EXCELing with Mathematical Modeling

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Week – 10

Lecture – 48 (Drug Delivery Model)

Hello, welcome to the course EXCELing with Mathematical Modeling.

Today we will be talking about a drug delivery model in the discrete case.

Let us define the model that suppose a patient is given drug to treat some disease, some infection and he or she is given the same dose of the medicine at some equally spaced time interval.

So, as you know when the drug gets into the body not the 100% of the drug works, a part of it works and let that portion or part be r of the original amount of drug that is injected in the body.

Our third assumption is after each dose the amount of drug in the body is equal to the amount of the given dose b plus the amount which is remained from the previous drug.

So, if you want to model this, it will be

$$x_{n+1} = r\, x_n + b$$

So, it is a very simple model. If you want to calculate the equilibrium solution, then we replace

$$x_{n+1} = x_n = x^*,$$

because there is no change from n to $n + 1$. And if you do that, you get

$$x^* = rx^* + b \Longrightarrow x^*(1 - r) = b$$

$$\Longrightarrow x^* = \frac{b}{1 - r}, \quad r \neq 1$$

Now, let us derive this in another way.

So, at

$$x_0 \text{ (no drug)}$$

and

$$x_1 = b \text{ (the first dose)}$$

So,

$$x_2 = rx_1 + b = rb + b$$

So, this is the amount remained from the previous dose and this is the new dose of drug that has been injected. So, I can write

$$x_3 = rx_2 + b = r(rb + b) + b$$

$$= b + br + br^2$$

Similarly,

$$x_4 = b + br + br^2 + br^3$$

In the similar manner,

$$x_{n+1} = b + br + br^2 + \cdots + br^n = b(1 + r + r^2 + \cdots + r^n),$$

Which is a GP series in r. So, the formula is

$$x_{n+1} = \frac{b(1 - r^{n+1})}{1 - r},$$

assuming $r < 1$ because r is a fraction of the drug so $r < 1$. So,

$$\text{as } n \longrightarrow \infty, x_{n+1} \longrightarrow \frac{b}{1-r}.$$

(Since $r < 1$, this quantity $r^{n+1} \longrightarrow 0$ as $n \longrightarrow \infty$)

So for large time it reaches a steady value

$$\frac{b}{1-r},$$

which coincides with our equilibrium solution and we can see that it is stable.

Let us now take a different scenario.

Assume that amount of drug in a patient's bloodstream decreases at a rate of 80% per hour and an injection is given at the end of each hour that increases the amount of drug in the bloodstream by, say, 0.2 units. So, if you want to model this, so

$$a_{n+1} = a_n - 0.8a_n + 0.2$$

$$\Rightarrow a_{n+1} = 0.2a_n + 0.2$$

If you want to find the equilibrium solution, you can easily put

$$a_{n+1} = a_n = a^*$$

and you will get

$$a^* = 0.2a^* + 0.2$$

and you can calculate

$$0.8a^* = 0.2 \Rightarrow a^* = \frac{0.2}{0.8} = \frac{1}{4} = 0.25$$

So, this is your equilibrium solution.

Let us take another example.

So, we assume that a certain drug is effective in treating a disease if the concentration of the drug remains above 100 mg/L. This L is some plasma concentration.

It is a unit commonly used, say, initial concentration is 640 mg/L. The drug decays at a rate of 20% of the amount present each hour.

So, if I take

$$C_n = C_{n-1} - \frac{20}{100} C_{n-1} = 0.8C_{n-1}$$

$$\Rightarrow C_n = 0.8 \times 0.8\, C_{n-2} = (0.8)^2\, C_{n-2}$$

$$\Rightarrow C_n = 0.8 \times 0.8 \times 0.8\, C_{n-3} = (0.8)^3\, C_{n-3}$$

So, in general,

$$C_n = (0.8)^n C_0$$

So, C_0 is the initial concentration, that is

$$C_0 = 640$$

which gives

$$C_n = 640(0.8)^n$$

So, the question we pose here is at what hour the concentration of the drug reaches 100 mg/L. So, please note the problem says that the drug is effective if the concentration of the drug remains above 100 mg plus L. So, we want to find in how much time or how many hours that concentration of drug will reach 100, provided it follows this particular model.

Let us quickly see the numerical solution of this particular model using Microsoft Excel.

