Model-Based Analysis (MBA) - Assignment 3

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PRISM MODEL OF THE GIVEN REACTION NETWORK

The designed model is available in the attached file `cov20.prism`. According to the specification was model designed as Continuous-time Markov chain (CTMC). It consists of one `module` named `cov20`, which includes three local *variables* and two *commands*. The local variables `z`, `n` and `u` represents the current numbers of the individuals in the relevant groups: *healthy* individuals, *infected* individuals and *healed* individuals. The commands represent the given reaction network, specifically its equations of the `infection` and `recovery`. At the global level are defined the global *variables* (`init_z`, `init_n` and `init_u`), which represents the initial numbers of the individuals in the relevant groups, and also their overall number (`sum_individuals`). Further we defined two global *variables* `k_i` and `k_r` without the initial values because the specific values will be defined when running experiments. The last part of this model are two *formulas* `r_i` and `r_r`, which represents the rates of the commands according to the *mass action kinetics*. For more details, please check the attached file `cov20.prism`.

FORMALISATION AND ANALYSING OF THE GIVEN PROPERTIES

In this task was required to formalise two given properties within the `PRISM` language for the property specification. The attached file `cov20.props` contains constructed properties according to the given specification. The first property queries to the probability that the infection will eventually disappear and it is described as follows: $\mathbf{P} =? \, [\, \mathbf{F}\ \mathbf{n} = \mathbf{0}\,]$. The second one queries to the probability that the infection lasts for at least **100**-time units and disappears within **120**-time units: $\mathbf{P} =? \, [\, \mathbf{n} > \mathbf{0}\ \mathbf{U}[\mathbf{100}, \mathbf{120}]\ \mathbf{n} = \mathbf{0}\,]$. To analyse these properties we need to select the specific values for both parameters and we decided to values, that will be significant later in the next section: $\mathbf{k_i} = \mathbf{0.003}$ and $\mathbf{k_r} = \mathbf{0.05}$.

First property. The probability of the first property is equal to **1**, because the infection disappears under any conditions after the expire some period of the time units. If we take a closer look at this property, when the infection can really disappear, then we see that after expires the **200**-time units is this probability equal to **0.99**. This probability was obtained with the following property $\mathbf{P} =? \, [\, \mathbf{F}[\mathbf{0}, \mathbf{T}]\ \mathbf{n} = \mathbf{0}\,]$ and the simulation was run with the interval $[\mathbf{100}, \mathbf{200}]$ for parameter $\mathbf{T}$ (step equal to **10**). The graph constructed by this simulation you can check in the file `end_time.jpeg`.

Second property. To analyse this property, we use some other properties which have some continuity on the analysed property. It is only for a better understanding and explanation of the overall result. Firstly, we take a look to the probability, that the infection will last for at least **100**-time units. This probability we describe as follows: $\mathbf{P} =? \, [\, \mathbf{G}[\mathbf{0}, \mathbf{100}]\ \mathbf{n} > \mathbf{0}]$ and it is also part of Figure 5. The value of the probability in this property is equal to **0.7630**, thus, we can conclude, that this is very likely. Let us now look at the opposite property, thus that the infection will spread even after the expiry of **120**-time units. This property is described in Figure 4 and we verify it with the following `PRISM` property: $\mathbf{P} =? \, [\, \mathbf{F} > \mathbf{120}\ \mathbf{n} > \mathbf{0}\,]$. With the specified values of the parameters $\mathbf{k_i}$ and $\mathbf{k_r}$ is this probability equal to **0.4170**, so it is a little less likely than the first case. Before we look at the final evaluation, we look at the property that describes that the infection disappears within maximally **120**-time units. This property also gives partial information on whether the analysed property is likely or not, and we introduce it at Figure 3: $\mathbf{P} =? \, [\, \mathbf{F}[\mathbf{0}, \mathbf{120}]\ \mathbf{n} = \mathbf{0}\,]$, and its value is equal to **0.5830**. We can see, that this value is a complement to the previously presented property $\mathbf{1} - \mathbf{0.4170} = \mathbf{0.5830}$, and check this complementary feature of both properties in Figures 3 and 4. From these partial properties, we can conclude, that the infection with such values of parameters $\mathbf{k_i}$ and $\mathbf{k_r}$ can spread in the following scenarios. Approximately one-quarter of the cases may disappear before expiry **100**-time units and slightly less than half of the cases may exceed **120**-time units. The result value of the probability of this analysed property is equal to **0.3460**, thus the infection can lasts for at least **100**-time units and disappears within **120**-time units, but also do not have. We will pay attention to the analysis of this property also in the next section.

