Megan Tsui 12N2

MODELLING THE COURSE OF A VIRAL ILLNESS AND ITS TREATMENT

Description:

When viral particles of a certain virus enter the human body, they replicate rapidly. In about four hours, the number of viral particles has doubled. The immune system does not respond until there are about 1million viral particles in the body.

The first response of the immune system is fever. The rise in temperature lowers the rate at which the viral particles replicate to **160%** every four hours, but the immune system can only eliminate these particular viral particles at the rate of about **50,000** viral particles per hour. Often people do not seek medical attention immediately as they think they have a common cold. If the number of viral particles however, reaches $\mathbf{10^{12}}$, the person dies.

Modeling infection

1) Model the initial phase of the illness for a person infected with **10,000** viral particles to determine how long it will take for the body's immune response to begin.

Since we know that in 4 hours the viral particles would double its number. Therefore we know that the formula for 4 hours would be

$$x_{n+1} = 2x_n$$

However to work out the growth rate of the particles in 1 hour we would need to work out

$$x_1 = x_0$$
$$x_2 = \text{[illegible]}x = \text{[illegible]}(x_0)$$
$$x_3 = \text{[illegible]}x_2 = \text{[illegible]}(\text{[illegible]}(\text{[illegible]}x_0))$$
$$x_4 = \text{[illegible]}x_3 = \text{[illegible]}(\text{[illegible]}(\text{[illegible]}(\text{[illegible]}x_0)))$$

From this we can work out that the general formula for would be:

$$U_{n+1} = U_n.2^{(\frac{t}{4})}$$

Since we need to work out the total number of particles for each hour, we put 2 to the power of t divided by 4.

This is because the body would only start response when the viral particles go up to 1 million. We could then put:

$$U_n = 1{,}000{,}000$$
$$N = 10{,}000$$

Solve t.

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$$U_n = 10{,}000 \cdot 2^{\frac{t}{4}}$$

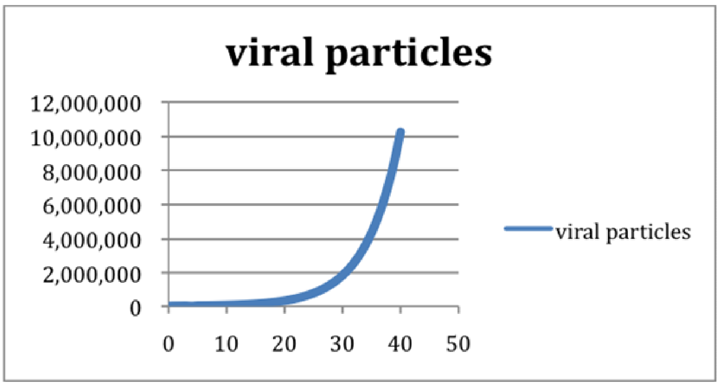
$$1{,}000{,}000 = 10{,}000 \cdot 2^{(\frac{t}{4})}$$

$$100 = 2^{(\frac{t}{4})}$$

$$\frac{\log 100}{\log 2} = \frac{t}{4}$$

$$t = 26.58 \ hrs.$$

Increasing rate = 200% per 4 hrs
Increasing rate per hr =
1.18920711500272



hour	viral particles	Fever?	hour	viral particles	Fever?
0	10,000	not yet	21	380,546	not yet
1	11,892	not yet	22	452,548	not yet
2	14,142	not yet	23	538,174	not yet
3	16,818	not yet	24	640,000	not yet
4	20,000	not yet	25	761,093	not yet
5	23,784	not yet	26	905,097	not yet
…	…	…	27	1,076,347	begin
20	320,000	not yet	28	1,280,000	begin

				29	1,522,185	begin
				30	1,810,193	begin

From this table we can see that after about 26 to 27 hours, the immune system starts to react to the viral particles.

2) Using a spreadsheet, or otherwise, develop a model for the next phase of the illness, when the immune response has begun but no medications have yet been administered. Use the model to determine how long it will be before the patient dies if the infection is left untreated.