So, as you can see this is the model which has been discussed previously, that is,

$$a_{n+1} = 0.2a_n + 0.2$$

So, I have taken two initial conditions 0.1 and 0.5 just to see how it will look.

So, this is

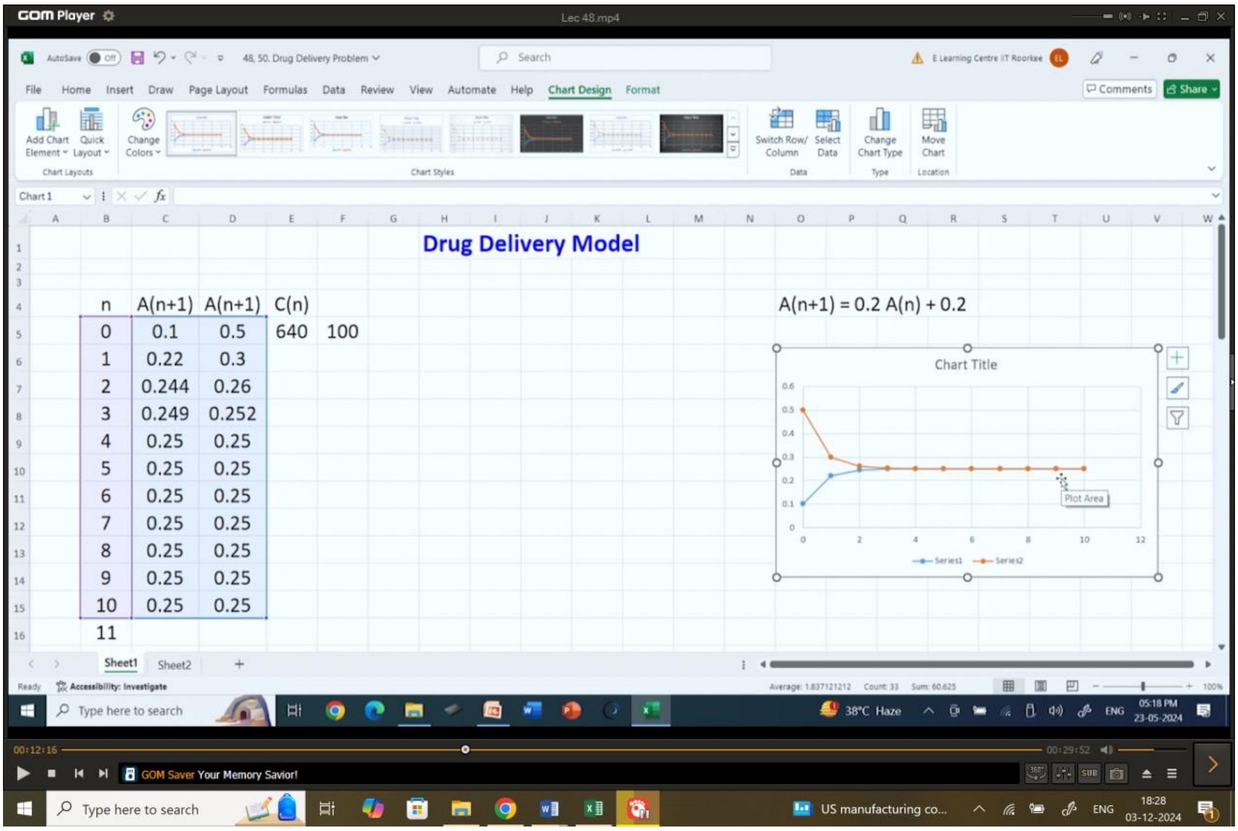
$$= 0.2 \times a_n(0.1) + 0.2 = 0.22$$

So, I get one value and this is

$$0.2 \times a_n(0.5) + 0.2 = 0.3$$

So, if I just highlight them and calculate the values, so, if I just plot this 10 values, I will see a graph like this.

So, if this particular problem has an equilibrium point as 0.25 and you can see that no matter from whatever initial condition it start it reaches the value 0.25 implying that the system is stable about the equilibrium point.



Now coming back to the recent problem where it says that you have a concentration of drug and you have shown that the model is

$$C_n = 640(0.8)^n$$

This is the model which we are discussing about.