ANALYSE THE IMPACT OF THE PARAMETERS

In this section, we introduce the analysis of the impact of the parameters $\mathbf{k_i}$ and $\mathbf{k_r}$ to the specified properties. All presented graphs were constructed by the experiment running in the `PRISM` tool, where we run the specified property with the following ranges of the parameters:

$$k_i \in [\,0.001,\, 0.011\,],\ \text{step} = 0.001 \qquad k_r \in [\,0.01,\, 0.11\,],\ \text{step} = 0.01$$

What is the probability that the infection will eventually disappear?

To analyse this property we define the following property specification within `PRISM` tool: $\mathbf{P} = ?\,[\,\mathbf{F}\ \mathbf{n} = \mathbf{0}\,]$, which exactly describe it. The graph below shows, that this probability is not affected by the values of the individual parameters and it is always equal to $\mathbf{1}$. Thus, regardless of the parameter values, the infection will sooner or later disappear.

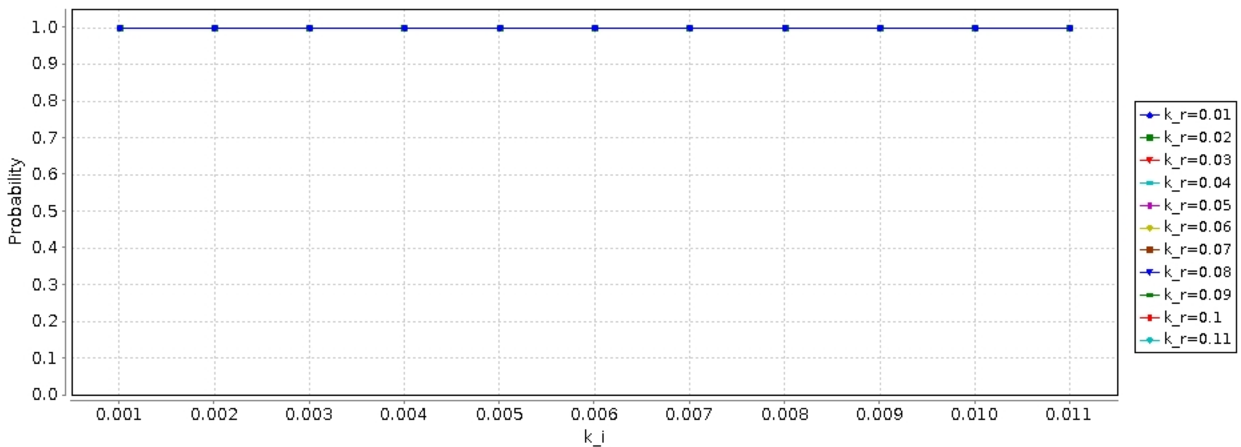

Figure 1. Graph constructed by the experiment running on the following property: $\mathbf{P} = ?\,[\,\mathbf{F}\ \mathbf{n} = \mathbf{0}\,]$. This property queries to the probability that exists the path where the infection disappears at some point along this path. This graph shows, that the queried probability is equal to $\mathbf{1}$ in all combinations of the parameters, thus the infection always disappears. We note, that the individual series are all folded on top of each other and therefore only first is visible.

What is the probability that the infection lasts for at least 100-times units and disappears within 120-time units?

