

**INDIAN INSTITUTE OF TECHNOLOGY ROORKEE
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**Mathematical Modeling:
Analysis and Applications**

Lecture-14

**Continuous Time Models in
Population Dynamics-II**

With

Dr.Ameeya Kumar Nayak

Departmental of Mathematics

Indian Institute of Technology Roorkee

Welcome, to the Lecture in the series of Mathematical modeling, analysis and application, in the last lecture, we have discuss have about the population and dynamics modeling and how we can formulate like, scientification deviation model, using a differential equation that we have discussed and in that lecture, we have also discussed that how we can just achieve this study state solution also, and this study state solution that, depends on like, resources have available and this resources, how it is just acting inside the like population growth, level we have also considered and in this lecture we will discuss about continuous study time models, in population dynamics So, like for different structures

(Refer Slide Time: 01:12)

Contents:

- Chemostat.
- Formulation of Chemostat Model.
- Dimensional Analysis of Chemostat Model.
- Non-Dimensionalization of Chemostat Model.

That is a first will go for like, chemostat, in a last lecture I have given the overview about chemostat also, and in this lecture will discuss about to in detail, how chemostat is acting for this like, population growth or like, decaying depth, then in second phase we just discuss about the formulation of chemostat model, and in the third phase we will discuss like, dimensional analysis of chemostat model, and in the final phase we will just go for like non-dimensionalization of chemostat model

(Refer Slide Time: 01:50)

Chemostat:

- In the last lecture, we introduced Chemostat which is a device used to study the behavior of micro-organisms with limited resource availability.
- The Chemostat can be represented as:

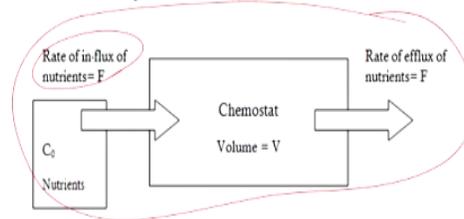


Fig 14.1 Chemostat

So, if you just will just go for like, the introduction of chemostat, chemostat is nothing but, it is a device used to study the behavior of micro-organisms with limited resource availability, this means that, the chemostat can be represented as, rate of influx of nutrients F , in to the system and which can be accumulated in volume V , then it can be extracted out, as a rate of efflux nutrient F , and the total system whatever, it just occurring like, supply of food and this, like cells utilization and what is the out food it is just coming, and the total system it is called chemostat (Refer Slide Time: 02:42)

Chemostat:

- A chemostat is basically a bio-reactor to which fresh medium is continuously added and the liquid inside chemostat is continuously removed in order to keep the volume inside chemostat constant.
- The liquid inside the chemostat should be well mixed so that conditions are homogeneous or uniform. This make it self-regularized i.e. when nutrients are more than micro-organisms, it accelerate their growth. When they are in sufficiently large numbers, they compete for nutrients and make them to reduce in number. Since the total volume of chemostat should be constant, this make nutrients to increase. This process repeats in cyclic manner in order to keep chemostat volume constant i.e. at steady state.
- The concept of chemostat is widely used in drug delivery.

So, chemostat is basically a bio-reactor to which fresh medium is continuously added, this means that like, we can say that, it is sufficient oxygen can be supplied to a medium then, this cell will growth in a uniform way, so, like if you just see our like new joints there also, requires like supply of, like external agents to get the activation of this leads and it should have like, uniform growth for that, and this is basically called tissue engineering scaples or tissue engineering bio-reactors, it has been used for chemostat process, and presently we are just discussing, the chemostat, which is used for like, culture of this cell, so culture of the cell means it, two types of

cell culture, it is used one it is called continuous culture techniques, one it is called base cultural techniques, and we are not going in detail that, but for in a general sense, if you just discuss here, chemostat is basically bio-reactor which a press medium is continuously added.

