell.line	string	Cell line name
drug1	string	Drug 1 name
drug1.conc	non-negative float	Drug 1 concentration (molar)
drug1.units	string	Must be `M`
expt.id	string	Experiment ID (optional)
expt.date	string	Experiment date `yyyy-mm-dd` format (optional)
drug2, drug2.conc, drug2.units		Defined analogously to drug1 fields

8.1.1.1 Notes Any other columns may be present but will be ignored.

8.1.2 Thunor HDF5 format

Files downloaded from Thunor, or from the Thunor Python package, in HDF5 format.

8.1.3 IncuCyte Zoom format

Thunor can also read files from the IncuCyte system from Essen BioScience. The IncuCyte Zoom software should be used to export a fluorescence marker proxy for cell counts. By default, the filename will be used as the plate name, unless a value is present in the `Label:` field.

The export can either contain one unified quantification per well (which by default is the median), in which case the header looks like the first example below, or each image can be exported separately, like the second example below. In the latter case, a unified score for each well is calculated as the sum of the values across all images at each time point.

```
Label:

Date Time   Elapsed A1  B1  C1 ...
```

In the above example, one count (fluorescence readout) is specified per well.

```
Label:

Date Time   Elapsed A1.Image1 A1.Image2 B1.Image1 B1.Image2 ...
```

8.2 Process

To begin, click **Create Dataset** on the home page, or using the icon in the menu at the top of the page. You'll need to be logged in to create a dataset.

1. Give the dataset a name, and click **Next**.
2. Drag and drop cell count files into the marked area, or alternatively use the **Browse** button to locate files on your computer.
3. The upload will start automatically. This process may take several minutes, depending on the size of the files.

4. Click **Proceed to Plate Mapper**. See the plate mapper documentation for more detail on the next step.

9 Dataset page

The dataset page shows you actions for the current dataset along with descriptive metadata. If viewing a dataset owned by another user, some of these options may not be available due to the permissions they have set.

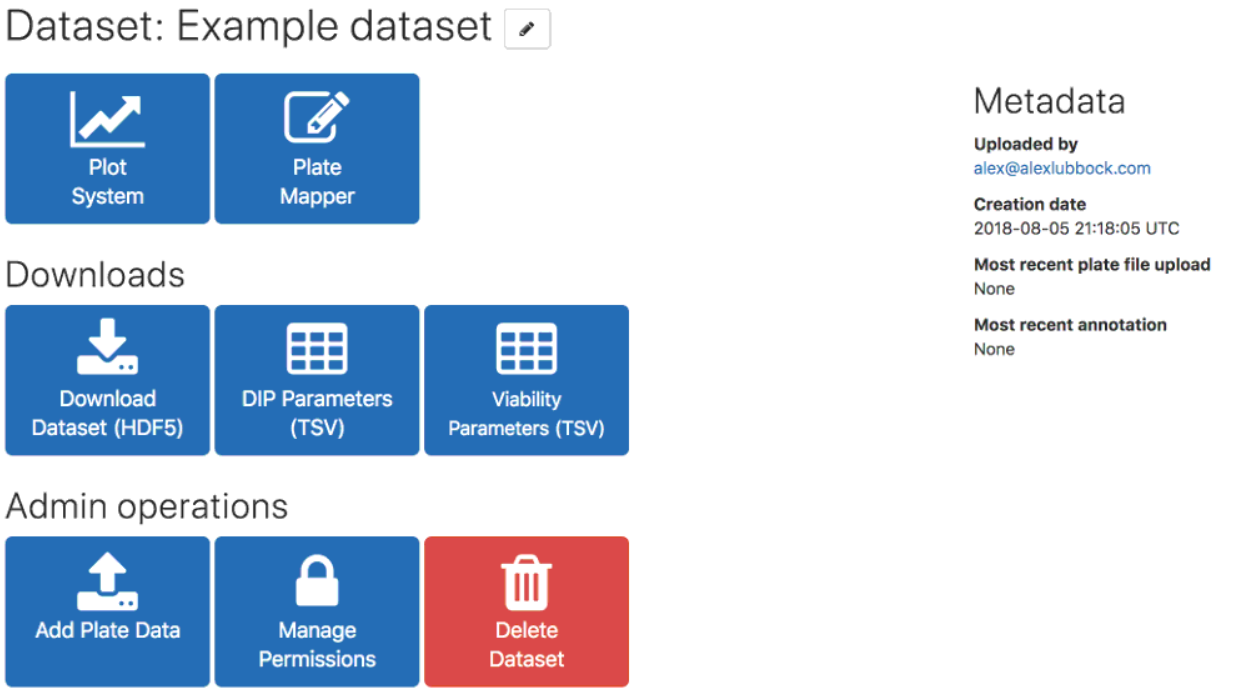

Image: Part of the Thunor Web dataset page

9.1 Dataset actions

- Plot system, for interactive visualization of datasets
- Plate mapper, for viewing and editing the plate annotations (labels for each well's cell lines, drugs, and drug concentrations)
- **Download as HDF5**, which is a compressed, hierarchical data format. The dataset can be used with other instances of Thunor.
- **Viability parameters (TSV)**, containing the viability curve fit metrics for each cell line/drug combination in tab-separated value format.
- **DIP parameters (TSV)**, containing the DIP curve fit metrics for each cell line/drug combination in tab-separated value format. Only available for datasets with multiple time points.
- **DIP rates (TSV)**, containing the DIP rate values for each well in the dataset. Only available for datasets with multiple time points.

9.2 Admin operations

These are only available to the owner of the dataset.

- **Add plate data**, to upload additional cell count data to the current dataset
- Manage permissions, to control who can access this dataset
- **Delete dataset**, to delete the current dataset.
- To **rename a dataset**, click the "pencil" icon next to the dataset's title.

9.3 Dataset metadata

This section shows the metadata associated with the dataset, such as the owner, the date it was upload to Thunor, and the date it was last edited.

10 Dataset permissions

Dataset permissions control who can access a dataset. Access control is handled by groups, which are collections of users created and managed by Thunor administrators. For managing group membership, see the admin interface documentation.

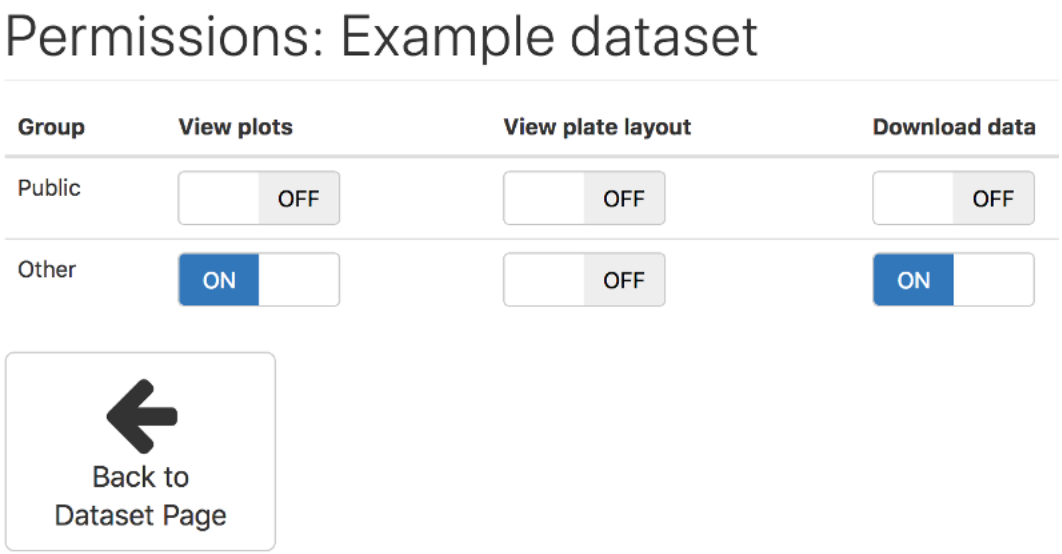

Image: Part of the Thunor Web dataset permissions page

10.1 Types of permission

- **View plots** allows users in the group to view and create interactive plots, including downloading the plots as images. Downloading the data underlying a plot (CSV or JSON format) requires **Download data** permission
- **View plate layout** allows users in the group to view the plate layout, including which drugs, cell lines, and doses were used. Only the owner can edit the plate layout regardless of this setting.
- **Download data** allows users in the group to download the complete dataset in HDF5 format, dose response parameters in CSV format, or the data underlying any plot in the plot interface in CSV or JSON formats.

10.2 Setting permissions

The current permissions are shown in a table, with groups in the rows and permission types in the columns. To set a permission, simply toggle the relevant switch by clicking (or tapping, on a mobile device). Likewise, toggle the switch back (shown as "OFF") to unset a permission.

11 Tag system

Tags can be applied to cell lines or drugs separately. The system works identically in both cases.

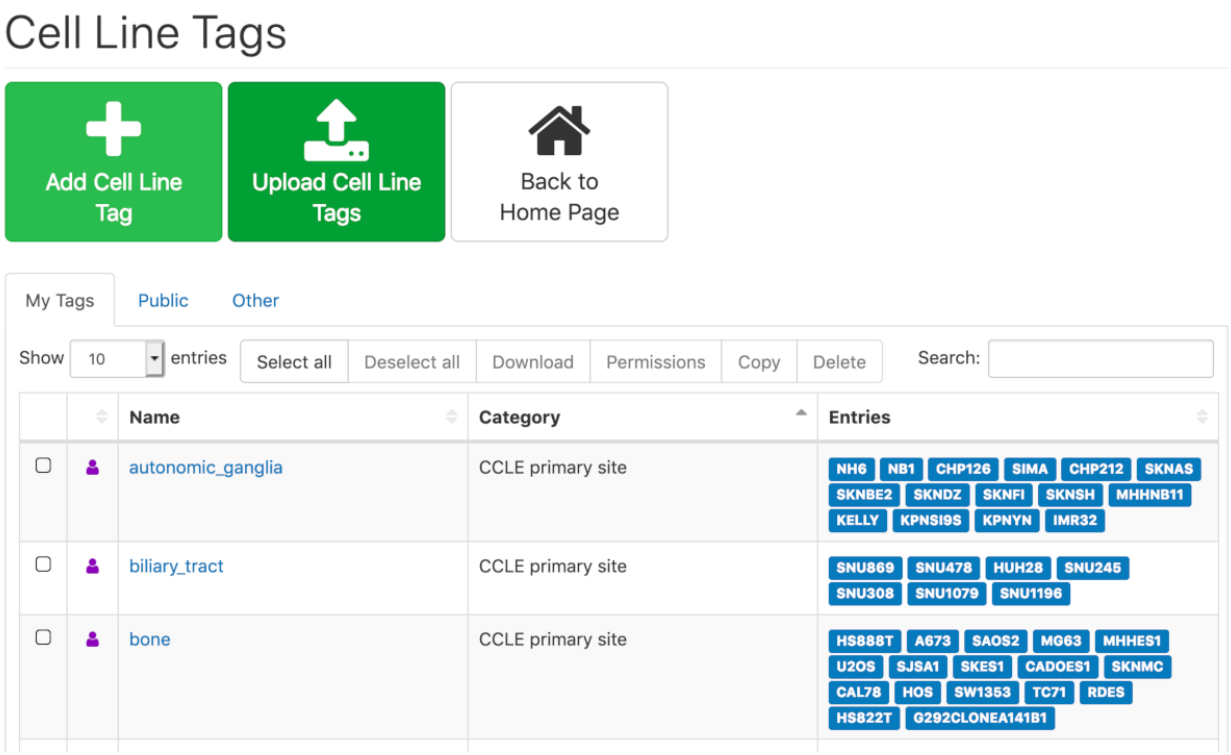

Image: Part of the Thunor Web tag interface

11.1 What are tags?

A tag is simply a label applied to one or more cell lines or drugs. Examples include cell line mutations, cell line tissues of origin, drug molecular targets, or drug classifications. Tags can be used for aggregating sets for visualization and statistical analysis, particularly in the plot system.

Tags can be grouped together into categories, and shared with other users.