To analyse this property we define the following property specification within `PRISM` tool: $\mathbf{P} = ?\,[\,\mathbf{n} > \mathbf{0}\ \mathbf{U}[\mathbf{100}, \mathbf{120}]\ \mathbf{n} = \mathbf{0}\,]$, which exactly describe it. For better understanding and explanation of the individual relations in this property, we use other partial properties which have continuity on the analysed property. These partial properties are described in Figures 3, 4, 5, common with their relevant graphs. Based on the results of individual properties, we decided to divide the whole interval of the parameter $\mathbf{k_r}$ to three following sub-groups: $[\mathbf{0.01}, \mathbf{0.02}, \mathbf{0.03}]$, $[\mathbf{0.04}, \mathbf{0.05}, \mathbf{0.06}, \mathbf{0.07}]$ and $[\mathbf{0.08}, \mathbf{0.09}, \mathbf{0.10}, \mathbf{0.11}]$. Now, we will gradually analyse the given property within individual sub-groups.

First group. From the presented graphs, we can conclude, that the group with $\mathbf{k_r} \leq \mathbf{0.03}$ does not pretty good prepositions to meet this property and therefore the relevant probabilities are the lowest. In this group is therefore very unlikely, that the infection will spread at least for a period of $\mathbf{100}$-time units and then at most for a period of $\mathbf{20}$-time units will disappear. This is caused by slow healing of the infected individuals, which ensures the long-term spread of the infection, regardless of the speed of spreading $\mathbf{k_i}$. Thus for this group is very likely, that the infection will be spreading also after the expiry $\mathbf{120}$-time units.

Second group. The presented graphs show, that this group with $\mathbf{k_i} \geq \mathbf{0.08}$ ensures the short-term spread of the infection. However, the feature of the fast recovery in the combination with the fast spread of the infection will cause the infection that it will not spread either for at least $\mathbf{100}$-time units. Therefore, we can see in Figure 2, that the members of this group achieve the maximal probability in the $\mathbf{k_i} = \mathbf{0.002}$, which represents the most adequate speed of spreading in combination with their rates of recovery. Subsequently, for $\mathbf{k_i} \geq \mathbf{0.003}$, the probability decreases with an increasing the value of the parameter $\mathbf{k_i}$, to almost identically low values of probability as in the first group. On contrary to the first group, there is very likely, that the infection disappears even before $\mathbf{100}$-time units, mainly with the higher vales of both parameters.

Third group. Figure 2 shows, that this group achieved the best results in the global view to the whole range of the parameters. The first two values of this group $[\mathbf{0.04}, \mathbf{0.05}]$ have a growing tendency with raising the value of