Like I have explained, suppose oxygen is supplied, and the liquid inside the chemostat is continuously removed in order to keep the volume inside the chemostat constant, so whatever it has been since, they contain or the volume is constant, so according to, like conservation mass whatever this amount has been supplied, the same amount it can be clocks out there, and the liquid inside the chemostat should be well mixed, so that conditions are homogenous for uniform and this make it self-regularized that is , when nutrients are more than micro-organisms, it accelerate their growth definitely if it will not properly mixed then we cannot find like, uniform structure of this, all the medium there, this growth will be amphere, when they are in sufficiently large numbers, they complete for nutrients , and make them to reduce in number, since the total volume of chemostat should be constant, this make nutrients to increase.

This process repeats in cyclic manner in order to keep chemostat volume constant, that is the study state we can just find, that in a cyclic form we can just find that always we will have like, constant level it should be maintained there, and this concept of chemostat is widely used for drug delivery systems, especially, when the drug delivery is applying, then there is a uniform distribution of ,they say nutrient are, they say chemical or whatever it is say, it should be supplied to our body should be maintained. So if you just go for this mathematical representation of

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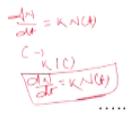
Formulation of Chemostat Equation:

- The mathematical model representing chemostat is:

$$\begin{aligned} N'(t) &= K(C)N - FN \\ C'(t) &= -\alpha K(C)N - FC + FC_0 \end{aligned} \quad \dots 14.1$$

here $-FN$ in first equation represents the total mixed outflow (= flow rate F * concentration of population N). We are assuming, bacteria are properly (well) mixed with resources in chemostat. This is to make mixture of resources and bacteria to be spatially independent. And hence they are only depending on time and therefore the model will be formulated by ordinary differential equation. (Note!) Now think the situation when bacteria's are not well or properly mixed inside the chemostat. (Exercise!)

Similarly, $-FC$ in second equation represents the depletion of total resources. The term $+FC_0$ represents the initial storage of resources.





Chemostat, then already in last lecture we have discuss that, this growth of population level, that is defined as $dN(t)$, which is return as like K in to $N(t)$, where there K is a rate of population and that level we have just consider, where if the resources are available or this C is the concentration of resources, we have just consider, then we have considering the K is a function of serer and our model is directly defined as the form of like $K N(t)$, okay, so, DN/DT , so DN/DT is just defined as in the form of , $K*N(t)$, and where they say K is depended on like, they say concentration

level of C is available, they are, the resources available they are and even if, there is population level it is sending to the respective time.

We cannot say that, this population growth rate, it just actively participate or actively it is just occurring inside the system, since if you will just see here, we have just $-FN$ here, so which represents the total mixed outflow over there, it means that inside the container or inside the volume whatever the change of population with respective time, you just consider, that depends on this total population size multiply with this like, proportional constant and whatever this outflow is that, occurring over there also, outflow means, we can just say that flow in with nutrients and it can just take out some of this constant some of the population from this system also.

So, that is why? we are just Writing here, the total mixed out flow is defined as flow rate of $F * \text{concentration of population } N$ there, so, maybe some dead cells are there, or some of the active cells that can removed out with the flow there, and we are assuming that, bacteria are properly mixed with resources in chemostat, this is to make like, mixture of resources and bacteria to spatially independent. And hence, they are only depending on time and therefore the model will be formulated by ordinary differential equation.

Since, we are just considering here, as a change of population or change of cell or number that whatever it has been just change with respective proportional constant with total population size and whatever it has been eff flux out from the system, and now think, if we will have like non-uniform distribution or it is not properly mixed inside the system, many constant it will come in to the picture that maybe in the next slides are in the next lectures, we can just consider, many restrictions it will be just followed in to that model

Similarly, equations, that you have see here, we are just assume this concentration or limited resources are available there, that will also get chance to a respective time, since, the cells that will consuming the concentration and this concentration chance, which effectively depended on this $-\alpha K (C) N$, that we have discussed or previous lecture that resources it will be just to used to by this cells, so that is why? Get like, used their depending on the population size N and finally we are just adding a term that is $-FC$, which is represents decaying of a total resources or a decrease of the resources, and FC_0 , we are just adding the extra term, which is just depending on initial storage of resources, that depends on whether it has been used by the cells or some remaining portion it has been used by the cell and it is kept there, that depend on. So, if you just go for this

(Refer Slide Time: 10:10)

Dimensional Analysis of Chemostat Equation:

- Let's consider the first equation of chemostat model eq. 14.1

$$\dot{N}(t) = K(C)N - FN.$$

- The dimension # of each term is:
 - $\#[\dot{N}(t)] = \text{number}/(\text{volume} * \text{time}),$
 - $\#[K(C)] = 1/\text{time},$
 - $\#[N] = \text{number}/\text{volume},$
 - $\#[F] = \text{volume}/\text{time}.$
- Now substitute all these dimensions in equation to verify the correctness of equation. **Have you observed any inconsistency?**
- To correct this problem, we need to divide the flow rate F by volume V. Practically, we should define flow rate per unit volume instead of flow rate



Dimensional analysis of this chemostat Equation, we can just find that, this equation $\dot{N}(t)$ which involves K, M and $-FN$ there, that is the flow rate out and which just can take out the total population size or the population size it can be just taken out, and if you just see here, $\dot{N}(t)$, is nothing but which can be defined as dn/dt there, and dn/dt that depends on this number per volume over time, this means that this change of number population that completely depended on this volume of the container and with respective time how it is getting chance to there, that is why? This Dimensional it can just define as number for volume * time.

And $K(c)$, that is your rate of change of like, population level, which depends on time only, so that, is why? it has been defined as one over time there, and the number means that is a total number of a population, total number of same size, that depends on the number volume there, and F there is a flow rate which depends on this volume, over the time and if you just substitute all this dimensions in equations here, to verify this correctness of equation, since it is very essential to do this dimensional analysis for all these different equations to get a solution.

So, we can just find there, the inconstancy is preserved inside the system, since if you have put all this dimensional number inside this system we can find that, whatever dimensional will get left hand side this not equal to right hand side, so that is why? it say in balance system or in considered system, to correct this problem, we need to divide the flow rate F by the volume V there, so practically, we should define flow rate per unit volume instead of flow rate for (Refer Slide Time: 12:23)

Dimensional Analysis of Chemostat Equation:

- So the dimensionally correct chemostat model is:

$$\frac{dN}{dt} = K(C)N - \frac{F}{V}N$$

$$\frac{dC}{dt} = -\alpha K(C)N - \frac{F}{V}C + \frac{F}{V}C_0$$

- To validate the model, we can now check the dimension of second equation:

$$\#[C(t)] = \text{mass}/(\text{volume} * \text{time}),$$

$$\#[\alpha] = \text{mass}/\text{number},$$

$$\#[N] = \text{number}/\text{volume},$$

$$\#[K(C)] = 1/\text{time},$$

$$\#[C] = \text{mass}/\text{volume},$$

$$\#[F] = \text{volume}/\text{time},$$

$$\#[V] = \text{volume}.$$



Instead of flow rate, so, for that what you will do is? We have to correct this like, chemostat model and for that what will do is, we will just divide a F/V in the right hand side, and then will have like corrected equations here, since you can see here, the left hand side it is a number for volume * time, this $=K$ is $1/\text{time}$, * N * number per volume $-F$, is a volume for time * N it is a number, for volume * time, so if you just see volume we can send it out, so this left hand side number for volume * time, this = number for volume * time, - number per times so, if you want to find in a compliancy here, that is a number per volume * time, so this one is the number per time square here, so F is defined as a volume per time, then will have like, N it is a number per volume, sorry this one not a time, number per volume here, so this will be time here, number per time, so we will see now here is number per volume * time, this = number per volume * time - number per time here, so that is why? There is a discrepancy of, there is like, deficit of this volume here, so that is why? We have to like, divide a volume to get in to a complete dimensional situation or to analyze this correctness of this dimensional, we have to divide the volume in the final term.

So, if you just divide this volume here, then we will have the equations like, dn/dt , which is defined as $K(c)N - F/V * N$ there, so now we just have a complete dimensional model and if you just see this second equation here, that is just defined as a like, $C(t) = -\alpha K(c)N - FC + FC_0$, we can just see that this $C(t)$, or like, concentration with respective time, which can defined as mass for volume * time this = α which is defined as a mass per number * K is defined as time, * N is defined as number, for volume - this is $F(v)$ F is return as volume per time, * C is defined as mass per volume divided by V here, V is defined as volume here, + $F(v)$ you will see here, F is return as volume per time, and C_0 is nothing about the constant here, so divided by volume is defined as volume

So, if you just see here, so the first one is mass per volume * time, and this is also the mass number * time, number, number in to is cancel it out, so we will have now mass by volume * time here, then if you just see here, volume, volume will cancel it out, so if you just see here, this is a mass per time * volume and if you just see here, this is just defined as F , F is volume per

time, by volume * C₀ can be return as mass per volume here, so volume, volume cancel it out, so this will just give you mass per time * volume.