11.2 View tags

From the home page, click the **drug tags** or **cell line tags** button. The tag browser is also accessible from any page by hovering the tag icon in the menu at the top of the page, and selecting either cell line or drug tags.

The tag browser interface contains a table with a list of tags. A set of tabs above the table list user groups: you will see a tab labelled “My tags”, for tags that you’ve created, plus a tab for each user group of which you’re a member (including “Public”). The table can be searched by tag name, category, or tag target (cell line or drug) using the search box.

In the first column of the table, a “person” icon shows each tag owner in a different color. To view the user, hover the cursor over the icon.

11.3 Create a tag

To create a tag, click the **Add cell line tag** or **Add drug tag** button. Give the tag a name and (optionally) a category, then click **Create**. Specify tag targets (cell lines or drugs) using the dropdown box and click **Save tag**.

11.4 Edit a tag and assign permissions

To edit a tag, click its name in the tag table. You will only be able to edit tags that you own. Click the dropdown selection, and enter select one or more cell lines or drugs (using the search box if desired). Afterwards, close the dropdown selection box, and click **Save tag** to save the changes.

To rename a tag or change it's category, click the **Rename** button. Enter a new tag name and/or category, and click **Save name** to save the changes.

To assign permission to a user group to use the tag, click the toggle switch next to the group name in the popup window.

For managing group membership, see the admin interface documentation.

11.5 Assign permissions in bulk

First, select a set of tags by clicking on each row of the table, or using **Select all**. You can also use the search facility, noting that **Select all** will limit itself to the search result. Click the **Permissions** button at the top of the table. In the popup window, click the toggle switch next to group name to share the selected tags with the group.

The toggle switches will show whether the set of tags are already shared with each of the groups. In the case that some of the selected tags are shared with a particular group and some are not, you'll see the switch in a "half on, half off" *indeterminate* state.

11.6 Delete a tag

To delete a tag, click its name in the tag table, then click the **Delete** button in the popup window. After a tag is deleted, it cannot be recovered.

You can also delete tags in bulk, by selecting several rows in the table as described above, then clicking the **Delete** button above the table.

11.7 Copy and merge tags

First, select a set of tags by selecting rows in the table, as described in the "assign permissions" section above. Then, click the **Copy** button. There are three tag copy modes:

- **Separate**, which duplicates each selected tag separately into a new tag category
- **Merge (union)**, which will generate a single new tag which contains all of the cell lines/drugs in the selected tags
- **Intersection**, which will generate a single new tag which contains the cell lines/drugs which are present in all of the selected tags

Enter a new **Tag category** in the text box (an existing tag category will work, providing there are no tags with the same name in that category already). Depending on whether the selected mode generates a single tag or multiple tags, you may be prompted to enter a new **Tag name**.

Click the **Copy tags** button to complete the process.

11.8 Upload a set of tags

A set of tags can be uploaded from a comma-separated or tab-separated values file (CSV or TSV). Here's an example of the drug tag file layout, containing two drugs which target BRAF.

tag_name	tag_category	drug
BRAF	Drug target	dabrafenib
BRAF	Drug target	sorafenib

Download drug tag example

And an example for cell line tags, illustrating cell lines with a BRAF mutation:

tag_name	tag_category	cell_line
BRAF-mut	Cell line mutation	SKMEL5
BRAF-mut	Cell line mutation	Jurkat

Download cell line tag example

11.9 Download a set of tags

To download a set of tags, first select them by clicking on each row of the table, or using **Select all**. You can also use the search facility, noting that **Select all** will limit itself to the search result. To download the current selection, click **Download**. The tags will download in a tab-separated format as described in the upload section, above.

11.10 Use tags for plots

The tags created in this system can be used in Thunor Web plots. See plot system.

12 Plate mapper

High-throughput screen datasets consist of one or more multi-well plates, typically containing 96, 384, or 1536 wells. *Annotation* is the process of connecting experimentally acquired data (e.g. cell counts) with the metadata describing what's in each well, typically a cell line, and one or more drug(s) with their associated concentrations. Depending on the data acquisition pipeline and equipment, the plates might get automatically annotated, or this can be left to the end user to do manually.

Thunor Web's plate mapper is a tool for viewing and editing plate annotations which has been optimized for efficient data entry. It has capabilities to reduce the amount of data entry, for example by applying a template layout to multiple plates, and by using a flexible "auto-stepper" which automates stepping between regions of plate (e.g. moving to the next column, next row, or even stepping in blocks of multiple columns/rows) to reduce keystrokes.

The plate mapper can be used in two modes:

- **Standalone mode** allows you to design a plate layout without attaching it to a dataset. The layout can be exported for later use in Thunor Web, or for use with external programs and pipelines. To start a standalone plate map, click the **Plate mapper** button on the bottom right of the Thunor Web home page, and select a plate size. You can try the plate mapper in standalone mode on the Thunor Web demo site.
- **Dataset annotation mode** allows you to view and edit the plate layouts of a recently uploaded dataset. The plate mapper is shown as part of the data upload process, or by selecting **Plate layout** from a specific dataset's page. Datasets uploaded with annotation data already present will be pre-populated in the plate mapper. Only the owner of a dataset can edit the plate annotations, but the owner may delegate access to view the plate layout.

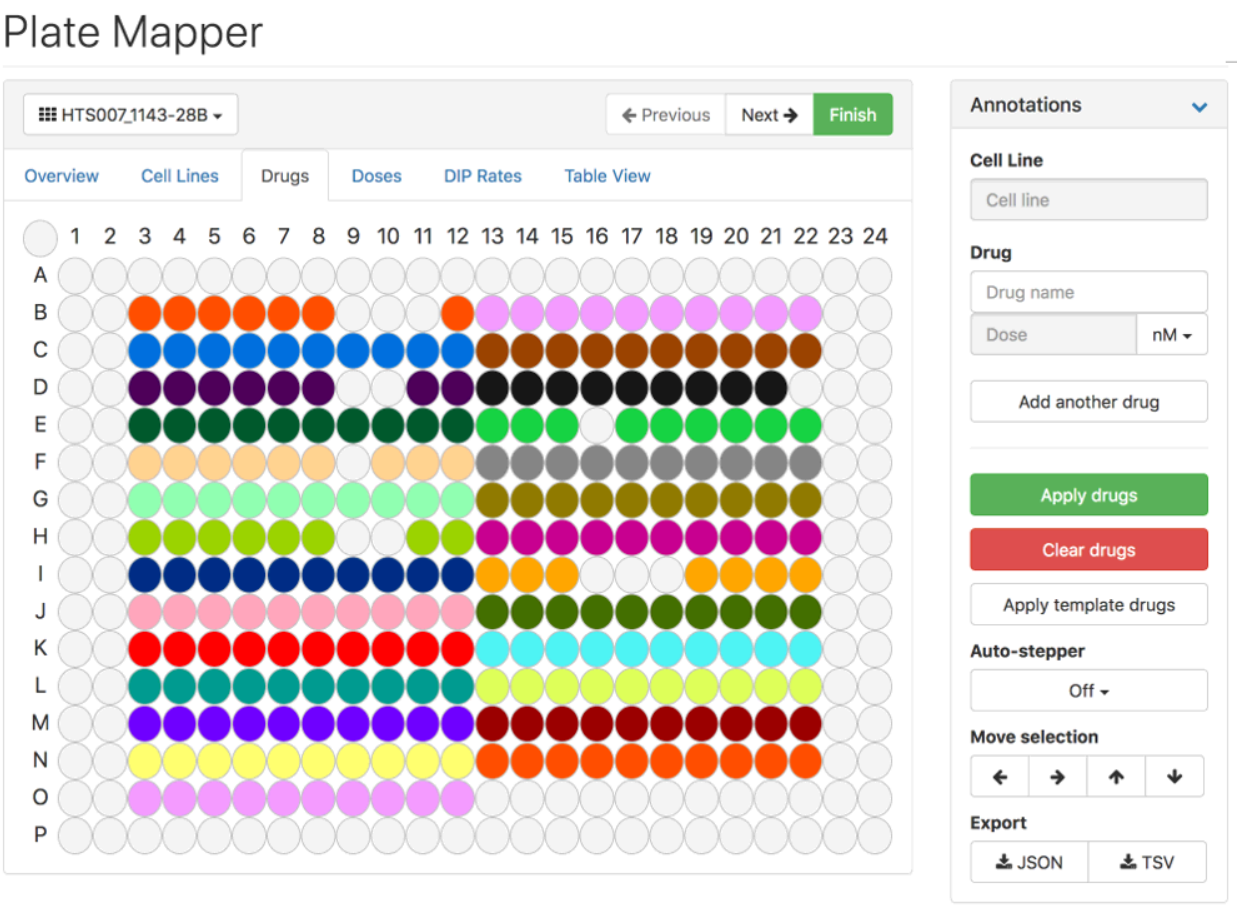

Image: Part of the Thunor Web plate mapper interface

12.1 Overview

The plate mapper consists of a representation of a multi-well plate, navigation to change the currently active plate in a dataset (dataset annotation mode only), an annotation panel for viewing and editing the currently selected wells, and a legend showing the color scheme of the currently active plate view.

In dataset annotation mode, the well annotations will show automatically if these data were present in the upload. If no changes are required, simply click **Finish**.

12.2 Navigate between plates

In dataset annotation mode, you can navigate between plates in the dataset. A dropdown box in the top left shows the name of the currently active plate. Click this box and select another plate name to change plate. You can also use the **Next** and **Previous** buttons to change plate.

If you have edit permissions for the dataset, the plate dropdown box will also show **Template master** at the top. Click this to enter template mode (see *Use a template* section, below).

12.3 Plate map views and legend panel

Plate map views change which annotations are displayed on the plate map. Click on one of the tabs to change the active view. For a description of the color scheme in each view, switch to that view and look at the **Legend** panel.

The **Annotations** panel can be hidden (collapsed) by clicking the chevron (down arrow) on the right-hand side of the header. This makes viewing the **Legend** panel, which is below the annotations panel, easier.

- **Overview** shows which wells have been annotated with cell lines, drugs, and doses, or a combination of these three.
- **Cell lines** colors the wells based on the cell lines in the dataset.
- **Drugs** colors the wells based on the drugs (or drug combinations) in the dataset.
- **Doses** colors the wells based on the unique doses (or dose combinations) in the dataset.
- **DIP Rates** colors the wells based on the drug-induced proliferation rate (DIP rate) in each well.
- **Table View** shows the complete annotation information in a table, which can be sorted (click on a column heading) and searched (type in the search box).

12.4 Well annotation

The annotation panel describes the currently selected wells, and allows editing the selected wells if the user has permission. If the user doesn't have edit permission, the text boxes will be greyed out, but the user can see the annotations of any well by hovering the mouse over the well (or tapping it, on touch devices).

The rest of this section applies only to users with edit permission, or when using standalone mode.

12.4.1 Select a set of wells

To select wells, click and drag across wells to make a rectangular selection. To make an irregular selection, hold Ctrl (Windows or Linux) or command (Mac) and make another selection, to build the desired selection out of a set of rectangular selections. To select entire columns or entire rows, click on the column numbers or row letters (or click and drag to select multiple). To select or deselect the entire plate, click the "well" in the top left (above the "A", left of the "1").

To manually move the current selection left, right, up, or down, click the arrows under **Move selection**.

12.4.2 Data entry

You can enter data in one or more of the fields at a time - cell line, drug name, or dose. You can tab between fields to enter more data. Pressing *Enter* or clicking **Apply** will apply the labels to the currently selected wells, and deselect them. If the auto-stepper is enabled (see below), the next set of wells will be selected.

For cell lines and drugs, begin typing a name. Thunor will offer suggestions matching existing cell lines or drugs in the system - click the selection to accept it. If no suggestion matches, press enter after typing the full name to create the cell line or drug in the system.

For doses, enter the dose numeric part in the dose box, then select the suffix from the dropdown box (nM for nanomolar, µM for micromolar etc.). Click **Apply** when complete. Alternatively, you can select the suffix first, then enter the numeric amount in the dose box, and press *Enter*.

To enter multiple drugs, click the **Add another drug** button. An additional set of drug name and dose fields will appear, defined analogously to the ones for the first drug. If some wells only have one drug, leave the fields for the second drug blank.