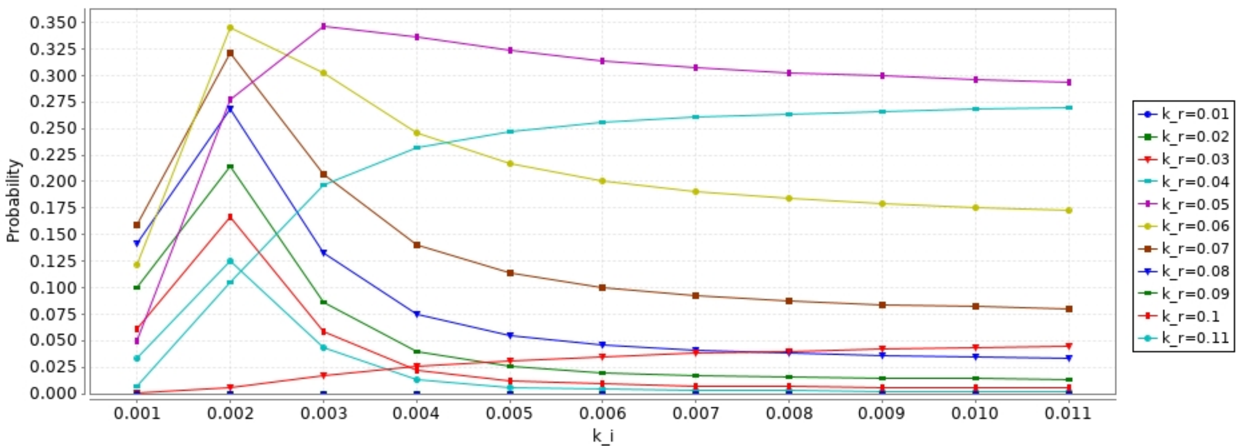

Figure 2. Graph constructed by the experiment running on the following property: $\mathbf{P} =? [\, \mathbf{n} > \mathbf{0}\ \mathbf{U}[\mathbf{100}, \mathbf{120}]\ \mathbf{n} = \mathbf{0}\,]$. This property queries to the probability, that the infection lasts for at least $\mathbf{100}$-times units and disappears within $\mathbf{120}$-time units. The results and consequences of this graph are discussed in the individual paragraphs of this section.

parameter $\mathbf{k_i}$, but the highest growth they achieved in the first values of this parameter: $\mathbf{k_i} \leq \mathbf{0.003}$. When the infection spreading increases over this value, then the probability stays almost at the constant value, thus the parameter $\mathbf{k_i}$ does not significantly affect this probability. We can conclude, that these values are most likely to meet the analysed property mainly with a high rate of the infection spreading, because of their appropriate rate of the recovery. The second part of this group, so the values $[\mathbf{0.06}, \mathbf{0.07}]$, have similar trends as the second group in the previous paragraph. They have the maximal probability in the $\mathbf{k_i} = \mathbf{0.002}$ and then with an increasing value of this parameter the probability slightly decreases. However, we can see that their local maximums are very close to the global maximum, so this combination has almost the best preconditions for fulfilling the given property. The division to these two subgroups is also indicated by the shown graphs, which we also mentioned for example in the description of Figure 4.

Conclusion. When the speed of the recovery is too slow ($\mathbf{k_r} \leq \mathbf{0.03}$) then regardless to the speed of the infection spreading is unlikely that the infection disappears within $\mathbf{120}$-times units and it will be last for a longer period very likely. On the contrary, when the speed of the recovery is too fast ($\mathbf{k_r} \geq \mathbf{0.08}$), then there is a small chance to meet the analysed property only at low speed of the infection spreading ($\mathbf{k_i} \leq \mathbf{0.003}$). The combination of the high values of both parameters very likely causes that the infection disappears even before the expires of $\mathbf{100}$-time units. In general, the best prepositions, that the infection lasts for at least $\mathbf{100}$-time units and disappears within $\mathbf{120}$-time units, has the combination with the low speed of the infection spreading ($\mathbf{0.002} \leq \mathbf{k_i} \leq \mathbf{0.003}$) and the average speed of the recovery ($\mathbf{0.004} \leq \mathbf{k_i} \leq \mathbf{0.007}$). In specific, the combination with the highest probability are the values $\mathbf{k_i} = \mathbf{0.003}$ and $\mathbf{k_r} = \mathbf{0.05}$, respectively $\mathbf{k_i} = \mathbf{0.002}$ and $\mathbf{k_r} = \mathbf{0.06}$. When we take a closer look to Figure 2, in the first pair of these values is an imaginary break within the third group, from where the probability decreases with the increasing rate of infection $\mathbf{k_i}$. Therefore we can consider this combination for an optimal to meet the analysed property, such indicated also the presented graphs.

CONSTRUCT THE REACTION NETWORK FOR THE FOLLOWING VARIANT OF THE EPIDEMIC

Description

Some infected individuals do not recover completely and can infect healthy (uninfected) individuals ($\mathbf{Z}$) even after healing. The *infection rate* from these partially healed individuals is twice as slow (at half the rate) as in the case of infection from infected individuals ($\mathbf{N}$).