So, now it is perfectly equal for dimensional analysis, so finally we have this mass per volume * time basically to mass per volume * time- mass per volume * time, + this is a mass per volume * time, so perfectly equal

(Refer Slide Time: 17:58)

Analysis of Chemostat Equation:

- So now we have got the dimensionally correct chemostat model.
- In previous model, we analyzed the rate of reproduction per unit time, K was linearly depending on resource concentration C i.e. $K = \kappa C$. This simply implies that for high amount of resources, the bacteria population will go on increasing. **Does this happen practically?** NO!! Hence we need a function $K(C)$ in such a way that it has some saturation limit i.e. resources are available only up to some limiting value.
- One such type of function is given by
$$K(C) = K_{max} \frac{C}{K_n + C} \quad \dots 14$$
 This function saturates to K_{max} when K_n tends to zero. Also at $C = K_n$, the function will give half the value of saturation limit K_{max} .

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So, if you just go for the analysis of chemostat equation, we can just find that, this is a dimensional correct now, and in the previous model, we analyzed the rate of reproduction per unit time, K was linearly depending on resource of concentration, so already we have defined that $K = \kappa C$ we can defined and this implies that for high amount of resources, the bacteria population will go on increasing, since available resource it is sufficient they are, then the population level will grow straight up, so, does it happen practically? Especially no, since, if you just see here, we need a function $K(C)$, in such a way that, it has some saturation limit resources are available only up to some limiting value.

After that, you can just find that, whatever the resources it will just grow up or it can come just to the picture, then it can be utilize in a uniform manner, especially if you just see that suppose one year population for existing for a practical chance if you just say, and suppose available graph it is the, and this one year population will just increase, if a sufficient graph is available to them and it suppose one year population level will get increased in high level and there will be a shortage of graph and after certain time you can find that, they will just struggle to find the food and some of the food will die over there, and is some of this population will die out, again that resources will be available there, since the graph will like, grow of, it will be like, after level that this deer's can eat and this will balance the nature and such a phase on that, this resources will be available to them.

In a such manner that, we will have a like, linear growth, and if you just consider such type of models then, one such type of function it is consider in the form of like, $K(C)$, this available of resources or the concentration which depends on this rate of change of population which it is defined in the form of $K_{max} * C / K_n + C$ okay, K_n is a constant parameter which balances this K_{max}

value and C value and this functions saturates to K_{max} when K_n trends to 0 if 20:93) will just to suppose to food here, and K_n hence to 0, over here, then $K(c)$, is especially to standing to K_{max} here, hence $C/C=1$, and if you just assume that, $C=K_n$ suppose then, the function will give half of this saturation value

So, this function is defined in a such matter either a maximized value, or it just give half of the value of this such ratio we can just accept, and in the graphical sense, if you, just visualize this one so it is just presented in the figure here, and this function is known as Michaelis –Menten Kinetics, and this model with is kinetics will be given as like if you just replace here, and the entity as the $K(c)$ $N-F/VN$ here, so it can be return as K is replaced by $K_{max} * C/K_n+C^n - F/V^n$, and dc/dx , dc/dt , it return as like, $-\alpha * K$, so that is why? $K_{max} C/K_n+C^n - F/V^C + F/V^C_0$ over here, now if you just observe this equations, the parameters if you just see the, the parameters are like, K_{max} then, K_n here, F is present, and then, V is present, α is present, and K_n it is also present here.

So, two more times we have just return here, K_n , so, K_{max} then, F , V , α and K_n , now let us do this non-dimensionalization to reduce the number of parameters, especially we have just discuss in one of the our earlier lecture about this non-dimensionalization things when we have just use to say descript logistic model, so there we have used to reduce a parameters to get this two parameters to one parameters solution there, so, especially this dimensionalization is made to reduce this parameters.