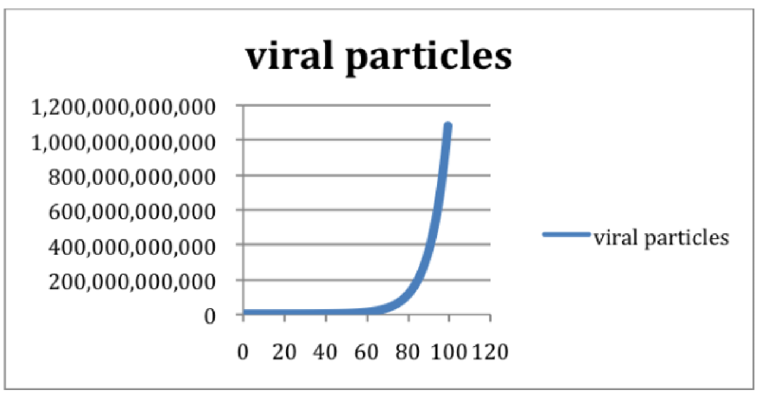
When the patient starts to fever, the replicate rate of the viral particles would decrease from 2.0 to 1.6 growth rate per 4 hours. When the growth rate is 1.6 per 4 hours, the equation would be:

$$x_{n+1} = (1.6)x_n - 200000$$

Therefore the equation of the replicate rate viral particles for 1 hour would be:

$$x_{n+1} = (1.6)^{(\frac{t}{4})}x_n - 50000$$

Since the replicate rate of the viral particles is cumulative, we could figure out the rate of 1.6 to the power of $\frac{t}{4}$, where t is time. The decreasing number of a 4-hour period is 200000, however if we are to work out the decreasing number of viral



particles in 1 hour, we would need to divide 200000 b y 4, which gives 50000

hour	**viral particles**	**Died?**
0	10,000,000	not yet
1	11,196,827	not yet
2	12,542,877	not yet

3	14,056,756	not yet
4	15,759,389	not yet
…	…	…
95	676,199,769,264	not yet
96	760,510,098,682	not yet
97	855,332,463,427	not yet
98	961,977,531,924	not yet
99	1,081,919,390,211	died

If medication were not administered, the immune system would not be able to eliminate a lot of viral particles. Then the particles would accumulate and grow faster and faster. When the particles reach to 10^{12}, which is between the 98th and the 99th hour, the person would die. This mean the patient would die on the 4th day if he or she has not taken any medicine.

Modeling recovery

An antiviral medication can be administered as soon as a person seeks medical attention. The medication does not affect the growth rate of the viruses but together with the immune response can eliminate 1.2 million viral particles per hour.

3) If the person is to make a full recovery, explain why effective medication must be administered before the number of viral particles reaches 9 to 10 million.

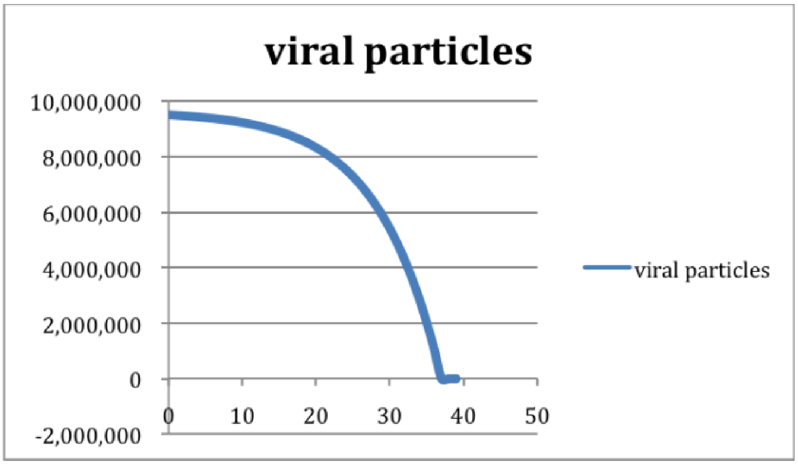
Now let's explore when the patient must take medication by latest in order to make a full recovery, assuming that once the particles reaches 9 to 10 million, the growth rate would maintain 1.6 even when the particles drop below 1 million.

Increasing rate = 160% per 4 hrs
Decreasing rate = 1,200,000 per hr
Increasing3 rate per hr = 1.1246826503807

All the table and graphs below will be base on this general formula:
$x_{t+1} = (1.6)^{1/4} x_t - 1200000$ if $x_t \geq 1{,}000{,}000$
<u>The Patient starts taking medicine when there is 9,500,000 viral particles inside his body</u>

Hour	No. of Viral Particles	Recovered?	Hour	No.of Viral Particles	Recovered?