Solution

According to the description of this epidemic model, we add to the population new group of the individuals called *partial healed* ($\mathbf{P}$). Individuals within this group are recovered not completely and can infect healthy uninfected individuals even after this partial healing. We can describe this epidemic model with the following reactions:

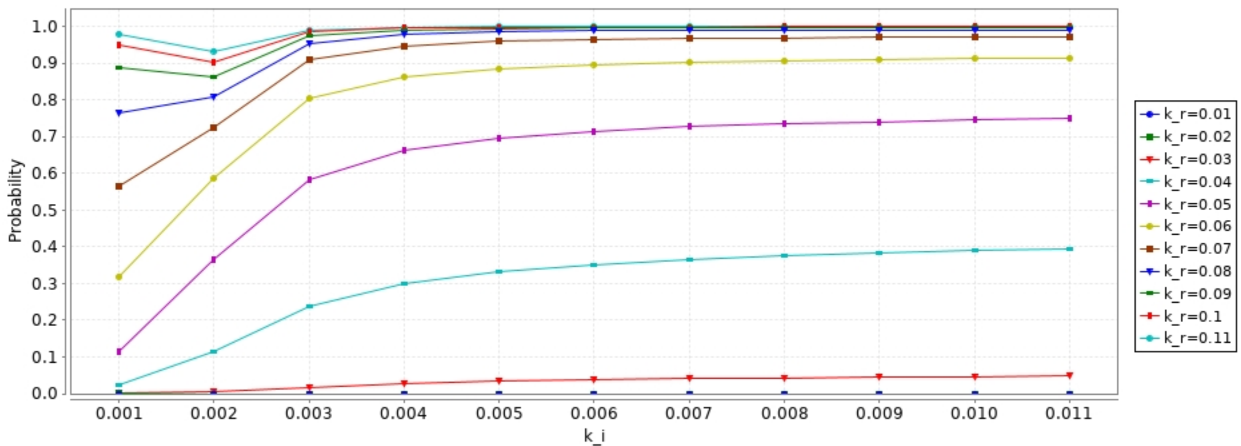

Figure 3. Graph constructed by the experiment running on the following property: $\mathbf{P} =? [\,\mathbf{F}[\mathbf{0},\,\mathbf{120}]\ \mathbf{n} = \mathbf{0}\,]$. This property queries to the probability that exists the path where the infection disappears at some point along this path, within maximally **120**-time units. This graph shows, that for $\mathbf{k_r} \leq \mathbf{0.03}$ is very unlikely the disappearance of the infection within **120**-time units. On the contrary, for $\mathbf{k_r} \geq \mathbf{0.08}$ is very likely, that the infection disappears within the given time interval, mainly, when we will consider $\mathbf{k_i} \geq \mathbf{0.03}$. For the remaining values, $\mathbf{0.03} < \mathbf{k_r} < \mathbf{0.08}$, the probability increases with an increasing value of this parameter $\mathbf{k_r}$, but it is not too low neither too high, as in two previous cases. In the first case, regardless of the rate of spreading the infection, the infection is maintained at all times, thanks to the slow rate of healing. Enough speed of healing ensures, in the second case, that the infection very likely disappears.

