TEST

"The Mutation process"

In this test, we check the **ONLY the The Mutation process and how it affects on Hallmark variables.** So, the normal reaction for test is the random changes in the Hallmark's variable with formula:
m'=m0 * CDS_length,
where m0 is the initial rate of mutation defined by user (see the table), CDS_length is a length of gene.

<table>
<tr><td colspan="7">MUTATION
$m' = m_0 \cdot CDS_{length}$ $u' = \begin{cases} u_0, & \text{for oncogene} \\ u_S, & \text{for supressor} \end{cases}$</td></tr>
<tr><td>Ga</td><td>Destroyed Genes / ALL Genes</td><td>Gi</td><td>Gim</td><td>-</td><td>Gd</td><td>Gb</td></tr>
<tr><td>$H_a = \sum_k (G_a)_k$</td><td>x – mutation density</td><td>$H_i = \sum_k (G_i)_k$</td><td>$H_{im} = \sum_k (G_{im})_k$</td><td>-</td><td>$H_d = \sum_k (G_d)_k$</td><td>$H_b = \sum_k (G_b)_k$</td></tr>
<tr><td colspan="2">Apoptosis
$a' = a - H_a$
$a = \frac{1}{1 + e^{-s_0(x-0.5)}}$</td><td>Hayflick limit (immortalization)
$i' = 1 - H_i$</td><td>Invasion/metastasis transformation
$im' = H_{im}$</td><td>Environmental death
k'</td><td colspan="2">Division process
$d' = \begin{cases} d - E' \cdot N & \text{, for normal cells} \\ d & \text{, for metastasis cells} \end{cases}$
$E' = \frac{E_0}{1 + F_0 \cdot H_b}$ and $d = H_d$
N – number of normal cells</td></tr>
</table>

Mutation of **driver** genes (and Hallmarks variable and mutation rate) depends on probabilities u_S and u_O (see the table) for oncogenes and suppressors.
Mutation of **passenger** genes depends on probabilities (1-u_S) and (1-u_O) without changes in Hallmarks variables for oncogenes and suppressors.
Mutation occurs only **during division process**, so the mutation must occurs ONLY **for parents and children** independently.
ONLY FOR TEST we changed the code and **switch off the death** of cell in order to check the mutation process.

The celling file is constant, it has the cells with all combinations of 4 genes + GD. The GD gene is needed, because the mutation occurs ONLY during the division process, what is why we need GD (GD switch on the division process with the probability 1).

Cellin file:

1 GA
2 GI
3 GD
4 GB
5 GIM
6
7 GD,GA
8 GD,GA,GI
9 GD,GA,GI,GB
10 GD,GA,GI,GB,GIM
11 GD,GA,GB
12 GD,GA,GB,GIM
13 GD,GA,GIM
14 GD,GI
15 GD,GI,GB
16 GD,GI,GB,GIM
17 GD,GB
18 GD,GB,GIM
19 GD,GIM
20 GD,GA,GI,GIM
21 GD,GI,GIM
22 GD,GA
23 GD,GI
24 GD,GB
25 GD,GIM

In this test we change only the **GENEFILE and u_S, u_O, m_0** to check formula and calculations of Hallmarks variables.

The genefile data are in the table below.

So the input and output data have several possibilities (see table below):

1

Genefile	U_S	U_O	m_0	Results
GA 1 apoptosis o 1 GB 1 angiogenesis o 1 GIM 1 invasion o 1 GI 1 immortalization o 1 GD 1 growth o 1	0	0	0	The cell divisions with the HD Hallmarks without mutations. Please, check the mutation rate. **Conclusion**: for oncogenes without mutation.
GA 1 apoptosis s 1 GB 1 angiogenesis s 1 GIM 1 invasion s 1 GI 1 immortalization s 1 GD 1 growth s 1	0	0	0	Same as previous. **Conclusion**: for suppressor same
GA 100 apoptosis o 1 GB 100 angiogenesis o 1 GIM 100 invasion o 1 GI 100 immortalization o 1 GD 100 growth o 1	0	0	1	The mutation occurs only in the **passenger** part of genes.

Genefile	U_S	U_O	m_0	Results
GA 100 apoptosis s 1 GB 100 angiogenesis s 1 GIM 100 invasion s 1 GI 100 immortalization s 1 GD 100 growth s 1	0	0	1	The mutation occurs only in the **passenger** part of genes.
GA 100 apoptosis o 1 GB 100 angiogenesis o 1 GIM 100 invasion o 1 GI 100 immortalization o 1 GD 100 growth o 1	0	1	1	The mutation occurs only in the **driver** part of genes.
GA 100 apoptosis s 1 GB 100 angiogenesis s 1 GIM 100 invasion s 1 GI 100 immortalization s 1 GD 100 growth s 1	0	1	1	The mutation occurs only in the **passenger** part of genes, because of U_S=0.
GA 100 apoptosis o 1 GB 100 angiogenesis o 1 GIM 100 invasion o 1 GI 100 immortalization o 1 GD 100 growth o 1	1	0	1	The mutation occurs only in the **passenger** part of genes, because of U_O=0.

Genefile	U_S	U_O	m_0	Results
GA 100 apoptosis s 1 GB 100 angiogenesis s 1 GIM 100 invasion s 1 GI 100 immortalization s 1 GD 100 growth s 1	1	0	1	The mutation occurs only in the **driver** part of genes.
GA 100 apoptosis o 1 GB 100 angiogenesis o 1 GIM 100 invasion o 1 GI 100 immortalization o 1 GD 100 growth o 1	1	1	1	The mutation occurs only in the **driver** part of genes.
GA 100 apoptosis s 1 GB 100 angiogenesis s 1 GIM 100 invasion s 1 GI 100 immortalization s 1 GD 100 growth s 1	1	1	1	The mutation occurs only in the **driver** part of genes.
GA 100 apoptosis o 1 GB 100 angiogenesis o 1 GIM 100 invasion o 1 GI 100 immortalization o 1 GD 100 growth o 1	0.5	0.5	1	The mutation occurs in the **driver** and **passenger** parts of genes.

Genefile	U_S	U_O	m_0	Results
GA 100 apoptosis s 1 GB 100 angiogenesis s 1 GIM 100 invasion s 1 GI 100 immortalization s 1 GD 100 growth s 1	0.5	0.5	1	The mutation occurs in the **driver** and **passenger** parts of genes.
GA 1000 apoptosis o 1 GB 1 angiogenesis o 1 GIM 1 invasion o 1 GI 1 immortalization o 1 GD 1 growth o 1	0.5	0.5	0.001	The mutation occurs only in the **driver** and **passenger** parts of gene with a longest CDS.
GA 1 apoptosis s 1 GB 1000 angiogenesis s 1 GIM 1 invasion s 1 GI 1 immortalization s 1 GD 1 growth s 1	0.5	0.5	0.001	The mutation occurs only in the **driver** and **passenger** parts of gene with a longest CDS.