12.4.3 Clear annotations

To remove annotations from wells, select the wells as described above, and click the **Clear** button. Note that this will remove annotations based on the currently selected view (cell lines in the cell line view, etc.). To remove all annotations from the wells, make sure the **Overview** tab is selected.

12.4.4 Use the auto-stepper

It is common to use repetitive patterns in plate designs, e.g. different drugs in columns, different doses in rows. The auto-stepper makes entering this annotation information faster by automatically moving the currently selected wells after data has been entered.

To use the auto-stepper, select the initial set of wells you wish to annotate. Then under **Auto-stepper**, select a mode from the options:

- **Move down 1 well** will move the selection down the plate one well after data entry
- **Move down selection height** will move the selection down by the height of the selection after data entry (e.g. to annotate pairs of rows at once)
- **Move right 1 well** will move the selection right along the plate one well after data entry
- **Move right selection width** will move the selection right by the width of the selection after data entry (e.g. to annotate pairs of columns at once)

12.5 Download the plate map

The plate map can be downloaded in either javascript object notation (JSON) or tab-separated values (TSV) formats. Under the **Export** section in the Annotations panel, click either **JSON** or **TSV** to download the plate map.

12.6 Upload a plate map

Previously downloaded plate maps can be used as the basis for a new plate map. Under the **Import** section in the Annotations panel, click the **Select file...** button to select a plate map (JSON or TSV format) from your computer.

12.7 Use a template

The template view provides a blank plate map which can be used to apply annotations to multiple plates at once (dataset annotation mode only, for users with edit permissions).

To switch to the template view click the dropdown box with the current plate name in the top left of the screen, and select **Master template**. Proceed to make annotations on the plate as defined above. Note that you can enter one, two or all types of annotation to apply to multiple plates, as desired (types of annotation means cell lines, drugs, or drug doses).

In the template view, a new dropdown box and button appears near the plate selection drop down box. Select the new dropdown box labelled **Apply to plates**, and select the plates you wish to annotate with what's currently on the template. Click **Apply template** to make the changes.

To exit the template view, click on the plate dropdown box (labelled **Master template**), and select a plate name from the dataset.

12.8 Exit the plate mapper

To exit the plate mapper, click **Finish**. This button may not be enabled if there are plates that remain unannotated in dataset annotation mode.

13 Plot system

Statistical tests within the plot system rely on certain assumptions that the user should verify before interpreting the results. See the statistical tests section for details.

The Thunor Plot System is an interactive visualization platform for high-throughput screen data. It supports multiple types of plots, a panelled interface for displaying multiple plots at once, plot interactivity (e.g. hovering mouse to view coordinates of a point), and exporting PNG or SVG graphics or raw data (JSON or CSV) from plots.

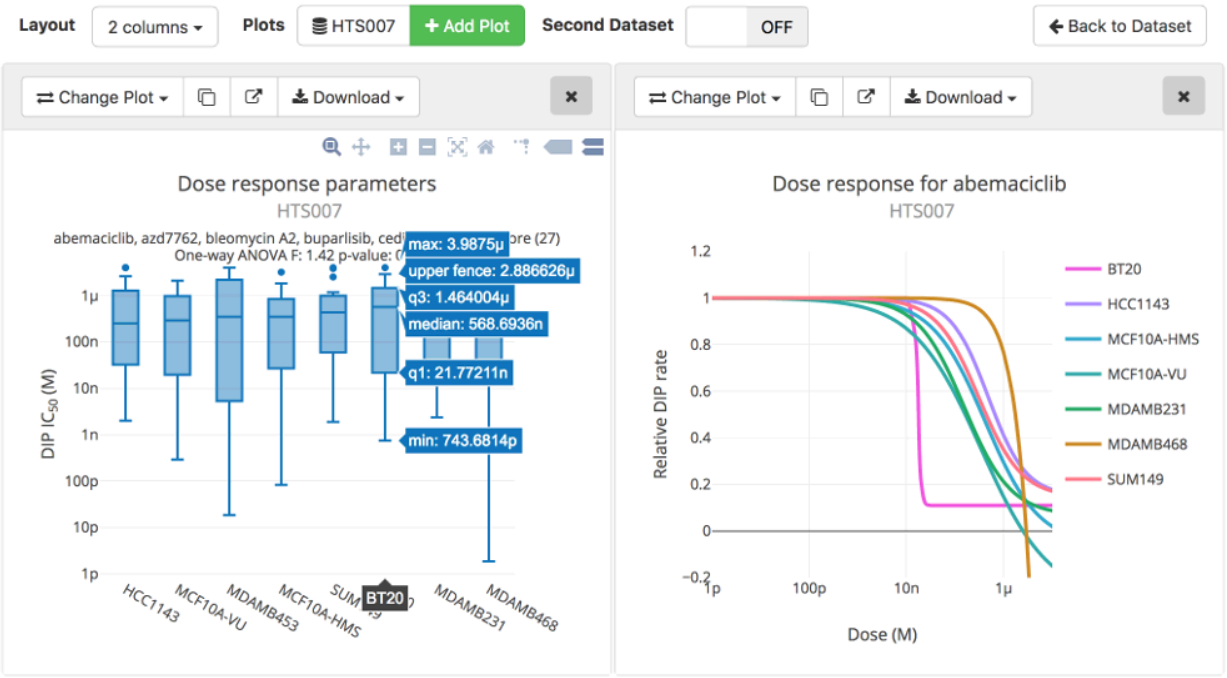

Image: Part of the Thunor Web plot system interface, showing box plots and dose response curves.

13.1 Plot System Layout

The plot system consists of a master toolbar (with **Layout**, **Plots**, and **Dual Dataset Plot** sections). The **Layout** section may not display on narrow devices (e.g. mobile phones). A **Quick start guide** is displayed until the first plot is loaded, whereupon it's replaced with the plot panel.

13.2 Select a dataset

Under the **Plots** section in the master toolbar, there is a button showing the currently active dataset, if there is one, or **Select Dataset** if no dataset is active. To change the currently active dataset, click on this button at any time.

Note that changing the active dataset(s) or Dual Dataset Plot mode (see next section) will only affect new plots - any plots already open will be unaffected. Thus, it is possible to compare plots from different datasets side by side in separate panels.

Clicking the dataset button will bring up a panel to select a new dataset. This panel is the same as the one on the home page of Thunor. Select a group from the available tabs at the top, then click a dataset name to select it. You can also search for a dataset by name using the search box. Click the *X* in the top right to close the panel without changing the dataset.

13.3 Dual dataset plots

Multiple plots can be loaded at the same time, by changing the active dataset (see above) and clicking **Add Plot** iteratively for each desired plot. By contrast, dual dataset plot is a feature that compares two datasets **on the same plot**.

To activate this feature, click the switch next to **Dual Dataset Plot** to *ON*. A second dataset button appears in the **Plots** section of the master toolbar, which can be clicked to change the active second dataset. Note that plot panels with two datasets loaded will have a different set of plot types available. This setting only affects new plot panels - already loaded plots are unchanged (you can sequentially load multiple plots from different datasets or dataset combinations).

To turn off this feature, toggle the **Dual Dataset Plot** switch to *OFF*.

13.4 Add a plot

To add a plot, click the **Add Plot** button. Note that if no dataset is currently active, you will be shown the dataset panel to select one first. A new "plot panel" will appear - a box with a grey header bar and a plot area, which is blank until a plot is selected.

The plot type is selected using the **Change plot** button, which is selected by default when a new plot is added. The *options panel* then appears with options for the current plot. For details, see **Choose plot options**, below.

13.5 Plot types

The plot type is chosen from the options panel, which can be accessed on any plot at any time by click on the **Change plot** button.

To use the options panel to create or modify a plot, first select a plot type, then enter options specific to the plot type, if applicable, then click the **Show Plot** button.

13.5.1 Time Course

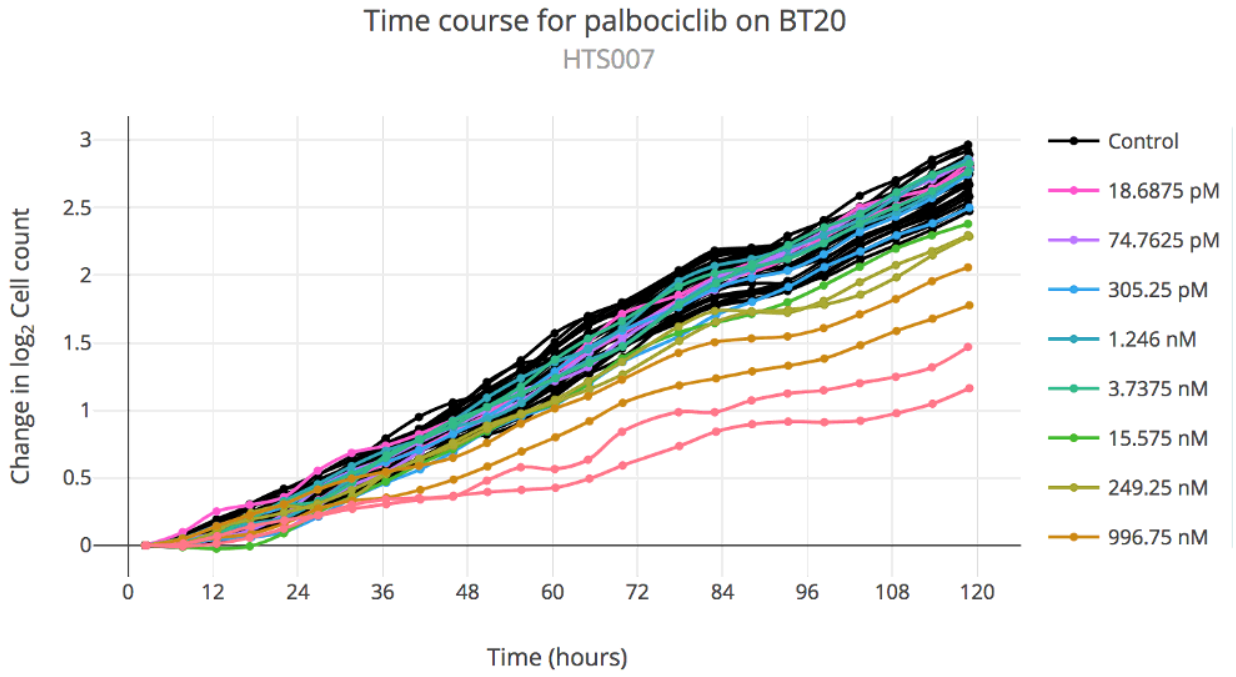

Image: Thunor Web time course plot example, showing the change in log2 cell count (i.e. cell population doublings) over time.

A Time Course plot show the change in an assay value (typically, cell count) over time. The x-axis shows time in hours, and the y-axis shows the change in assay value. It is not available for panels with two active datasets. The following plot options are available:

- **Cell Line**. Only a single cell line can be selected at a time for this plot type. Select from the list or type a name.
- **Drug**. Only a single drug (or drug combination) can be selected at a time for this plot type. Select from the list or type a name.
- **Vertical Axis** (DIP rate only): *Doublings (log2)* uses a log base 2 y-axis showing change from baseline (i.e. the axis starts from zero), *Linear* uses a linear (untransformed) y-axis.

- **Overlay Dip Fit** (only available for log2 vertical axis on DIP rate data) Turn this option on to overlay the DIP rate fit on the cell count data (a straight line on a log2 plot). Allows a visual assessment of goodness of fit.