(Refer Slide Time: 22:36)

Non-Dimensionalization of Chemostat Equation:

- To reduce the number of parameters, let's re-scale all the variables as:

$$N = N^* \times N1,$$

$$C = C^* \times C1,$$

$$t = t^* \times t1,$$

where N^* , C^* , t^* are new variables and $N1$, $C1$, $t1$ are parameters.
- The dimension of $N1$, $C1$, $t1$ are same as that of N , C , t respectively while N^* , C^* , t^* are dimensionless parameters. The values of $N1$, $C1$, $t1$ are left open for now and will be determined strategically.
- The chemostat model with new variables will be:

$$\frac{d(N^*N1)}{d(t^*t1)} = K_{max} \frac{C^*C1}{K_n + C^*C1} N^*N1 - \frac{F}{V} N^*N1$$

$$\frac{d(C^*C1)}{d(t^*t1)} = -\alpha K_{max} \frac{C^*C1}{K_n + C^*C1} N^*N1 - \frac{F}{V} C^*C1 + \frac{F}{V} C_0$$

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10

To reduce the number of parameters, let us re-scale all the variables that is in the form of like, $N=N^* \times N1$ here, and $C=C^* \times C1$ and $t=t^* \times t1$, if you just see here that N^* is a new variables, C^* is a new variable and t^* is the new variables here, and especially, we can just write this variable N^* is $N/N1$ here and C^* can return as $C/ C1$ here, and t^* can return as $t/t1$ here, and if you just see here all this variables whatever is associated in newly that N^* C^* and t^* all are like, dimension variables here, and if you just see here, $N1$ $C1$ $t1$, all are parameters which are taking this dimension null values here, this means that, if N as certain dimension $N1$ has also certain

dimension and if C has certain dimensions, and C1 has also certain dimension and where we are just reducing directly to the variables in the form of a N *, C * and t * which will provide as a new equation which is free from this like, dimension variables and the chemostat model with new variables, if you just put this variables in the equations, then directly we can replace here, N/N * to N1, and this t can replace by t * x t1
 Similarly, C can replace by C * x C1 and N can be replaced by N * N1, so similarly we can just replace in the second equation also, the non-dimensional form of this equation can return as in this form here.

(Refer Slide Time: 24:32)

Non-Dimensionalization of Chemostat Equation:

- Now we need N1 to be in such a manner that $\alpha(N1)(t1)K_{max} / C1 = 1$ or

$$N1 = \frac{C1}{\alpha K_{max}} = \frac{FK_n}{\alpha K_{max} V}$$

- So the new model after non-dimensionalization is:

$$\begin{aligned} \frac{dN^*}{dt^*} &= \alpha_1 \frac{C^*}{1+C^*} N^* - N^* \\ \frac{dC^*}{dt^*} &= -\frac{C^*}{1+C^*} N^* - C^* + \alpha_2 \end{aligned} \quad \dots 14.6$$

where $\alpha_1 = (V/F)K_{max}$ and $\alpha_2 = C_0 / C1$. So here, we have only two parameters α_1 and α_2 . Now all the parameters and variables are dimensionless. So we will write the same model without asterisk marks for simplicity.

$$\begin{aligned} \frac{dN}{dt} &= \alpha_1 \frac{C}{1+C} N - N \\ \frac{dC}{dt} &= -\frac{C}{1+C} N - C + \alpha_2 \end{aligned} \quad \dots 14.7$$

And since, all of this N1 and t1 and C1 all are constant, so we can just take out this terms outside this differential operators which can be return as N1 * d N * here, and d (c) * x C1 can be return as C1 x d (c)* and t1 can be return as a t1 d * here, so after putting all this systems finally this equations will be reduce in the form of d N * by dt* just see here, so this N1 and t1 has been taken out obviously can multiply in the right hand side as t1/ N1 there, so t1/N1 so that is why? N1 got cancel it out and t1 it is just multiple by there, similarly second equation see here, so t1, if you just multiply by here also t1/C1 the same one we have to do here also t1/C1 so it can cancel it out and t1/C1 it can be multiply by here, so C1 is cancel it out, and C1 is cancel it out here, so that is why? T1 can be multiple by here, so t1 can be multiple by here, and C1 obviously it will be there

So, this is the factor completely you can just get, now if you just see here the total number of parameters involved in this model are like, t1 K_max K_n/C1, F/V alpha and C1 so the total number of parameters are still same but some of the parameters has been changed, since it is a definition of time out there, if you substitute suppose here, C1=K_n, since K_n is the arbitrary parameter and we can just change according to flexibility.