So, what we have to find that it says that the drug concentration cannot be less than 100 mg/L sample plasma concentration.

So, we want to find it from the graph that what is the time that will make the graph of the drug to reach that 100 mg/L. So, what you do here is, this is the initial concentration. This is

$$= 640 \times (0.8)^{n=0} = 640$$

and I drag it say up to 30 values.

Now this is 100, I keep it the constant value 100 because I need a straight line. So, all of them are 100.

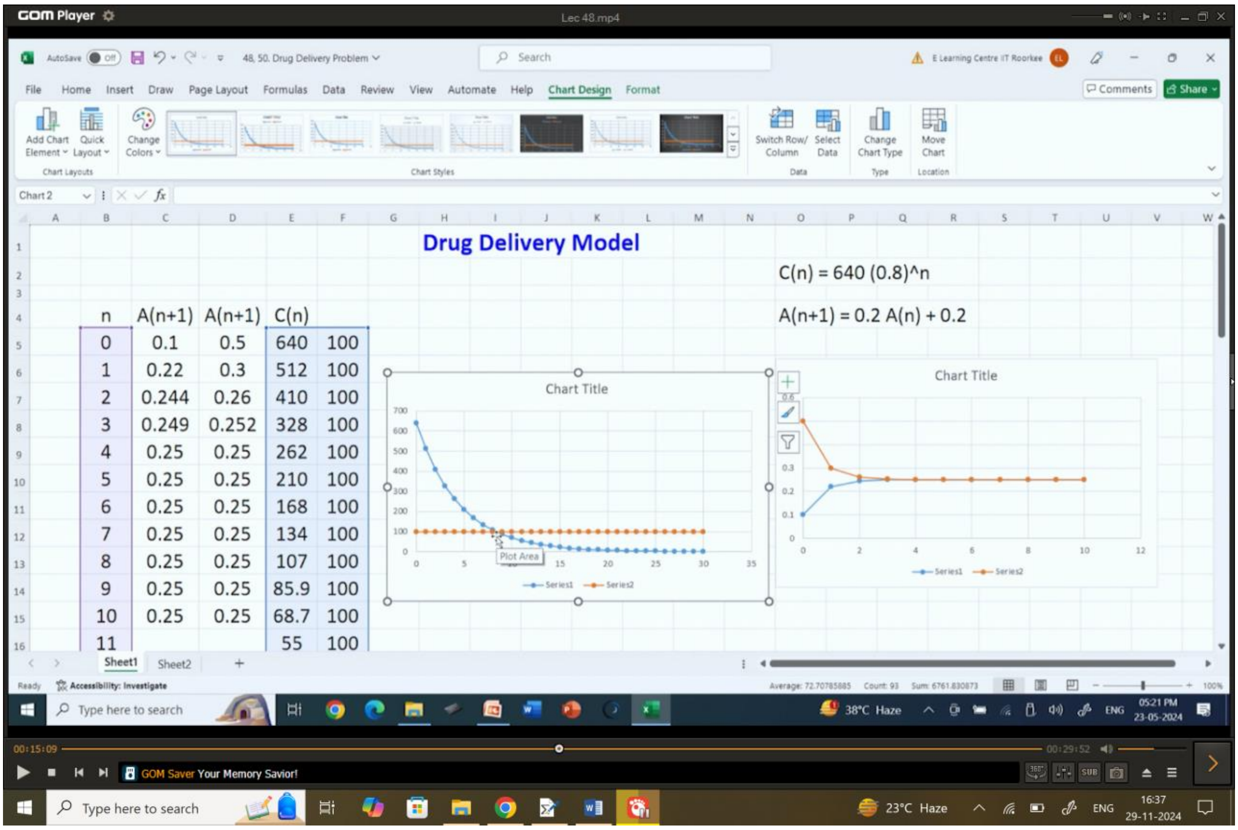
Now let me plot this. This is zero, I highlight till 30 values.

When you click the control, you press this, you press shift and the down cursor. So, it will highlight this row, this column.

Again, press control, select this, press shift and the down cursor. So, these three columns have been selected. You go to insert, go to the chart, see the chart.

So, what you see here is that this is the drug the curve and it goes to 0 and this is the line of 100 mg/L. So, this is the point of intersection and that value is approximately equal to 9 time unit in this case it is hour.

