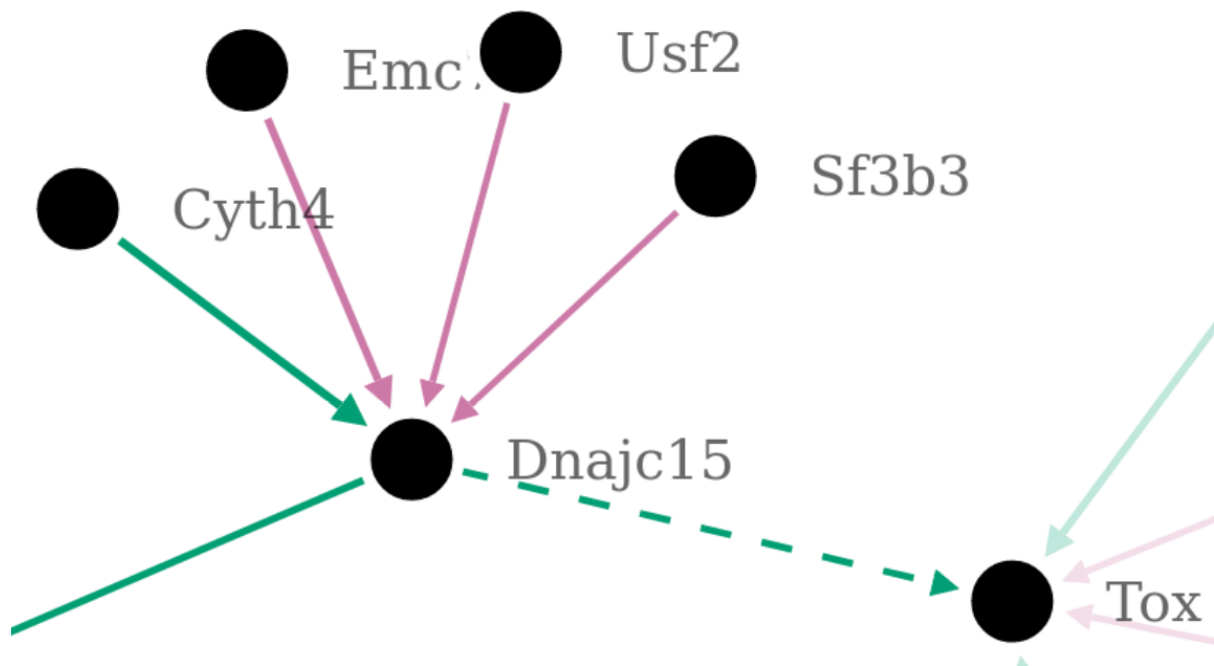


DGRN Explanation

This is a step by step explanation of a resulting network of our pipeline and how to correctly interpret it.

In the figure below you can see a part of a resulting network. We will use this example to explain everything that you can see and the meaning behind it.

- Stronger in Doc_Spleen_d28 (Activator)
- - Stronger in Doc_Spleen_d28 (Repressor)
- Stronger in Arm_Spleen_d28 (Activator)
- - Stronger in Arm_Spleen_d28 (Repressor)



The network consists of nodes (black circles) and edges (green/pink arrows). There are two different types of edges (fully drawn/dashed), we will get to the difference between these edges later on.

Nodes:

Each node represents a gene, which is identified by the name to the right side of it. In this example the nodes (genes) are “Cyth4”, “Emc7”, “Usf2”, “Sf3b3”, “Dnajc15” and “Tox”. You can see that “Emc7” is partially covered by the node belonging to “Usf2”. You can move the nodes around by dragging them with your mouse for better visibility.

Edges:

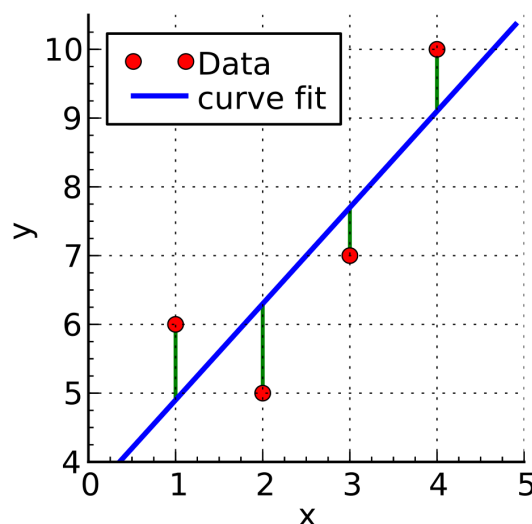
This section generally describes the meaning of the edges at first and gives concrete examples how to interpret the edges in the figure shown above at the end.

- Each edge represents an interaction between two genes. The start of an edge is the source gene and the end of an edge (indicated by the arrow) is the target gene. **An edge between two genes tells you that the source gene is predictive of the target gene.**

- There are two types of colors (green/pink) that an edge can have. **Each color represents the condition that the edge belongs to.** The two conditions are listed in the top left corner. In this example we have Doc_Spleen_D28 (pink) and Arm_Spleen_D28 (green) as our two conditions. The exact meaning of these conditions is specific to the data used to compute the network.
- There are two types of edge styles (fully drawn/dashed). **Fully drawn edges (e.g. “Cyth4 -> Dnajc15”) represent an up regulatory interaction between two genes and dashed edges (e.g. “Dnajc15 -> Tox”) represent a down regulatory interaction between two genes.** This means that if the source gene is up/down regulated, the target gene will be up/down regulated as well. We call this Activator/Repressor in the legend.

We compute this with the following process:

- 1) Take the gene expression of the source gene **x** and the target gene **y**
- 2) Fitting a line with $y = m * x + t$ based on the data using linear regression (example picture shown below). We refer to this often as “fitting a linear model”



- 3) The interaction is an upregulatory interaction if the line has a positive slope and a down regulatory interaction if the line has a negative slope

- **Example:**

We will go over the figure shown at the top and how to interpret every edge. We have the edges “Cyth4 -> Dnajc15”, “Emc7 -> Dnajc15”, “Usf2 -> Dnajc15”, “Sf3b3 -> Dnajc15” and “Dnajc15 -> Tox”. Additionally, we have the two conditions “Doc_Spleen_D28” and “Arm_Spleen_D28”. We will go through all the edges and their correct interpretation:

- “Cyth4 -> Dnajc15”: “Cyth4 is predictive of Dnajc15 in the condition Arm_Spleen_D28 and it is an up regulatory interaction”.
- “Emc7 -> Dnajc15”: “Emc7 is predictive of Dnajc15 in the condition Doc_Spleen_D28 and it is an up regulatory interaction”.

- “Usf2 -> Dnajc15”: “Usf2 is predictive of Dnajc15 in the condition Doc_Spleen_D28 and it is an up regulatory interaction”.
- “Sf3b3 -> Dnajc15”: “Sf3b3 is predictive of Dnajc15 in the condition Doc_Spleen_D28 and it is an up regulatory interaction”.
- “Dnajc15 -> Tox”: “Dnajc15 is predictive of Tox in the condition Arm_Spleen_D28 and it is a down regulatory interaction”.