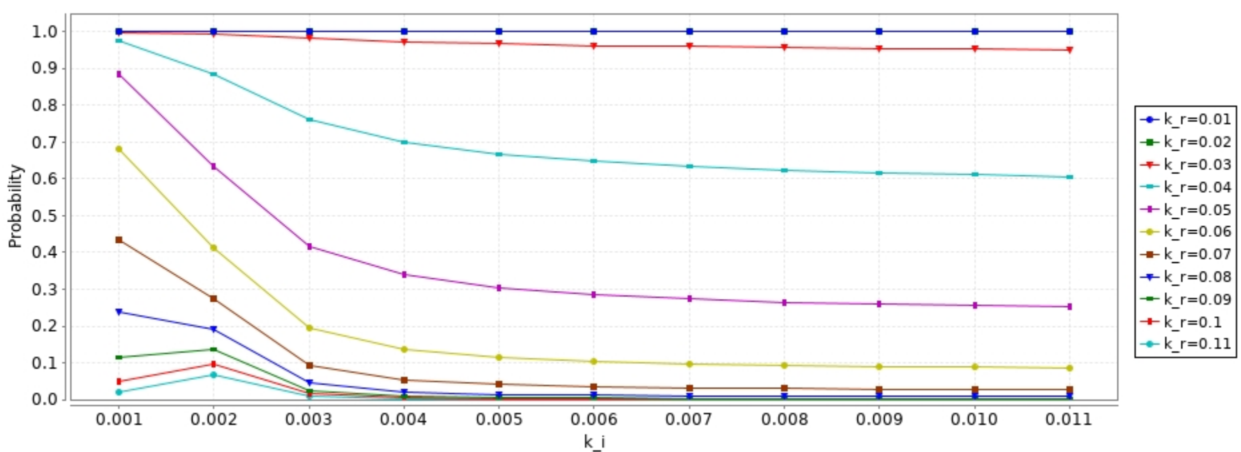

Figure 4. Graph constructed by the experiment running on the following property: $\mathbf{P} =? [\,\mathbf{F} > \mathbf{120}\ \mathbf{n} > \mathbf{0}\,]$. This property queries to the probability that exists the path for the infection to spread even after **120**-time units. This graph shows, that for $\mathbf{k_r} \geq \mathbf{0.08}$ is very unlikely the spreads of the infection after expiry the given time units. We argue this in the same way as in the first graph, thus by enough speed of the healing parameter. The second extreme case, where the querying probability is almost equal to one, includes values $\mathbf{k_r} \leq \mathbf{0.03}$. The low values of this parameter ensure the long-term spread of infection. We emphasise that in this graph from the remaining values, $\mathbf{0.03} < \mathbf{k_r} < \mathbf{0.08}$, the two smallest values differ the most from the described extreme cases ($\mathbf{0.04} \leq \mathbf{k_r} \leq \mathbf{0.05}$). Note also that when $\mathbf{k_i} \geq \mathbf{0.003}$, then all cases have a constant trend and they do not depend on the value of $\mathbf{k_i}$ parameter.

- **infection**: the healthy individual in contact with an infected individual becomes infected – the infection rate depends on the parameter $k_i \in \langle 0.001, 0.011 \rangle$
- **recovery**: the infected individual will recover – the recovery rate depends on the parameter $k_r \in \langle 0.01, 0.11 \rangle$
- **partial infection**: the healthy individual in contact with a partially healed individual becomes infected – the infection rate is twice as slow as in the case of the *infection* ($k_i/2$)