So, approximately in 9 hours the concentration of the drug will reach the 100 mg/L.



Let us now go back to our slides.

So, the answer to our question that what hour the concentration of the drug reaches this 100 mg/L is approximately 9 hours which we have shown by solving this model numerically.

The next part is what is the maintenance dose that will keep this drug above 100 mg per L and below 800 mg/L. So, how much drug you should give?

It should have a range such that it always lies above 100 mg which is required for the drug to be effective and below 800 mg per L so that there is no overdose.

So, for that you go back to the model which is

$$C_n = 0.8C_{n-1}$$

and we have our x,

$$C_n = 0.8C_{n-1} + x$$

suppose x is the dose.

So, if we want to find the equilibrium solution, we will replace this

$$C_{n+1} = C_n = C^*$$

So

$$C^* = 0.8C^* + x \Longrightarrow x = 0.2C^* \Longrightarrow C^* = 5x$$

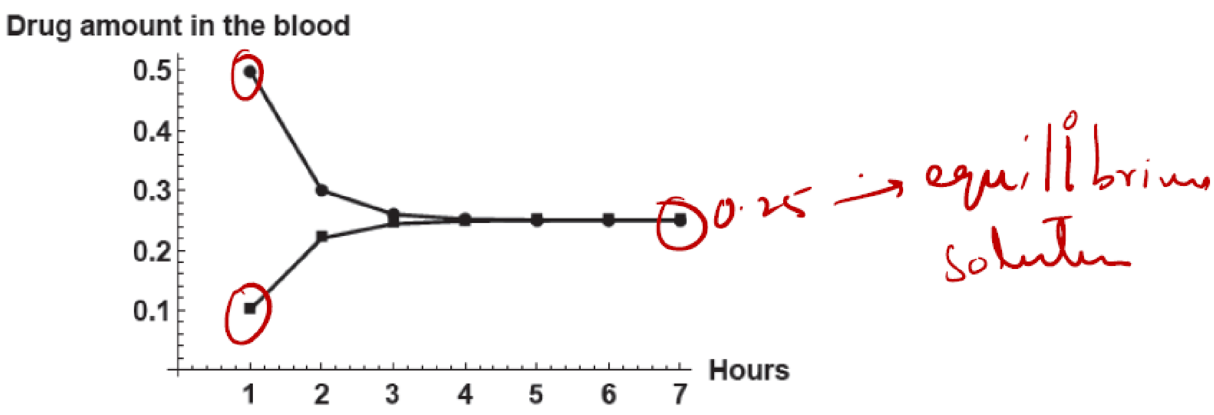
Now, this value should not cross this 100 and it should lie between this 100 and 800.

So, you have

$$100 < 5x < 800 \Longrightarrow 20 < x < 160$$

So, this will imply that you want to give to the patient such that the drug concentration is never below 100 and never cross the value 800, is that the dose must lie between 20 and 160.

Let us quickly see the numerical solutions. So, this is the one which we have shown in Microsoft Excel.

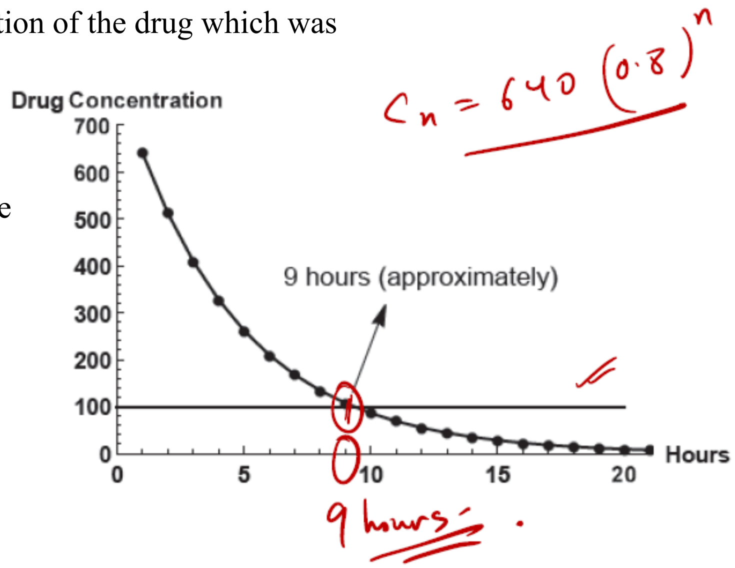


So, it says that this value reaches 0.25 it starts with an initial condition 0.5 and 0.1 but since the system is stable it goes to the value 0.25 which is the equilibrium solution.