13.5.2 Dose Response Curves

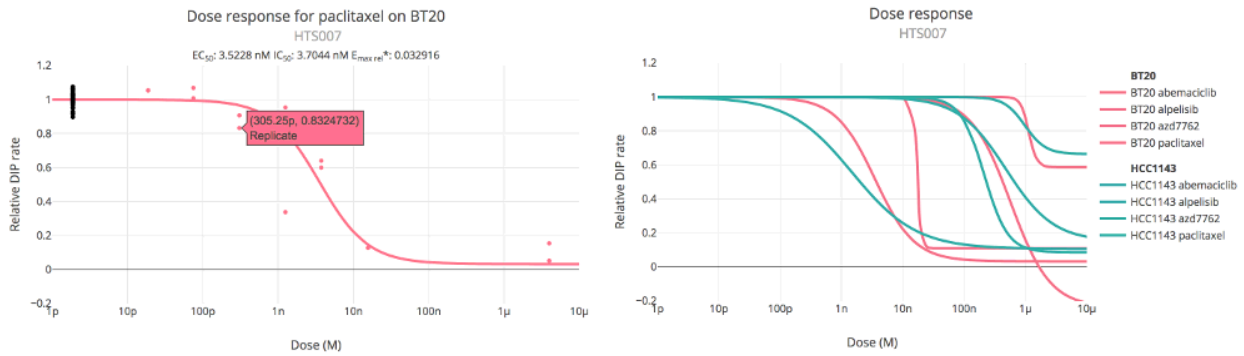

Image: Thunor Web dose response curve examples, showing the relative DIP rate by dose. **Left**: A single dose response curve with experimental (*red*) and control (*black*) data points. Values can be displayed by hovering the mouse, or tapping on touch devices. **Right**: Multiple dose response curves can be overlaid, and colored by cell line, drug, or tag.

A dose response curves plot shows fitted dose response curves to the DIP rates. If only a single cell line/drug (or drug combination) is selected, the DIP rate data points are shown, to allow a visual assessment of goodness of fit. The following plot options are available:

- **Cell Line**. One or more cell lines can be selected by name or by tag. Tags are collections of cell lines annotated with a label (see Tag System). Select cell lines by clicking on them or typing a name to search after clicking the dropdown box. To use tags, click the **Tags** button and select one or more tags, by clicking or typing their names.
- **Drug**. One or more drugs can be selected by name or by tag. Tags are collections of drugs annotated with a label (see Tag System). Select drugs by clicking on them or typing a name to search after clicking the dropdown box. To use tags, click the **Tags** button and select one or more tags, by clicking or typing their names.
- **Color overlay**: Specify how to color and group the dose response curves. By default, each curve will receive a different color. You can also color the curves by cell line or drug by selecting those options.
- **Response metric**: Show response curves for *Viability* or *DIP rate*. This option is only shown if the dataset has the multiple time points required for DIP rate calculation.
- **Vertical axis** (DIP rate only): Select *Relative* to use relative DIP rate (minimum effect, E0, is set to 1), or select **Absolute** to use an absolute scale y-axis.

For details on the curve fitting process, see curve fits.

13.5.3 Dose Response Parameters

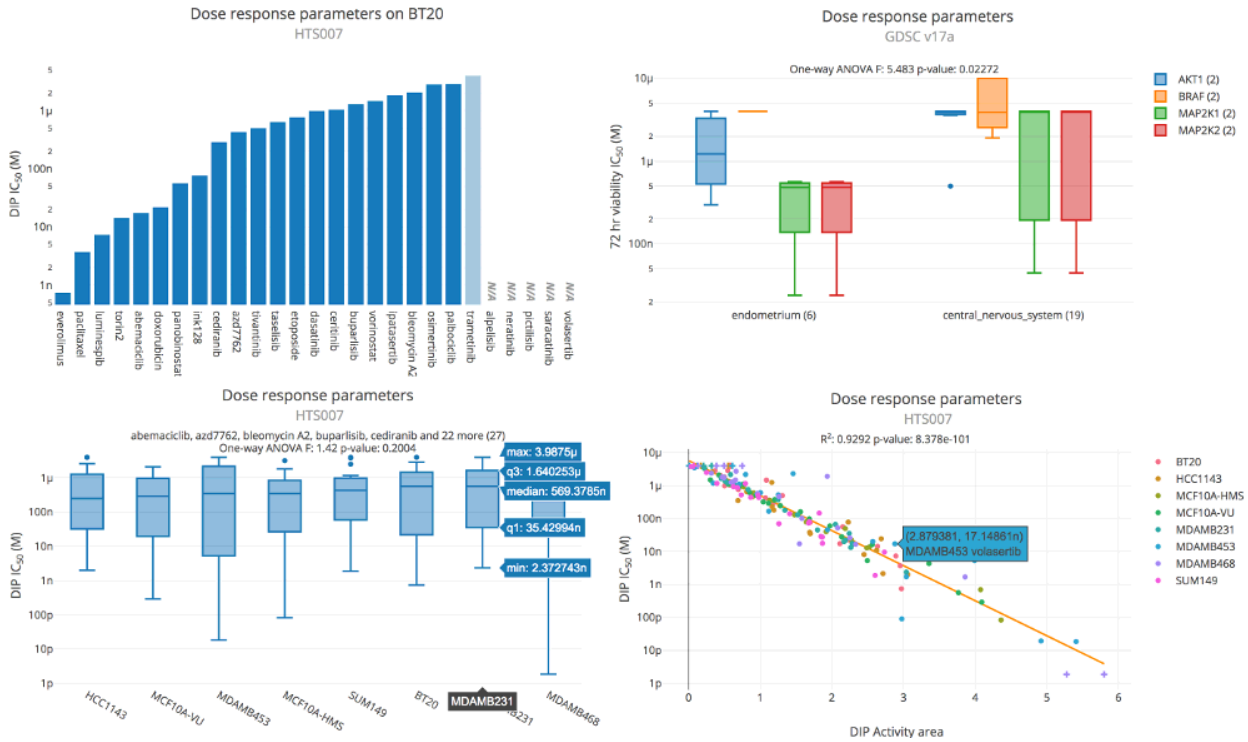

Image: Thunor Web dose response parameter plot examples. **Upper left**: Bar plot showing DIP rate IC50 across a selection of drugs. **Upper right**: Box plot showing viability IC50 across two tissue types (endometrium and central nervous system) and four molecular drug targets (AKT1, BRAF, MAP2K1, MAP2K2). The tissue types and drug targets are defined as tags (see tag system). **Bottom left**: Box plot showing DIP IC50. Each box shows the IC50 values across 27 drugs for a particular cell line (x-axis label). **Bottom right**: Scatter plot showing DIP activity area (x-axis) versus DIP IC50 (y-axis). Each point represents a cell line/drug combination, colored by cell line. The orange line represents the best fit from linear regression.

A Dose Response Parameters plot shows parameters extracted from dose response curve fits, such as IC50 and EC50. Depending on the plot options, the plot may be a bar plot, box plot, or scatter plot. Bar plots are used to visualize a single parameter, box plots for a range of parameters on aggregated data, and scatter plots for comparing two different parameters, or the same parameter across two datasets.

On scatter plots, some parameter values get "truncated" - the value is set to the outer limit of the measured range, where the model estimate lies outside of that range (e.g. an EC50 which is higher than the maximum measured concentration). This is denoted with a red cross symbol.

Bar and box plots are sorted in ascending order of the selected parameter by default, but this can be overriden by the **Ordering Parameter** option described below.

For descriptions of each of the parameters, see dose response parameters.

The following plot options are available:

- **Cell Line**. One or more cell lines can be selected by name or by tag. Tags are collections of cell lines annotated with a label (see Tag System). Select cell lines by clicking on them or typing a name to search after clicking the dropdown box. To list parameters for each cell line separately, click the **Separate** button, otherwise use **Aggregated** to combine them as a group. To use tags, click the **Tags** button and select one or more tags, by clicking or typing their names. Parameters are shown for each tag separately if **Separate** is selected, otherwise they can be **Aggregated** (all constituent cell lines are shown as a group).

- **Drug**. One or more drugs can be selected by name or by tag. Tags are collections of drugs annotated with a label (see Tag System). Select drugs by clicking on them or typing a name to search after clicking the dropdown box. To list parameters for each drug separately, click the **Separate** button, otherwise use **Aggregated** to combine them as a group. To use tags, click the **Tags** button and select one or more tags, by clicking or typing their names. Parameters are shown for each tag separately if **Separate** is selected, otherwise they can be **Aggregated** (all constituent drugs are shown as a group).
- **Color overlay**: Specify how to color and group the plot data. The plot traces can be colored by cell line or drug if required. This option also affects the groups defined for statistical tests, if applicable. Color overlays are not currently supported with box plots.
- **Response metric**: Show response curves for *Viability*, *DIP rate*, or *Compare*. This option is only shown if the dataset has the multiple time points required for DIP rate calculation. The *Compare* option uses the viability version of a metric on the x-axis, and the DIP rate version of a metric on the y-axis.
- **Parameter** defines the dose response parameter to visualize. These are grouped by inhibitory concentration (e.g. IC50), effective concentration (e.g. EC50), effect size (e.g. Emax, E50), or other (Hill coefficient or Activity Area). When selecting a parameter marked with `(custom value)` a custom integer value between 0 and 100 may be entered. This allows parameters like EC25.
- **Second Parameter** can be toggled on or off with a switch. Toggle to *ON* to compare two parameters against each other. The available parameters are the same as the first parameter.
- **Ordering Parameter** can be toggled on or off with a switch. It cannot be combined with a Second Parameter. The Ordering Parameter defines the x-axis ordering. This can be used to aid direct comparisons between two parameters, by keeping the ordering the same across two plots. In addition to sorting by a specific parameter, there is an option for alphabetical sorting by x-axis label.

The following statistical tests are performed:

- On **scatter plots**, a line of best fit is calculated using linear regression and shown as an orange line. Data points which are truncated in either axis are excluded from the fit. The R2 and p-value for the fit are shown above the plot.
- On **box plots**, a one way analysis of variance (ANOVA) is calculated, which tests for statistically significant difference in means of a dose response parameter across the groups. Please note that, depending on the groups used for the box plots, an ANOVA test may not be statistically appropriate - it is down to the user to consider whether it is so. In particular, one-way ANOVA assumes that

(1) Response variable residuals are normally distributed; (2) Population variances are equal; (3) Responses for each group are independent and identically distributed (i.i.d.), and normally distributed random variables.

- On **bar plots**, if certain criteria are met, a two-sided Mann-Whitney U test is calculated, which tests for statistically significant difference in the *ranks* of two random variables. Here, Thunor will test for the difference in the ranks of a dose response parameter (e.g. IC50) between two groups (cell lines, drugs, or tags). The test will only be run if the plot contains exactly two groups (defined by the number of cell lines/drugs/tags and the "color by" option), and both groups contain more than 20 data points. The test has continuity correction applied. The test assumes that data points are independent.

13.5.4 Quality Control

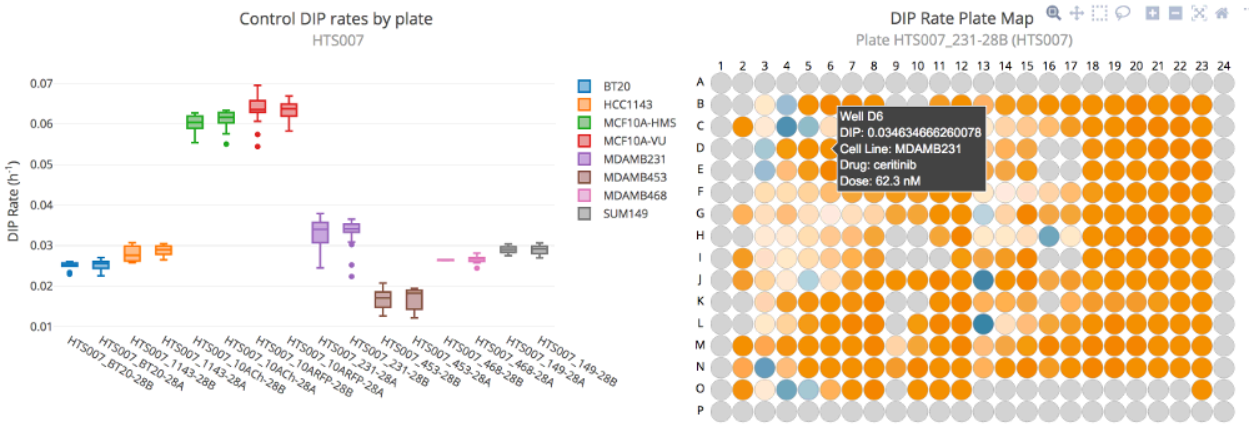

Image: Thunor Web quality control plot examples. **Left**: Box plot of control DIP rates by plate and cell line. **Right**: Plate map showing DIP rate as a heat map across a plate. Positive DIP rates are shown in orange; negative in blue.