0	9,500,000	not yet	37	7,191	not yet
1	9,484,485	not yet	38	0	recovered
2	9,467,036	not yet	39	0	recovered
…	…	…	40	0	recovered

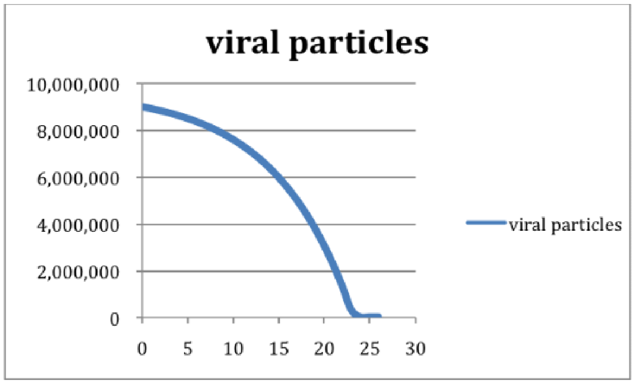


From the table and the graph above, we can see that when the patient start taking medicine when there are 9,500,000 viral particles in the body, the patient would eventually recover in the 38th hour. This is because the immune system is eliminating the viral particles in a faster rate than the growing rate of the viral particles.

We can see from the graph, the curve goes down and eventually the viral particles goes down to 0, which is a full recovery.

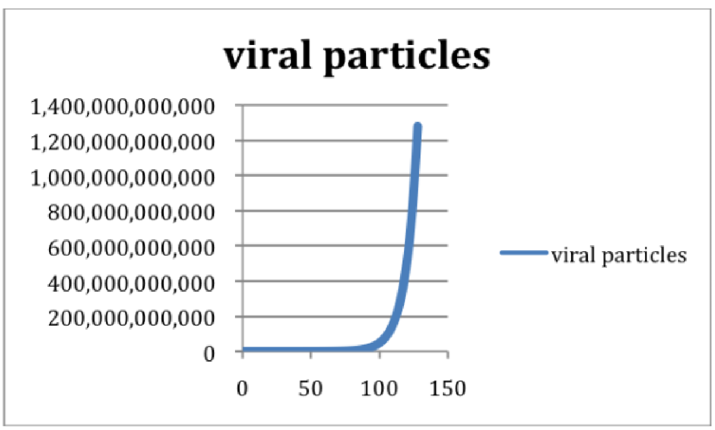
The Patient starts taking medicine when there is 9,00,000 viral particles inside his body

Hour	No, of Viral particles	Recovered?	Hour	No. of Viral particles	Recovered?
0	9,000,000	not yet	23	309,565	not yet
1	8,922,144	not yet	24	0	recovered
2	8,834,580	not yet	25	0	recovered
…	…	…			



From the table and the graph above we can see that if the patient starts taking medicine when there are 9,000,000 viral particles inside his body, the patient would recovery in around 23 to 24 hours. If the patient starts taking medicine, the viral particles would decrease and eventually in between the 23rd and 24th hour, the patient would make a full recovery. This is because the rate of the immune system eliminating the viral particles is greater than the growth rate of the viral particles, therefore the viral particles would decrease as time passes.

<u>The Patient starts taking medicine when there is 10,000,000 viral particles inside his body</u>



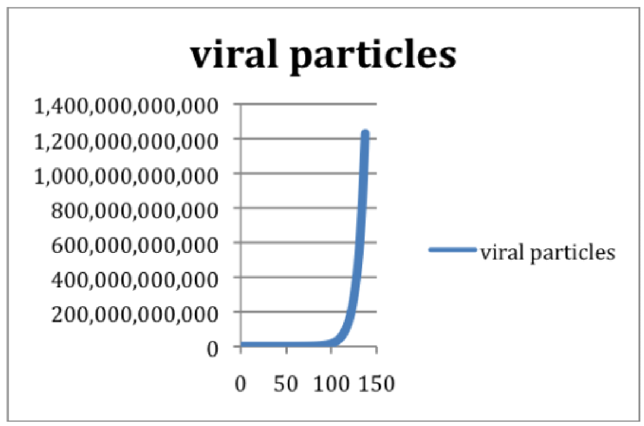
hour	viral particles	Recovered?
0	10,000,000	not yet
1	10,046,827	not yet
2	10,099,491	not yet
…	…	…
125	898,338,099,074	not yet

126	1,010,344,074,204	dead
127	1,136,315,251,173	dead

From the graph and the table we can see if the patient starts taking medicine when the viral particles reaches 10,000,000, the patient would not recover. This is because the growth rate of the viral particles is bigger than the rate of the immune system and the medicine eliminating the viral particles. This would accumulate more and more viral particles as the particles are increasing in the rate of 160% per 4 hours. We can see from the table that even the patient has taken medicine per hour, however the viral particles still increases in his body after each hour and until around the 125^{th} and 126^{th} hour, which is around 5 days the patient dies. We can also see this from the graph, the curve goes up instead of down.