In this, it is shown that this is the concentration of the drug which was

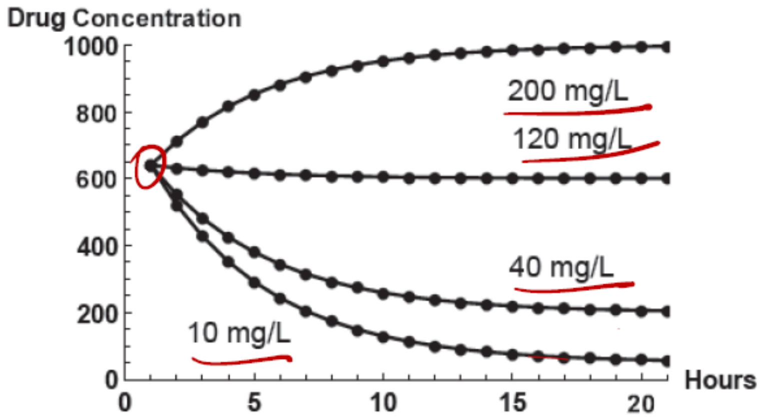
$C_n = 640(0.8)^n$

and we have plotted this and this is the line for 100 mg/L. So, both intersect somewhere here and it shows that approximately 9 hours will be needed so that the concentration of the drug reaches 100.



And finally, this one is where we have shown that the range of the constant input of the drug must lie between 20 and 160.

So, this particular figure shows that it starts with an initial condition which is 640 and the amount of drug here is 10, 40, 120 and 200.



So what will happen that if this concentration of drugs is maintained so if it is 10 as you can see that it is going down below 100 whereas if it is 40 and 120 it lies within the range and if it is 200 it will go beyond.

We now take another example say a person with an ear infection takes 150 mg ampicillin tablet once in every 4 hours. So, that is the time interval. About 15% of the drug in the body at the start of a 4-hour period is still there at the end of the period.

So, a person with certain ear infection, he takes 150 mg of ampicillin tablet every 4 hours and 15% of the drug is in the body in this 4-hour period.

So, the first question which we ask, (i) what quantity of ampicillin is in the body right after taking the third tablet.

So, as we have modelled this before, the model equation is

$$x_{n+1} = rx_n + b$$

So, r is the amount of drug which is present in the body and so in this particular case r=15%

$$r = 15\% = \frac{15}{100} = 0.15$$

and the dose every 4 hour is 150 mg.

And we have shown that this is

$$x_{n+1} = \frac{b(1 - r^{n+1})}{1 - r}$$

So, after taking the third tablet, we have to calculate x_3, with $b = 150$

$$x_3 = \frac{b(1 - r^3)}{1 - r} = \frac{150(1 - 0.15^3)}{1 - 0.15} = 150 \times \frac{0.996625}{0.85} = 175.875 \text{ mg}$$

So, the quantity of ampicillin tablet which is in the body right after taking the third tablet, the amount of ampicillin is 175.875 mg.

Next, we pose another question, say, what quantity of ampicillin is in the body

(a) at the steady state level right after taking the tablet

and second question is

(b) at the steady state level right before taking the tablet.

So, the first question is what is the quantity of ampicillin in the body at the steady state level right after taking the tablet and we know that the equilibrium point or the steady state is obtained by replacing

$$x_{n+1} = x_n = x^*$$

as there is no change from n to n+1.

So, this gives

$$x^* = rx^* + b,$$

which implies the value at the equilibrium point or at the steady state level is

$$x^* = \frac{b}{1-r} = \frac{150}{1-0.15} = 176.47 \text{ mg}$$

So, the quantity of ampicillin right after taking the tablet at the steady state level is 176.47.

And the quantity of ampicillin at the steady state level before taking the tablet, it is going to be $x^* - b$. So this is the dose which you take every four hours.

So just before taking the tablet, that is,

$$176.47 - 150 = 26.47,$$

gives you the amount of ampicillin in the body at the equilibrium point or at the steady state level before taking the tablet.

Let us now solve this model or this particular problem numerically using Microsoft Excel.