Quality Control plots are used to check for experimental anomalies within a dataset.

Three options are available:

- **Control DIP Box Plot** shows the distribution of control DIP rates across each plate as a box plot. This can be used to spot plates with a wide distribution of control proliferation rates, or large differences in control proliferation rates across different plates with the same cell line.
- **DIP Rate Plate Map** shows a representation of the plate map, with wells colored by DIP rate. This may be useful for spotting spatial effects within a plate, e.g. cells at the plate edge grow more slowly in control.
- **Control Cell Count Box Plot** shows the distribution of control cell counts for a viability (single time point) dataset. Note that this is only a meaningful quality control check if starting cell counts (seeding density) for each cell line are tightly controlled and equal across wells and plates at the start of the experiment. Assuming this is so, the plot can be used to spot plates with a wide variation of control cell counts at the end-point or large differences in control cell counts across different plates with the same cell line.

13.6 Why are some cell line or drug names shown in italics?

On the drop down boxes to select cell lines and drugs, you may notice that entries may appear in black, grey, or gold. The colors indicate the availability of data for the currently selected cell line(s) on the drug dropdown box, and vice versa. For example, if the cell line SKMEL5 is selected, drugs in the drug dropdown will reflect the availability of data for each drug for SKMEL5. The color scheme is as follows:

- *Black* indicates data for the drug is available for the currently selected cell line(s) (or vice versa)
- *Grey* indicates data for the drug is *not* available for the currently selected cell line(s) (or vice versa)
- *Gold italics* indicates data for the drug is available for a *subset* of the currently selected cell lines. In the case of a plot with two datasets, data might only be available for one of the datasets.

Therefore, for datasets where all cell line/drug combinations have data, all cell line and drug entries will appear in black.

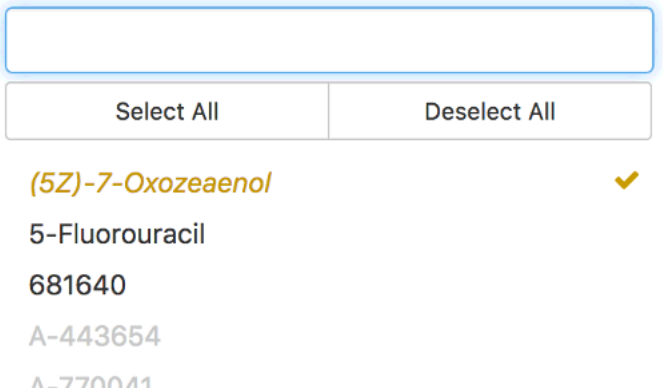

Image: Thunor Web drug selection color indicator, which shows data availability by drug for the currently active selection of cell lines.

The color scheme is not used when cell lines or drugs are selected by tag.

13.7 Notes on using tags

Tags can be used to select and group cell lines or drugs (see tag system). Tags are listed by category and can be searched using the search box.

At the bottom of the list is a special tag, **Everything else**. This selects every cell line or drug that is not otherwise selected by the list of tags. This is useful for comparing a tag to everything else in the dataset. This option works best either with aggregation switched on (to get box plots), or with aggregation switched off and a single entry in the other dropdown box (i.e. a single drug if using **Everything else** with cell line tag(s), or vice versa).

13.8 Create a tag from a plot

In bar and scatter plots, one can create new tags from within the plot interface. This can be useful for defining new tags based on patterns, trends, or outliers observed in a dataset. First, you'll need to create a selection. Hover over the plot, and you'll see the *plotly modebar* in the top right of the plot (a set of icons). Click either the **Lasso select** or **Box select** option, and draw round a set of points (scatter plots) or bars (bar plots). You can add to the selection by holding *Shift* and drawing another box/lasso. To deselect, double click within the plot area.

With a selection active, you'll see a new menu on the main plot toolbar, illustrated by an arrow, next to the **Download** button. The number in parentheses on this button indicates the number of selected data points. Click on this menu, and you'll have to the choice to create either a **Cell line tag** or **Drug tag** based on the selection. When clicking either of these options, a pop-up window will appear showing the cell lines/drugs the selection contains, each with a checkbox next to it (checked by default). You can uncheck any of the cell lines/drugs to remove them from the new tag if desired. Give the new tag a name and category (text boxes at the bottom of the popup). Then click the **Save as tag** button. The plot selection menus will automatically refresh, giving access to the new tag.

13.9 Modify an existing plot

To modify an existing plot, click the *Change plot* button.

13.10 Duplicate a plot

An existing plot can be duplicated by clicking the **Duplicate** button in the plot header. This is useful for comparing a plot against a similar plot with a slight modification.

13.11 Open a plot in a new window

An existing plot can be opened in a new window by clicking the **Open in new window** button in the plot header. The icon is a box with an arrow pointing outwards.

13.12 Rearrange plots

Plots can be rearranged by clicking and dragging (or tapping and dragging, on touch devices) on the plot header grey area (not on any button). If the screen is wide enough, the number of columns can be changed by selecting it from the dropdown box under **Layout** in the master toolbar.

13.13 Close a plot

Click the "X" button in the top right of the plot header.

13.14 Interact with a plot

Thunor's plot interface uses plotly, which provides interactivity and vector graphics which look sharp on any size screen.

Hover over a plot (or tap, on touch devices) to see a toolbar in the top right of the plot area. This provides options for adjust the plot view. Some useful options are:

- **Hover** the mouse over any data point or plot object to view the raw data values.
- **Autoscale** adjusts the axes to what plotly considers a sensible range. Either double click on the plot when the "crosshairs" are showing, or select the **Autoscale** button from the plotly toolbar.
- **Zoom** by using the options in the plotly toolbar, or by clicking and dragging a bounding box on the plot area.

13.15 Download graphics or data

Plot graphics and data can be downloaded using the **Download** button on any plot header.

- **PNG image** is a bitmap image type, well supported by most graphics software. Bitmap images have a fixed resolution and may become pixellated when printed or when zooming in.
- **SVG image** is a vector image type (Scalable Vector Graphics), supported by most graphics software. Vector images contain data on the constituent graphic objects, which means they look good at any resolution. Ideal for publications or poster printing.
- **Plotly JSON** contains the code used to render the plot using the plotly library. This option is useful for those who want to edit their plot using the plotly library, e.g. in R or JSON, or to host a copy of the plot on their website.
- **CSV** contains the plot data in comma-separated value format.
- **HTML** contains the plot as a web page (HTML), with all of the required software to display the plot saved in the single HTML file. This creates a relatively large file size (typically around 1 Mb), but is suitable for archiving a plot without any external dependencies.

13.16 A note on graphics formats

For publication quality images, we recommend using the **SVG image** format. SVG is a vector graphics format, which can be rescaled without loss of quality.

SVG can be converted into PDF or EPS formats using Inkscape. You can use Inkscape's graphical interface, or the following command:

```
inkscape fig.svg --export-pdf=fig.pdf
```

13.17 Share or save a plot session

The URL of the page is updated as plots are displayed. Therefore, to save a plot session, simply bookmark the page. To share the plot session, you can share the URL. Note that the URL can get rather long if many plots are open.

13.18 Exit the Plot System

Click the **Back to Home Page** button at the top right of the page. Please note that any currently open plots will not be saved automatically.

14 Dose response curve fits

14.1 Viability curve fits

Viability is the cell count relative to control at a specific time point (usually 72 hours). As a ratio of two positive numbers, it cannot go below zero.

Thunor fits viability data to a three parameter log-logistic model. The three parameters are Emax, EC50, and Hill coefficient. A constrained fit is used: Emax is constrained to be between 0 and 1, and the Hill coefficient (slope) is constrained to be non-negative.

$$f(X, b, c, e) = c + \frac{1 - c}{1 + e^{b(\ln X - \ln e)}}$$

Equation: Three parameter Hill curve (log-logistic curve)

14.2 DIP rate curve fits

The drug-induced proliferation rate (DIP rate) is defined as the steady-state rate of proliferation in the presence of a particular concentration of drug. It is quantified as the slope of the line on a plot of population doublings versus time. Unlike viability, DIP rate can go negative, indicating a cytotoxic drug effect.

Thunor fits DIP data to a four parameter log-logistic model. The four parameters are Emin, Emax, EC50, and the Hill coefficient. For ease of comparison, the relative DIP rate is often used, where the effect is shown relative to the minimum. Thus, on the relative scale, DIP curve fits will start from 1 on the y-axis.

$$f(X, b, c, d, e) = c + \frac{d - c}{1 + e^{b(\ln X - \ln e)}}$$

Equation: Four parameter Hill curve (log-logistic curve)

14.3 Curve fit parameters

For details on derived metrics like IC50, see dose response parameters.

15 Dose response parameters

This page discusses metrics derived from curve fits, like IC50s. For details on the curve fitting process and differences between viability and DIP rate dose response curves, see curve fitting.

15.1 IC50 and inhibitory concentrations

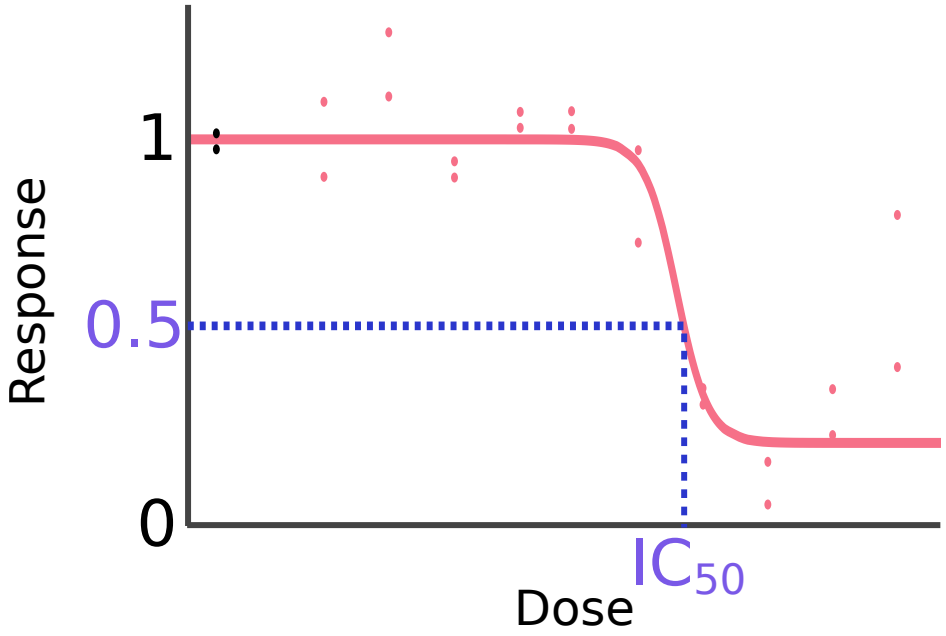

Image: Definition of IC50 shown on a dose response curve

Half-maximal inhibitory concentration (IC50) is a measure of drug potency expressed in molar units (M). It specifies the concentration at which the dose response curve reaches 0.5 on the y-axis (for DIP rate dose response curves, this is 0.5 on a relative scale y-axis). The IC50 may be undefined in the event that the maximum effect on the fitted curve does not reach 0.5 on the y-axis. On some plots in Thunor, this will show as `NA`.

Other inhibitory concentrations are defined analogously for any response value between 0 and 1. For DIP-based dose response curves, which can go below zero on the y-axis, IC100 denotes the concentration at which the dose response curve crosses the y-axis.