<u>The Patient starts taking medicine when there is 9,750,000 viral particles inside his body</u>

hour	viral particles	Recovered?
0	9,750,000	not yet
1	9765655.841	not yet
2	9783263.694	not yet
…	…	…
135	9.72577E+11	not yet
136	1.09384E+12	dead
137	1.23022E+12	dead



When we take the midpoint of 9,500,000 and 10,000,000 we have the value 9,750,000. However we can still see from the table and the graph, the viral particles increases as time passes. After 135 to 136 hours, the patient dies. We can see if the patient taken medication when there are 9,750,000, it would only delay the time of death of the patient, however the patient would not recover.

We can see the patient would not recover if he starts taking medication when there is 9, 750,000 or 10,000,000 viral particles in his body. But we can see that the patient would survive longer if he takes medication when there are 9,750,000 particles in his body. It would take him 136 hours until his death.

The antiviral medication is difficult for the body to adapt to, so it must initially be carefully introduced to the body over a four-hour time period of continuous intravenous dosing. This means the same amount of medication is entering the body at any given time during the first 4 hours. At the same time, however, the kidneys eliminate about 2.5% of this medication per hour. The doctor has calculated that the patient needs at least 90 micrograms of medication to begin and maintain the rate of elimination of 1.2 million viral particles.

4) Create a mathematical model for this four-hour period so that by the end of the four hour period the patient has 90 micrograms of medication in their. Find the solution to your model analytically, or estimate its solution with the help of technology.

The dosage is 4 hours per does. Since the kidney would eliminate 2.5% per hour, we know that the medicine would decrease 2.5% every hour

Let x be the amount of medication entering the body for each hour
At first: x micrograms
At the end of the four hour period: 90 micrograms

Model:

Let the patient take 1 dose per hour. In the 1st dose between 0 to 1 hour, there would be 0,975 of medicine left in the body.

X is the gram of dosage and every time, after each hour, the dosage would have 0.975% left over since the kidneys eliminate 2.5%. Therefore we must times 0.975% with x for every hours and make it equals to 90, because there will be 90μg of medicine left over after a 4-hour period.

Therefore the 0.975^4x would be 0 hour, 0.975^3 would be the 1st hour, 0.975^2x would be the 2nd hour and 0.975 would be the 3rd hour and x would be the last hour. We can

Solve :x

$\{[(0.975x + x)0.975 + x]0.975 + x\}0.975 + x = 90$

$[(0.975x + x)0.975 + x]0.975^2 + 0.975x + x = 90$

$(0.975x + x)0.975^3 + 0.975^2x + 0.975x + x = 90$

$0.975^4x + 0.975^3x + 0.975^2x + 0.975x + x = 90$

$x = 18.92278\mu g$

Once the level of medication has reached 90 micrograms the patient is taken off the intravenous phase and given injections every four hours. The kidneys will still be working to eliminate the medication, so the doctor must calculate the additional dosage, D accordingly. Dosage D should allow for maintenance of a minimum of 90 micrograms within the patient's bloodstream throughout the treatment regimen.

5) What dosage, D, administered every four hours from the end of the first continual intravenous phase, would allow for the patient to maintain at least 90 micrograms of the medication in his system? Make sure you take into account the kidneys' rate of elimination. Explain carefully how you came to this number.

We know that each hour the body would eliminate 2.5% of medicine. In order to calculate the dosage (D) of injection every hour, this is the formula:

$90(0.975)^4 + D = 90$

where :

$90(0.975)^4$ = the amount of medicine that is maintained in the body after 4 hours