So, I already have the equation

$$x_{n+1} = rx_n + b,$$

$$r = 0.15 \text{ and } b = 150$$

So, I have n and I have $x(n)$, so, we put here $n = 0$, the initial value here is $x(0) = 0$.

So, we increase here by 1 and drag this to a few values.

This value is

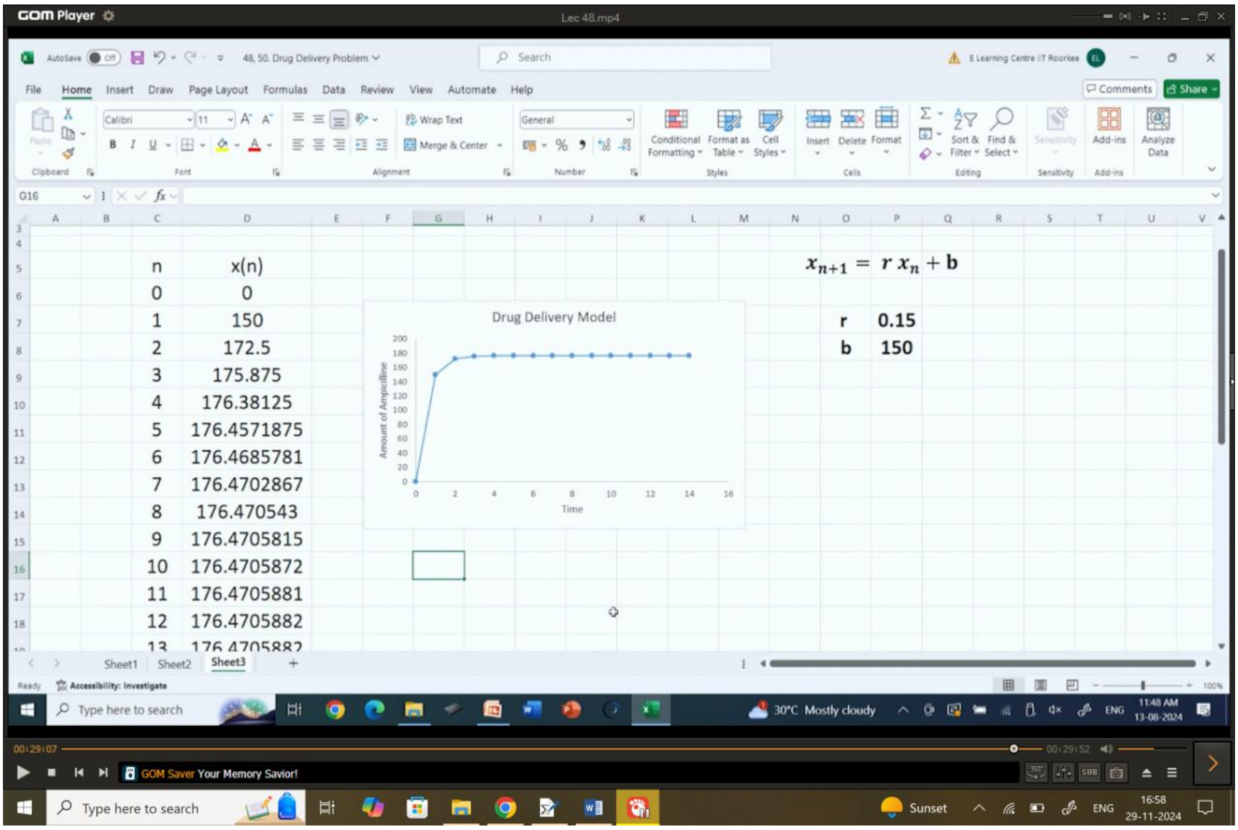
$$rx_n + b$$

So the value of r is constant and the value of b is constant. So I put a dollar and enter.

So I drag it to some values and then I plot this graph, go to insert, go to chart and click this.

So this is white drug delivery model we remove the grid lines go to the axis title this is the time and this is the amount of ampicillin.

So, as you can see that this value over time reaches the value 176.47 which matches with our analytical result.



So, with this we come to the end of this lecture where we have shown the discrete case of a drug delivery model.

In my next lecture, we will be talking about combat models, namely, discrete Lanchester's combat model.

Till then, bye-bye.