So if you just replace this K_n/C1 here and t1=v/F will get rid of 2 parameters and thus we will left with only 4 parameters and now if you just proceed that we can just consider N1 in a such passion that, alpha N1 * (t1), K_max/C1=1 suppose, if just consider like, a particular case, then we will have like, N1 can be calculated as C1/ alpha t1 K_max, which can be return as also F K_n/alpha K_max *V, so if

you just do this new model after this non-dimensionalization it will be reduce in the form of like, $\frac{dn^*}{dt^*} = \alpha_1 \frac{C^*}{1+C^*}$, if you just see the previous model here, we are just replacing all this variables in terms of this $\alpha_1 \frac{N_1}{K_{max} C_1} = 1$ so, that is why? this will be reduce in the form here, that is a $\frac{dn^*}{dt^*} = \alpha_1 \frac{C^*}{1+C^*} \frac{N^*}{N^*}$ here, and $\frac{dc^*}{dt^*}$ this can be return as $\alpha_2 \frac{C^*}{1+C^*} \times N^* - C^* + \alpha_2$, where α_1 can be return as like, $\frac{V}{F} \frac{K_{max}}{C_1}$ and α_2 can be return as $\frac{C_n}{C_1}$ so here we will have like only two parameters α_1 and α_2 , now all the parameters and variables are dimensionless, so easily we can just obtain this solution so we will write this same model without since, this N^* or any parameters we can put their so obviously we can just replace as N in the form of like, $N C^*$ as C , then obviously this model will be reduce in the form of $\frac{dn}{dt} = \alpha_1 \frac{C}{1+C} \frac{N}{N}$, this is just represented as $-C \times C^*$ is replaced by C here, so that is why? $\frac{C}{1+C} - C + \alpha_2$
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Summary:

- Introduction of chemostat – need of properly mixed resources with bacteria suspension to avoid the spatial dependence, if it doesn't happen so then it will lead to PDE instead of ODE.
- Formulation of chemostat model.
- Analysis on chemostat model.
- Non-dimensionalization of chemostat model.

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So, in this lecture we have discuss about, the chemostat modeling and how it can just develop a chemostat or bio-reactor using this self culture technique and which is a restricted that medium should be properly mixed, we are not consider the in homogeny in homogenous mixed are here, and which restricts many conditions so, that is why? We have not consider that one and we have just consider that the resources will be properly mixed with bacteria suspension to avoid the spatial dependence with respective time

It should having uniform chance and if it does not happens and then it will be partially differentially equation instead of a co-ordinary equation and in second phase we have discuss the different equations which is a in the form of differential equation and which can be used to formulation of chemostat model since, earlier model we have not consider without flow conditions that, if there is a inflow all of this resources are like, some of this cells so, in flux conditions are all like, out flow conditions will have not restricted so that is why? It is a formula has get chanced or this formulation of the differential equation get chanced

And then, we have try to analysis this chemostat model, with a various parameter values and finally we have non-dimensional equation based on this total number of population size like total

number of cells with this limited resources constant so in the next lecture maybe we will just go for this solution of this chemostat model and all other stops thank you for listening this lecture

For Further Details Contact

Coordinator, Educational Technology Cell

Indian Institute of Technology Roorkee

Roorkee-247667

Email: etcell@iitr.ernet.in, etcell.iitrke@gmail.com

Website: www.nptel.iitm.ac.in

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Prof. Ajit Kumar Chaturvedi

Director, IIT Roorkee

NPTEL Coordinator

Prof. B.K.Gandhi

Subject Expert

Dr. Ameeya Kumar Nayak

Department of Mathematics

IIT Roorkee

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