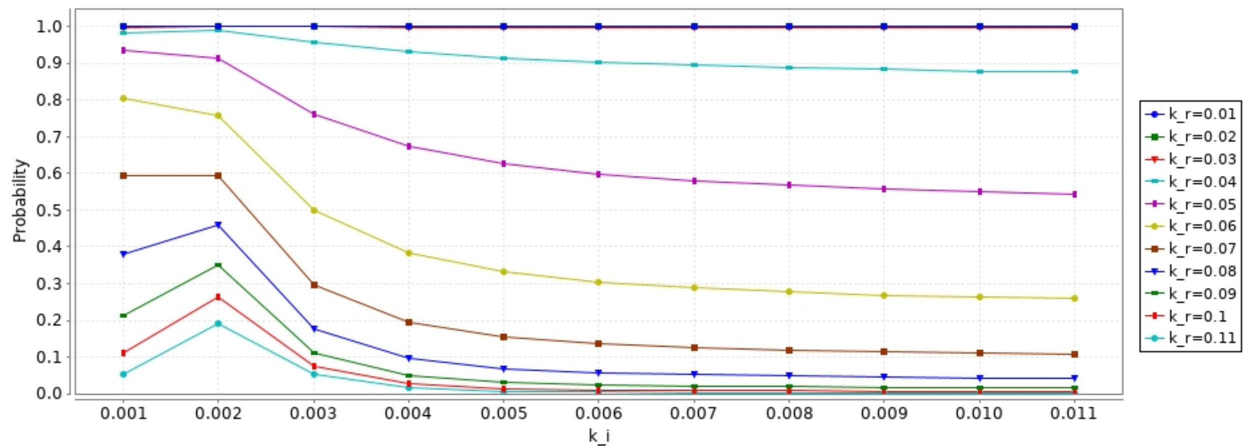

Figure 5. Graph constructed by the experiment running on the following property: $\mathbf{P} = ?\,[\,\mathbf{G}[\mathbf{0}, \mathbf{100}]\;\mathbf{n} > \mathbf{0}]$. This property queries to the probability that exists the path where the infection does not disappear in each point along this path until **100**-time units. We can see, that this graph has a similar arrangement as the previous graph, because of the similar semantics of both properties. Therefore, again we can conclude, that the probability of the disappearance of the infection until **100**-time units at $\mathbf{k_r} \leq \mathbf{0.03}$ is very unlikely, whereas at $\mathbf{k_r} \geq \mathbf{0.08}$ very likely. The middle range $\mathbf{0.03} < \mathbf{k_r} < \mathbf{0.08}$ can be re-assigned to the neither of these groups, whereby the probability, in this group, decreases with increasing value of this parameter $\mathbf{k_r}$. The individual reasons are the same as in the previously presented graph and the constant trend at $\mathbf{k_i} \geq \mathbf{0.003}$ stay also unchanged.

- **partial recovery**: the infected individual will partially recover – the partial recovery rate depends on the parameter $k_p \in \langle 0.005, 0.055 \rangle$

This model then responds to the following reaction network:

$$\textbf{infection} : Z + N \xrightarrow{k_i} N + N \qquad \textbf{recovery} : N \xrightarrow{k_r} U$$

$$\textbf{partial infection} : Z + P \xrightarrow{k_i/2} N + P \qquad \textbf{partial recovery} : N \xrightarrow{k_p} P$$

As it seems at first glance, in contrast to the original model `cov20`, this time the infection does not always disappear. The reason is that there will be a partially healed individuals (P) in the population, which will never totally healing. For the purpose of the demonstration, the original model was modified according to the above-listed reaction network (see file `cov20_4.prism`), and in Figure 6, we can see that the complete disappearance of the infection is now very unlikely. If we always want to achieve complete disappearance of the infection, it would be necessary to add a reaction

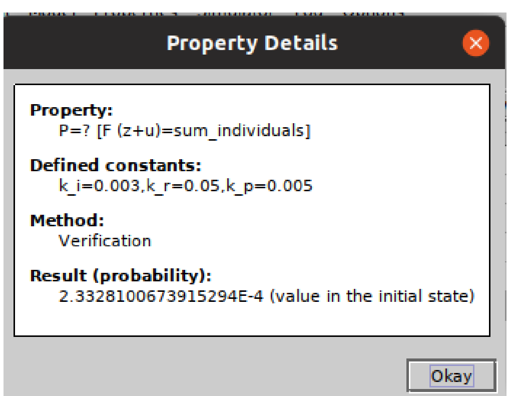

Figure 6. Without totally healing of group **P**.

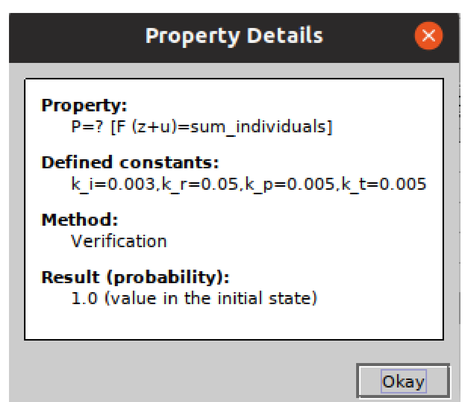

Figure 7. With totally healing of group **P**.

describing the complete recovery of partially healed individuals: **totally recovery** : $P \xrightarrow{k_t} U$.