15.2 EC50, E50, and effective concentrations

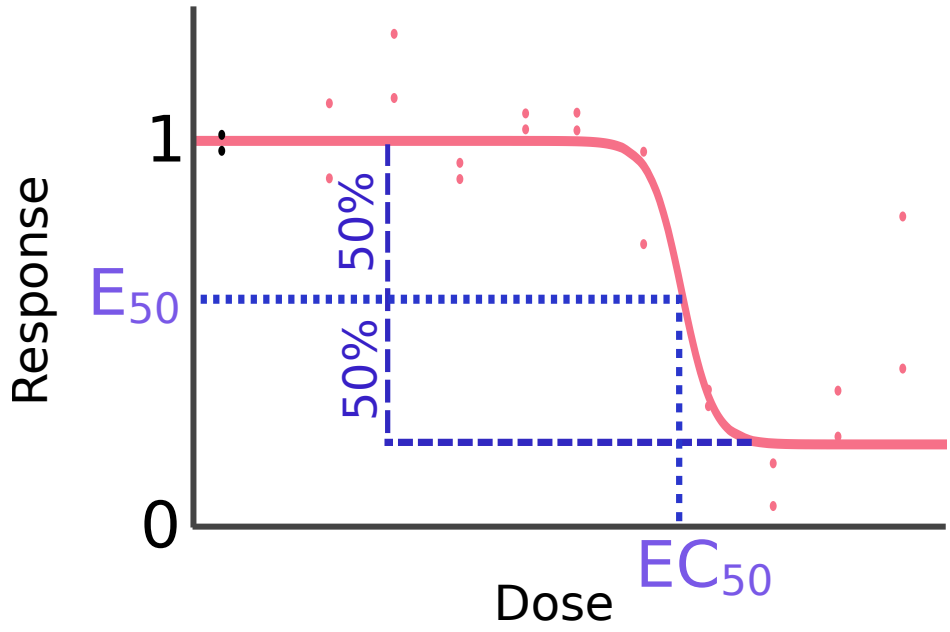

Image: Definition of EC50 shown on a dose response curve

Half-maximal effective concentration (EC50) is a measure of drug potency expressed in molar units (M). It specifies the concentration at which the dose response curve reaches 50% of the maximum effect observed, based on the fitted model - i.e. the halfway point between the curves maximum and minimum y-values. The response/y-value of the curve at this point is the half-maximal effect (E50).

15.2.1 Relative vs absolute values

For DIP rate curve fits, EC and E values can be measured on a relative DIP rate axis, or an absolute one. Thus, metrics with “relative” in their name are measured on the relative axis. Viability is already a relative metric, so this distinction does not apply (all values correspond to viability relative to control).

15.3 Emax

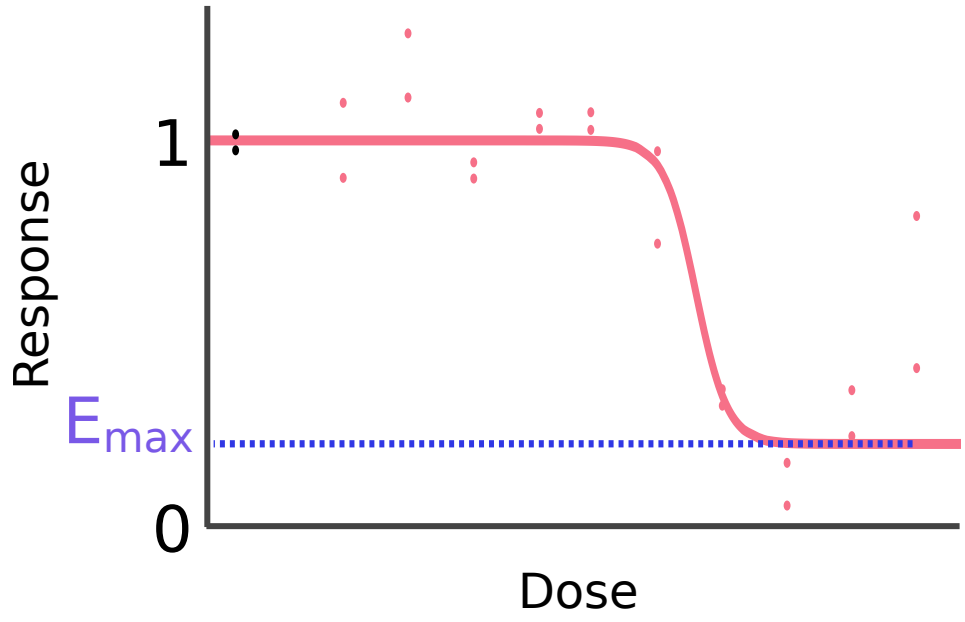

Image: Definition of Emax shown on a dose response curve

The maximal effect (Emax) denotes the fitted curve's effect (i.e. the y-value) at the maximum observed concentration (the highest drug concentration for which there is data).

15.4 Emax (observed)

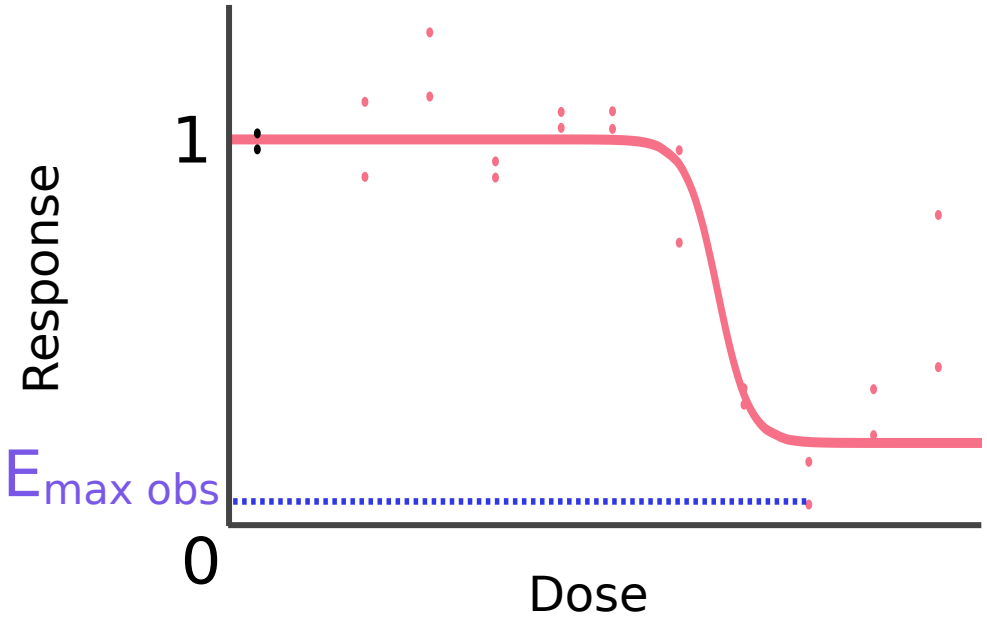

Image: Definition of Emax observed shown on a dose response curve

The observed maximal effect (Emax (observed)) is the maximum effect observed experimentally. Note that this is not necessarily observed at the maximum concentration.

15.5 Activity Area

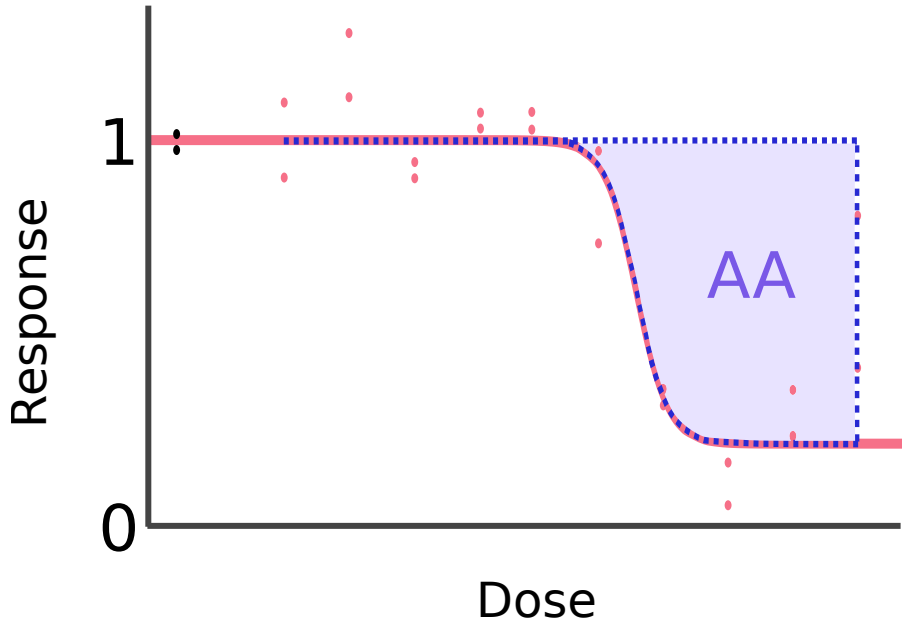

Image: Definition of Activity Area shown on a dose response curve

Activity area is the area above the dose response curve, up to the no response value (1 on the y-axis), bounded by the minimum and maximum observed concentrations.

15.6 Activity area (observed)

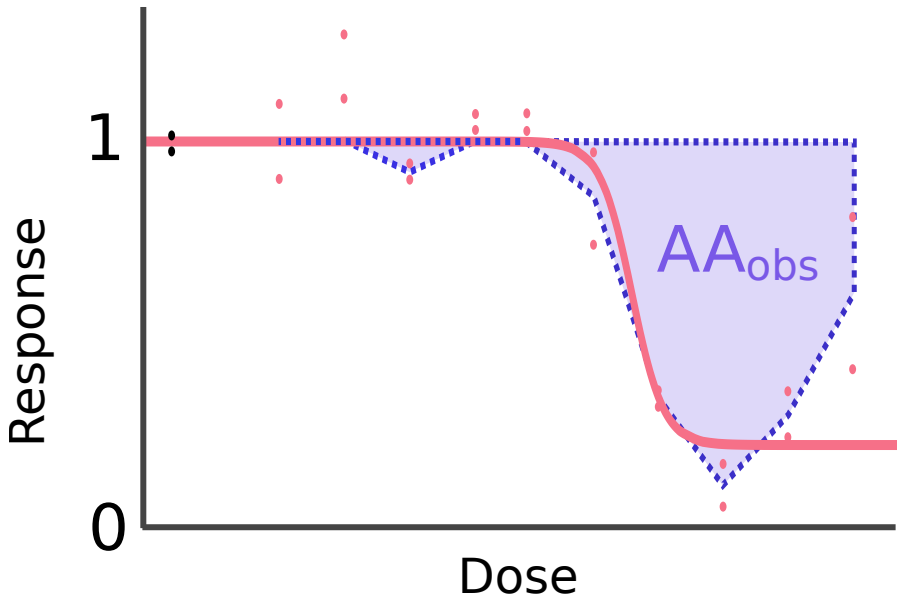

Image: Definition of Activity Area (observed) shown on a dose response curve

Activity area (observed) is the area above the observed response values, up to the no response value (1 on the y-axis). Between doses, a straight line extrapolation is used (on a log10 dose x-axis). Response values above 1 are truncated at 1. If there are multiple response values for a particular concentration (replicates), the mean average is used.

15.7 Hill coefficient

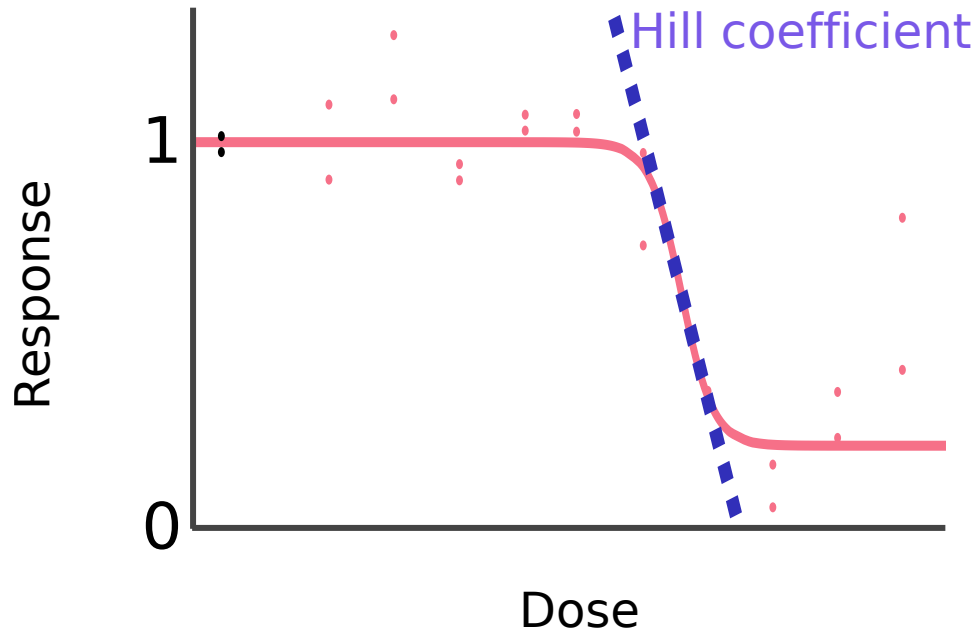

Image: Definition of Hill coefficient shown on a dose response curve

The Hill coefficient quantifies the rate of onset of a drug's effect as drug concentration increases. It affects the steepness of the dose response curve.