D = the dosage of injection

90 = the microgram that is needed in the body to fight off viruses

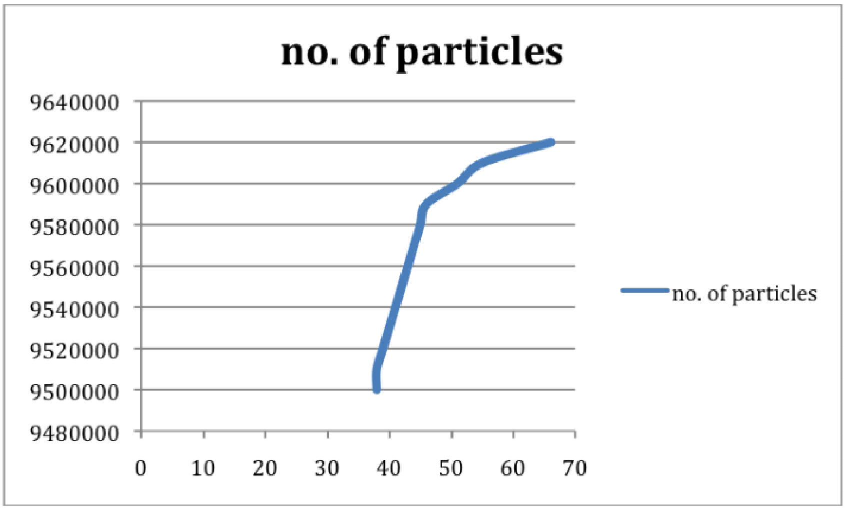
$90(0.975)^4 + D = 90$

D = 8.66808984375001

6) Determine the last possible time from the onset of infection to start the regimen of medication. How long it will take to clear the viral particles from the patient's system? Show on a graph the entire treatment regimen from the time treatment begins until the viral particles are eliminated.

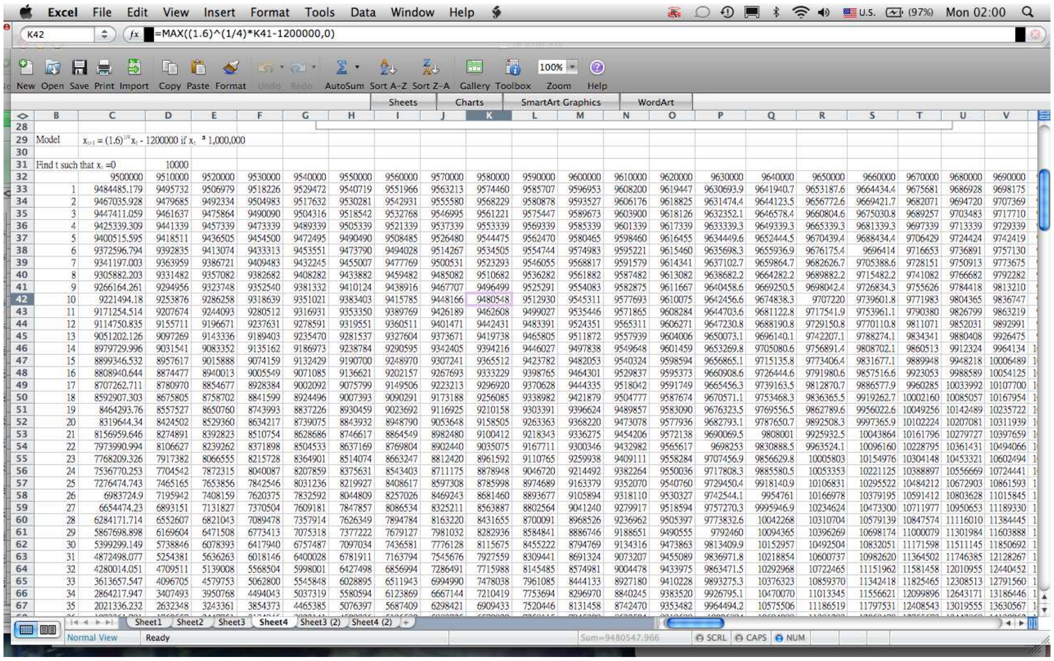
	viral particles	Time t (hr) elapsed
Initial	10,000	90
At t	59,316,416,015	

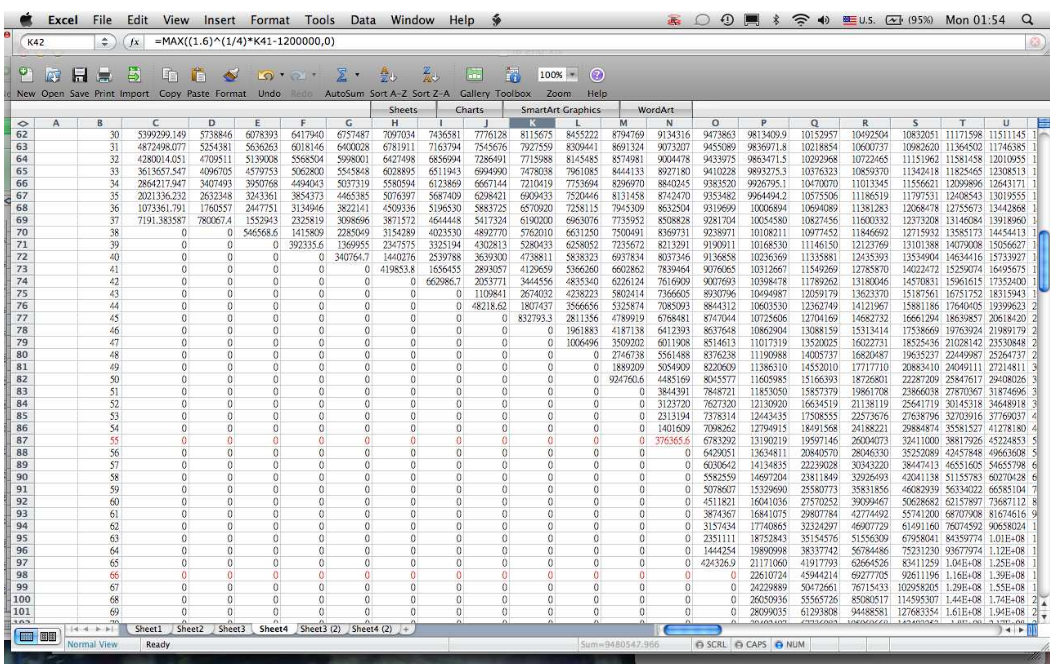
Model: $x_{t+1} = (1.6)^{\frac{1}{4}} x_1 - 12000$



Since the full table is too big to plot a graph I decided to focus on the critical point, which determines the death of the patient. If the patient starts taking medication when the viral particles inside the patient's body are 9,630,000, the patient would eventually die. Therefore the patient should start the medication before the viral particles reaches 9,620,000.

These are the print screens of the full table. I know that the critical rate of the patient's death would be somewhere between 9,500,000 and 9,750,000 therefore I used the trial and error method to see where is the critical point that determines weather the patient survives or dies.





From the 2 print screen table, we can see the O and P column, which is at 9,620,000 and 9,630,000. When the viral particles reaches between these two numbers, it is the critical point of die and full recovery for the patient. This mean the patient must take medication when the viral particles increases to around 9620000 to 9630000, in order to recover, if not the patient may die after a while. This is the critical moment that determines weather the patient would survive or not. The more viral particles there is in the body, the longer it takes for the patient to fully recover and as the particles gone up to a certain amount, the patient would not survive even if he or she takes medicine continuously.

Analyzing your models

Analyze all your models discussing any assumptions you have made, the strengths and weaknesses of the models, and the reliability of your results.

Applying your model

7) Explain how your models could be modified for use if the patient were not an adult, but a young child.

In question 1 we assumed that the viral particles are increasing in a very steady rate and therefore work out the growth rate of the viral particles in each hour.

In question 3 we assumed that once the particles inside the patients' body are over 1 million, the growth rate of the particles would be 160% every 4 hours, even when the patient has taken medicine and the particles are dropped under 1 million. This basically means tat once the patient starts to fever, the growth rate of the particles would maintain in a growth rate of 160% until the viral particles die.

In question 4 we assume that the patient take the medicine per hour, so that we could calculate how many viral particles the kidneys would eliminate in every hour.

The model should be modified if the patient were not an adult but a child. Since the children's immune system would be weaker. The immune system of the adult would be 50000 but the children would smaller than 50000. The medicine that the children take should be less than the adults' proportion as the children's body is not capable to take in too much medicine. Therefore it might means that the children might need to administrate effective medication before 9,000,000 to 10,000,000, in order to survive.

Weakness is that we had made assumptions and therefore we cannot from time to time check the growth factor of the particles. Another weakness is that we estimate by the graphs, therefore it may be in terms of the hours, but not minutes, therefore it is not accurate to the patient. The reliability is also not as reliable because the units are in hours which is very general and it is not precise enough. In order to solve this problem we might need to change the units to minutes to seconds, so that we can estimate precisely what exact time the patient would die. To be more precise I can also work out the exact value of the particles that would cause the death of the patient.