16 Installation options

Thunor Web can be installed in a variety of configurations, depending on the required level of security, scaling, and integration with existing infrastructure.

- For most use cases, we recommend the typical installation. This uses Docker Compose to manage Thunor Web, an nginx web server, and a PostgreSQL database.
- If you are just trying out Thunor Web and only need a single user account without network access, you can try the developer installation. This is also the option to pick if you might want to make edits to the Thunor Web source code. The developer installation doesn't use a Docker container for Thunor Web itself and doesn't run a full web server, instead relying on a lightweight, single user web server (Django's development server). This option still requires a PostgreSQL server, which by default is started in a Docker container during the installation process.

17 Typical installation

This section will show you how to install Thunor Web for testing or production use.

Thunor Web consists of several components, which are controlled together by a system called Docker Compose. Each component runs in a separate container, which makes the system modular and increases security.

A typical installation will use the following components:

- Thunor Web application server, written in Python using the Django framework.
- nginx web server, to handle HTTP requests
- Postgres database server

- Redis key-value server, used for caching time-consuming calculations and database queries.

17.1 Requirements

- **Docker** and **Docker Compose v2** (i.e. `docker compose` should work, without a dash). Follow instructions for your platform:
  - Docker for Windows
  - Docker for Mac
  - Docker for Linux
  - Other platforms: Docker installation instructions
- A **Python** installation. Python 3.6 or later is recommended, but other versions will probably work - it is only used for the configuration script.
- **Git**

If you use MacOS or Linux, you probably already have Python and git installed. If you use Windows, we recommend installing Anaconda, a Python distribution which includes lots of useful software.

17.2 Installation steps

1. **(Optional) Configure a DNS name**. If you're only testing Thunor Web on your local machine and don't need network access, this step is unnecessary. A DNS name is an entry like `thunor.example.com` which points to the machine hosting Thunor Web (specifically, an "A record"). Contact your domain provider for further information.

2. **Retrieve the Thunor Web quick start tool** using git

   ```
   git clone https://github.com/alubbock/thunor-web-quickstart thunor-web
   cd thunor-web
   ```

3. **Run the Thunor Web deploy script**.

   Choose an option: (a) for local only installation (single computer), or (b) network accessible installation.

   (a) To install a **local only** version for testing, use:

   python thunorctl.py deploy –hostname=localhost

   OR (b) To install a **network accessible** version at `thunor.example.com`, and to activate TLS encrypted connections using certbot, use:

   ```
   python thunorctl.py deploy --hostname=thunor.example.com --enable-tls
   ```

4. **Create an admin account**. You can use this to log in.

   ```
   python thunorctl.py createsuperuser
   ```

That's it! Thunor Web is now ready to start.

17.3 Starting and stopping

To start Thunor Web:

```
python thunorctl.py start
```

To stop Thunor Web:

```
python thunorctl.py stop
```

These commands must be run from the `thunor-web` directory.

17.4 Next steps

- Check the installation FAQ if you're having issues.
- Configure the system by changing settings in `thunor-app.env` (described in configuration options). After changing configuration values, restart Thunor Web using `python thunorctl.py restart`.
- You can add and invite new users, and create user groups in the admin interface.
- If you enabled TLS encryption, you may wish to schedule a job to renew those certificates automatically (they only last 90 days). See the section on TLS Encryption for details.

17.5 Uninstallation

Simply stop the system with `python thunorctl.py stop`, then delete the Thunor Web directory (noting that this will delete all data in Thunor Web, of course).

17.6 Upgrade Thunor Web

Check your current version with:

```
python thunorctl.py version
```

To upgrade to the latest version, run:

```
git pull
python thunorctl.py upgrade
```

In production, a database backup is recommended before performing an upgrade.

18 Developer installation

The developer installation allows the user to edit the Thunor Web source code, and is intended for use by those wishing to customize, develop, or contribute to the Thunor Web software. It is NOT a secure configuration to run across a network, and should not be run on a publicly accessible server. For that, see full installation, which is simpler to get up and running and recommended for most users.

This installation uses Python directly on your computer (i.e. not in a Docker container), Django's built in webserver, and a PostgreSQL database. Some Python/Django experience is recommended.

18.1 Requirements

- The quickstart procedure requires **Docker** and **Docker Compose v2** (i.e. `docker compose` should work, without a dash), which are used to launch a PostgreSQL database server. Advanced users may prefer to install their own PostgreSQL server or utilize an existing one instead. To use PostgreSQL in a Docker container, install one of the following:
  - Docker for Windows
  - Docker for Mac
  - Docker for Linux
  - Other platforms: Docker installation instructions
- A **Python >= 3.6** installation. If you have not used Python before, we recommend installing Anaconda.
- **Git**. If you're not sure if you have git, it will be provided with the Anaconda download in the previous step.

18.2 Getting Started

1. **Create a virtual environment**. This allows Thunor Web to keep its Python dependencies separate from other programs on your machine. You can do this with Anaconda (described here), or with

`virtualenv` or `pyenv`, if you prefer. On Anaconda, to create an environment called `thunor` and activate it, run the following:

```
conda create -n thunor pip python=3.6
conda activate thunor
```

2. **Download Thunor Web**. Change directory to where you want to download the software, then type:

```
git clone --recurse-submodules https://github.com/alubbock/thunor-web
cd thunor-web
```

3. **Run the Thunor Web initialization script**

```
python thunorbld.py init
```

4. **Create an admin account**. You can use this to log in.

```
python manage.py createsuperuser
```

5. **Start the development server**

```
python manage.py runserver
```

That's it! You can now access Thunor Web on your local machine by accessing http://localhost:8000 through a web browser.

18.3 Shut down the system

When you're done with testing, you can shut down the system as follows.

1. **Stop the development server** if it's running, by pressing Ctrl+C
2. **Shut down the database** by running `docker compose down` in the `thunor-web` directory.

18.4 Re-start Thunor Web at a later date

To re-start Thunor Web at a later date:

1. Activate the virtual environment: `conda activate thunor`
2. Change directory to the `thunor-web` installation location
3. Make sure the database is started: `docker compose up -d`
4. Start the development server: `python manage.py runserver`

18.5 Uninstallation

Simply shutdown the system as above, then delete the `thunor-web directory` (noting that this will delete all data in Thunor Web, of course). If you're using Anaconda, you can deactivate the virtual environment with `conda deactivate` and delete it with `conda env remove -n thunor`.

18.6 Further configuration options

For more configuration options that can be set as environment variables, see configuration options. You can set those environment variables in the `thunor-dev.env` file.

18.7 Making modifications

Changes to Python files should be reloaded automatically by the development server. If changing any static files (within `thunorweb/webpack/thunorweb`), you'll need to trigger a webpack build:

```
python thunorbld.py --dev makestatic
```

18.8 Unit tests

To run the unit test suite on the host machine's Python environment:

```
python thunorbld.py --dev test
```

Generally, the above test suite is sufficient, but to run the test suite in a Docker container (to mimic the production environment), run

```
python thunorbld.py test
```

19 Password reset

19.1 Reset password by email

You can reset your password by clicking on the **forgotten your password?** link on the login page. Simply enter your email address, and an email will be sent to that address with a link. Click on that link in the email, and you'll be able to enter a new password.

The above procedure will only work if the server administrator has entered a working email configuration. If that's not the case, the password will need to be reset on the command line by an administrator. Otherwise, the administrator can enable self-service password resets by entering details of a working email server.

19.2 Command line password reset

Enter the following command, replacing `user@example.com` with the email address of the relevant user:

```
docker compose exec app python manage.py changepassword user@example.com
```

You will be prompted for a new password, and asked to confirm it by entering it again. The password change will take effect immediately (no restart required).

This approach is recommended only for single-user servers, since the administrator needs to set the password. For security, it is highly recommended to use the reset by email option on multi-user servers.

20 Enable HTTPS encryption

HTTPS encryption uses transport layer security (TLS) to encrypt connections to Thunor Web via the web browser. It is strongly recommended for any use of Thunor Web over a network.

20.1 Enable TLS encryption

Encryption requires a specific domain name to be configured, which you can purchase from any domain name registrar. For demonstration purposes, we'll use `thunor.example.com`, but replace this with your own domain throughout the tutorial. Configure a DNS A record to point to the the server IP address.

Thunor Web automates the process of generating encryption certificates and deploying them. The certificates are generated with the help of certbot.

To generate the certificates and deploy them, run:

```
python thunorctl.py generatecerts
```

After the above command successfully completes, you should find that accessing http://thunor.example.com automatically redirects to https://thunor.example.com.

The certificates only last 90 days, so you'll probably want to automatically renew them, described below.

20.2 Manually renew TLS certificates

Certificates can be renewed with

```
python thunorctl.py renewcerts
```

20.2.1 Automatically renew TLS certificates on Linux

To automatically renew TLS certificates on Linux, you can use a cron job. Edit your crontab using `sudo crontab -e` and type the following entry (**replace `/thunor` with the location of the `thunorctl.py` script**):

```
0  5  *   *   0   python /thunor/thunorctl.py renewcerts
```

Edit the run times to your requirements, following the cron syntax (briefly: the columns are minute, hour, day of month, month, day of week [0-6, where 0 is sunday]). This example runs at 5am every Sunday.

20.2.2 Automatically renew TLS certificates on a remote Docker Machine

If you installed Thunor Web using Docker Machine, it's useful to automatically renew certificates on the remote instance, which may not have Python available (outside of the container) or Docker Compose.

A `renew-certs.sh` script is automatically copied to the remote instance when you set up TLS encryption. Add the script to your crontab by adding the following entry using `sudo crontab -e` (replace `/home/ubuntu/thunor` with the correct path, if necessary):

```
0 5    *   *   0   /home/ubuntu/thunor/renew-certs.sh
```

Edit the run times to your requirements, as described in the previous section.

21 Configuration options

21.1 How to change settings

Settings are stored in the `thunor-app.env` and `thunor-db.env` files as environment variables: one variable per line, in the format `VARIABLE=value`. Most configuration will go in `thunor-app.env`, except the database configuration, which goes in `thunor-db.env`.

To change a variable, simply open the relevant file in a text editor, and enter in the new value. Allowed values are shown in a table below.

For the changes to take effect, you must restart Thunor Web:

```
python thunorctl.py restart
```

21.2 Public user signup

By default, only administrators can create users, and the public signup facility is disabled. To enable it, set the environment variable `THUNOR_SIGNUP_OPEN=True`. Users can then create an account by visiting the URL `/accounts/signup` on your server. It is strongly recommended that you also set `THUNOR_EMAIL_VERIFICATION=mandatory` to require new users to verify their email addresses if your server will be publicly accessible (see **Email server configuration**).

21.3 Dataset access without login

By default, users will need to be logged in to access any dataset or tag labeled "Public". To enable anonymous access (i.e. without an account, or when logged out), set the `THUNOR_LOGIN_REQUIRED` environment variable to `False`.

21.4 Email server configuration

An email server is required to enable the `THUNOR_EMAIL_VERIFICATION` option. Enter the details of an SMTP server using the `DJANGO_EMAIL_HOST`, `DJANGO_EMAIL_PORT` etc. variables.

21.5 Integration with Sentry

Sentry is an error monitoring and aggregation system. For example, if an error occurs when a user loads a page on the site, the error will be logged in Sentry. Administrators can be alerted by email.

Sentry is available as a service (free for small use cases and academic use), or can be installed locally.

See the Sentry quickstart guide to create a project to track Thunor alerts. When you have a Sentry DSN (a URL to which software can report errors), set that value as the environment variable `DJANGO_SENTRY_DSN` to enable Thunor's Sentry integration.

21.6 Complete list of settings

Thunor Web is configured through the use of environment variables, which are listed below.

Remember to **restart Thunor Web after changing configuration**: `python thunorctl.py restart`

Name	Default	Description
THUNOR_LOGIN_REQUIRED	`True`	Set to `False` to allow anonymous access to public datasets. Set to `True` if an account is required to use the system.
THUNOR_SIGNUP_OPEN	`False`	Set to `True` to allow anyone with access to the server to create an account.
THUNOR_EMAIL_VERIFICATION	`none`	`none`: Don't verify accounts by email`mandatory`: Require email verification of accounts (recommended)
DJANGO_SENTRY_DSN	None	A Sentry DSN value to enable Sentry, a system for logging and aggregating errors.
DJANGO_EMAIL_HOST	None	Hostname of email server
DJANGO_EMAIL_PORT	None	Email server port, e.g. 587 for a TLS connection
DJANGO_EMAIL_USER	None	User account name on email server
DJANGO_EMAIL_PASSWORD	None	User password on email server
DJANGO_EMAIL_FROM	Same as user	Account to send email from, e.g. `An Example <an.example@example.com>`
DJANGO_SECRET_KEY	(random)	A secret key for this instance used by Django. Typically 50 random characters. You can use an online tool to generate one, if desired.

Name	Default	Description
DJANGO_DEBUG	`False`	Set to `True` to enable debug information. Do not use in production or on publicly accessible servers.
DJANGO_HOSTNAME	None	Hostname of the server e.g. `thunor.example.com`
DJANGO_STATIC_URL	`/static/`	Location to serve static files from. This only needs changing if you wish to serve static files from a separate domain.
DJANGO_ACCOUNTS_TLS	`False`	Set to `True` to use `https://` links for account emails, e.g. password reset
DATA_UPLOAD_MAX_NUMBER_FIELDS	1000	The maximum number of form fields the server will process. If you have datasets with lots of cell lines and drugs, you may wish to increase this number, at the expense of system memory.
POSTGRES_HOST	`localhost`	Hostname of the postgres server, or `postgres` to use the Docker Compose-launched postgres instance.
POSTGRES_USER	`postgres`	Postgres username
POSTGRES_PASSWORD	(random)	Postgres password
DJANGO_REDIS_URL	`redis://redis:6379/1`	A Redis URL. If provided, the Redis instance will be used as a system cache, to improve response times. The default URL uses a Redis instance provisioned by Docker Compose.
DJANGO_DB_CACHE	`False`	Set to `True` to use a database cache. The cache table must be created before first use, as described in the installation procedure. If a DJANGO_REDIS_URL is provided, that option supersedes this one.
UWSGI_PROCESSES	5	Number of processes to use for the application server (uWSGI)
UWSGI_BUFFER_SIZE	32768	Buffer size for the application server (uWSGI)

22 Admin interface

During installation, you should've created a super user account. This account can be used to log in to the admin interface, which is available at `/admin` on your server. E.g. if your server is hosted at `http://localhost`, visit `http://localhost/admin` and log in with the super user account.

22.1 User accounts

User accounts can be created manually by an administrative user (including the super user), by email invitation, or by open signup if enabled.

22.1.1 Manually add user

To manually create a user, log in to the admin interface as described above. Under the **Custom User** header, there's a row labeled **Users**. Click the + **Add** button to create a new user. All that's needed is an email address and password.

22.1.2 Invite user by email

To invite a user by email to create an account, simply click the + **Add** button under the **Invitations** header, and enter their email address.

22.2 Group administration

Groups can be added or modified in the admin interface by the super user (the account created during installation) or users marked as "staff".

22.2.1 Add a group

Under the **Authentication and Authorization** header, there's a row labeled **Groups**. Click the + **Add** button to create a new group. Give the group a name. Leave the Permissions box blank. In the Users box, add users to the group by double-clicking them, or use the add/remove arrows between the Available Users and Chosen Users boxes. Click the **Save** button at the bottom right when done.

22.2.2 Modify group membership

Under the **Authentication and Authorization** header, there's a row labeled **Groups**. Click the word **Groups**, then select a group from the list. Adjust the group membership by selecting users from the list, and using the add/remove arrows between the Available Users and Chosen Users boxes. Click the **Save** button at the bottom right when done.

23 Design and Components

23.1 Infrastructure diagram

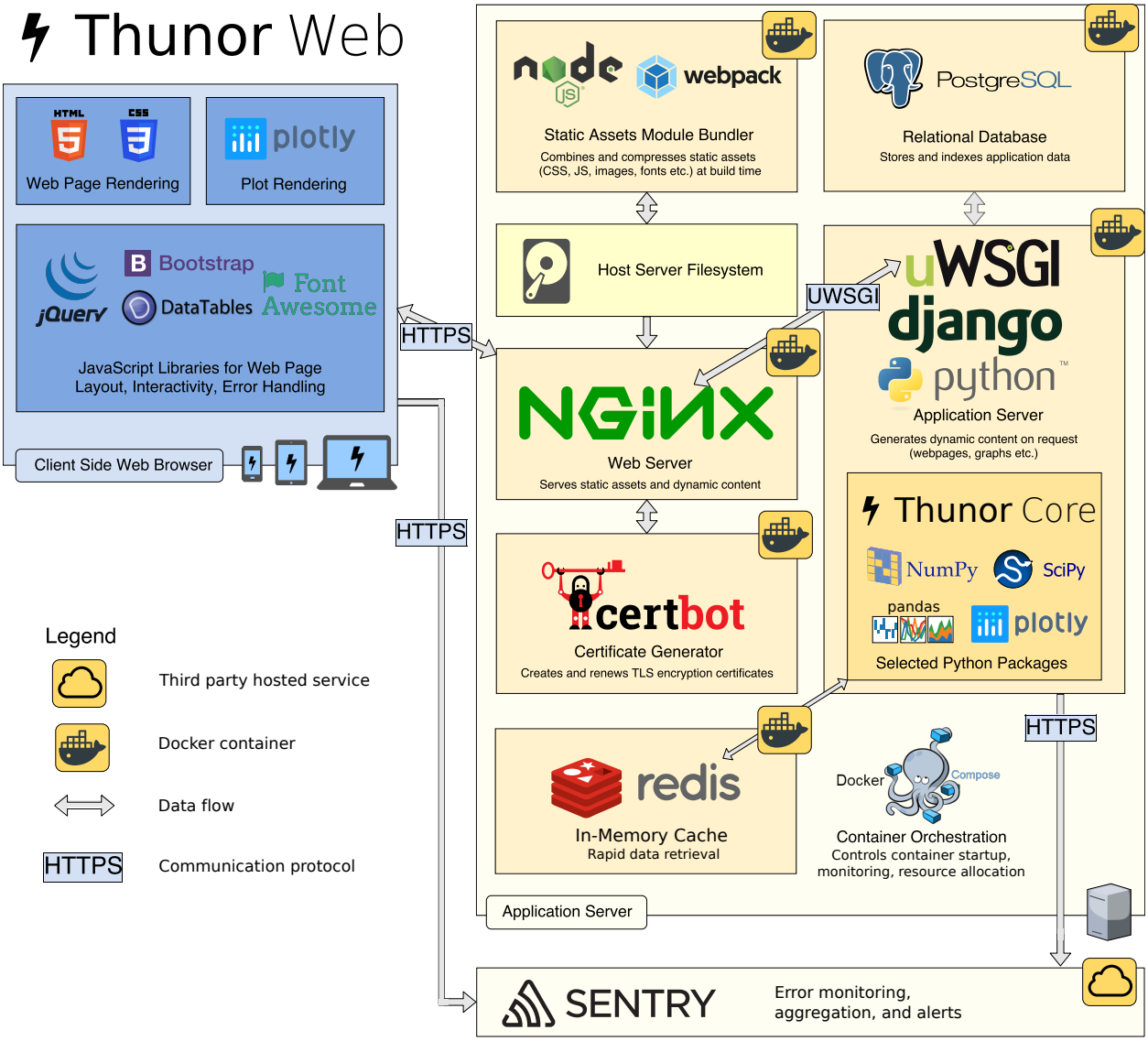

Image: Thunor Web software infrastructure. Users access Thunor Web through a web browser. Thunor Core produces plots using the plotly library, which can be delivered through Thunor Web. On the server, Thunor Web runs in multiple Docker containers: nginx web server, PostgreSQL database, and application server. The application server runs uWSGI and Django, a Python web application framework, which interfaces with Thunor Core. Encryption certificates are generated using Certbot in a separate container, run on demand. Static files (CSS, Javascript etc.) are compiled into bundles using Webpack to improve server performance. Error reporting and aggregation use the Sentry platform. The server system is "orchestrated" using Docker Compose.

23.2 List of software components

The following is an alphabetical list of software components used in Thunor Core and Thunor Web.

Component	Role
Bootstrap	Front end layout
Certbot	TLS certificate provisioning
Datatables	Interactive web tables
Django	Web application framework
Docker	Application containers
Docker Compose	Multi-container orchestration
Docker Machine	Remote control and deployment
jQuery	Front end interactivity
Nginx	Web server
Numpy	Numerical operations
Pandas	Data manipulation
Plotly	Plot rendering, interactivity
PostgreSQL	Relational database
Redis	Cache
Scipy	Curve fitting, statistics
Sphinx	Code documentation
Sentry	Error aggregation, logging
uWSGI	Application server
Webpack	Static file bundling

23.3 Database Entity Relationship Diagram

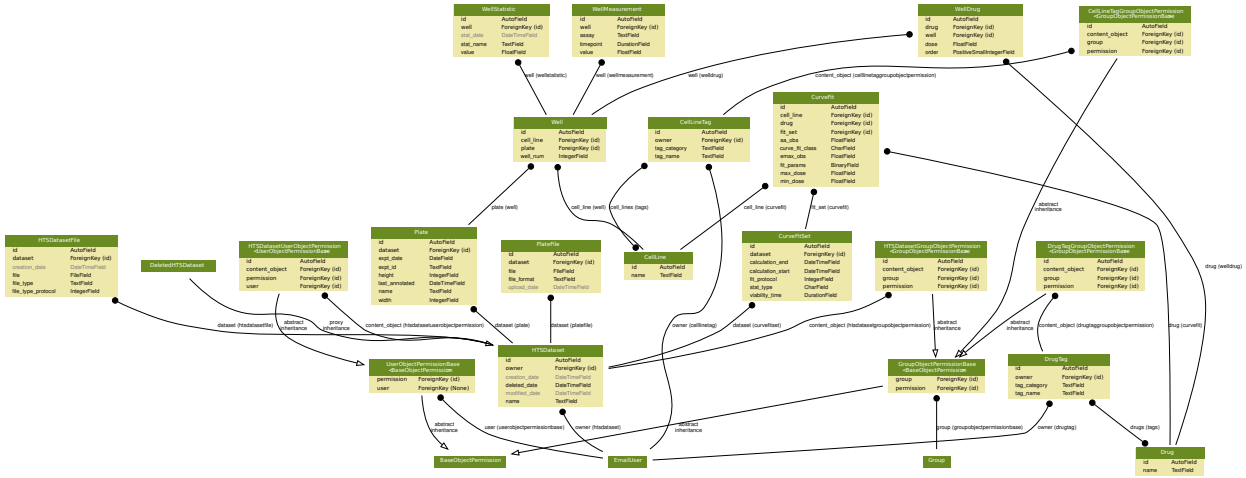

Image: Entity relationship diagram for Thunor Web's relational database. Each box shows a database table with its fields. Foreign key relationships are denoted by lines terminated with circles, inheritance is denoted by arrows.