Microbial population age studing

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Abstract: - This paper presented population modelling method in treating microbial cells growth in time and cells age.A rigorous description of the features of the of microorganism in biochemical process was derived. It is assumed that two properties need to observed to desribe the state of a cell the mass and cell age. Cells in vivo have various ages, masses and so on, which need to be taken into account. This paper illustrates a complex situation for various birth and death processes. The Hanseula polymorpha DL-1 growing up was investigated. The obtained results illustrates the microbial population dynamic changes. This work is the first report in literature which giving population time age function.

Key-Words: -Microbial culture, dynamic model, cell mass, cell age, Hanseula Polymorpha, distribution function.

I. INTRODUCTION

A mathematical treatment is indispensable if the dynamics of microbial system are to be analyzed and predicted quantitatively. The method is essentially the same as that used in such fields as classical and quantum mechanics and molecular biology. In a quantification of macrobiology, however one has no access to such established principles as Newton's equations of motion or Schrodinger wave equation. If only diffusion is considered, it may be noted that although molecular diffusion obeys Fick's law.

It must be realized that quantum mechanics, as well established as it is now, was as vague as mist in its early stages. In that mist, Planck's quantum hypothesis and Rutherford – Nagaoka's atomic model bases on a solar system analogy were born. Bohr formulated the model and was able to explain the spectral lines of hydrogen by introducing the quantum hypothesis. Thus, the method of constructing a model based on analogy, formulating it, and solving it by introducing a hypothesis or hypotheses. The mere fact that mathematical model agrees well with a small amount of data does not suffice, insofar as the agreement could be coincidental. Moreover, models should not be confused with fundamental equations or laws. Only, those hypothesis that have withstood large amounts of critical scrutiny can be elevated to the status reserved for laws.

It is nevertheless true that time and space are inseparable, sister coordinates, and only when populations of organisms are considered in both time and space. The time rate of change of the number of the number of individuals N in a population may be expressed as the derivative with respect to t, dN/dt. The equations of biosystem are then established by equating this derivative to another relation expressing the effect of species interaction on population. Such a simple analysis is not possible when spatial variations are considered. What is directly related to species interaction is the net population flux through an arbitrary infinitesimal piece of space, rather than the spatial rate of change of the population itself, and thus a proper expression is unattainable without knowledge of the mechanism of movement of the organisms.

A rigorous microbial description of the features of the growth of microorganisms in biochemical processes falls naturally into the framework of general population balance methods. The cells (microorganisms) have various ages, masses, and so on, which need to be taken into account [1]-[4]. A classical description of microbial study has been given in literature before. Modelling microbial growth kinetics has beengiven with complex models which including general population balances and probabilistic projection in previously papers [5].

This paper is intended to illustrate a complex population where growth as well as birth and death processes are accounted for. Distribution function has considered as a function of cells age and cells mass. This work is the first report in the literature showing the population model which including cells age, cells mass and time.

II.BIOLOGICAL POPULATION

With the work [6] the basics of the theory of random dispersion of biological populations took shape. Skellam's method involved applying the analytical expression among and between species. Is treates constitutes one of the classic works on biological dispersion.

However, the process of biological diffusion cannot be said to be purely random, rather as can be seen in the activities of most entities, a special portion of space is preffered for use, and there is an element of choice in location [7]. The motion of entity populations does not simply consist of spreading. Entities often concentrate together to form groups. In such cases, an effect that opposes diffusion occurs due to behavioral patterns and interaction between individuals. One of the important features that distinguishes the movemnts of biological entities from the random motion of inorganic material is the delicate balance between spreading and concentrating . Entities dispersion can not be analyzed without an understanding of these processes. Although, the random work forms the point of depature and can not simply rest peacefully with it. In addition, species propagation and intra – and inter- species relations work in the direction of the formation of spatially concentrated patterns of organisms. When, of the other hand, two much crowding occurs, population pressure causes the commencement of organism dispersion.Here again the endless interplay between order and disorder occurs.

Airborne bacteria, fungi, pollen, etc., have been of continuing interest to botanists wind transport and

atmospheric diffusion have been considered as processes that contribute to the determination of spore diffudion.

identifying, marking, each individual And following the subsequent motion. in Eulerian viewpoint the flow of population individuals past a fixed point is observed. These two viewpoints represent concepts originating in fluid mechanics, but observation of the Lagrangian flow of fluid particles is decidedly more difficult than that of Eulerian flow and can in fact be impossible in some cases. The basic nature of Langragian observation is, however, much more suited to the study of biological organisms. This fact allows for a glimmer of optimism to fall on the otherwise nearly intractable study of individual motion, the development of elementary techniques together with the computer has opened up a new horizon of research.

III. STOCHASTIC METHOD

Mathematical models can also be delineated into those of either a deterministic or stochastic nature. Rougly speaking, educational models often employ deterministic methods, while practical models tend to be stochastic in approach. Strictly speaking, nearly all biological processes are stochastic. However, a greater portion of the individuals involved in a process may be said to follow a single deterministic path *on the average.*

As an example, consider a population subject to exponential growth . According to deterministic theory, the rate of population increase, *dN/dt,* is proportional to the number of individuals at that time, N(t). If μ denotes the coefficient of growth , pure birth rate, the following holds

$$\frac{dN}{dt} = \mu N \qquad (1)$$

Solving this equation under the initial condition, $N=N_0$ at t=0, it is obtained:

$$N = N_0 e^{\mu t} \qquad (2)$$

The change in population is uniquely given by eq.(1), and if μ is held constant for each run it will get the same result deterministically.

However, the process of population growth is ussually stochastic, and at given instant the growth does not necessarly take place at a rate μN, as shown in experiments. Thus, on must consider the probability *p(N,t)* that at a given time population will be N[8],[9].

$$p(N,t) = \frac{(N-1)!}{(N_0-1)!(N-N_0)!e^{-\mu N_0 t}(1-e^{-\mu t})^{N-N_0}} \qquad (3)$$

where μΔt represents the probability that in a small time interval Δt one individual will give birth to another individual.In this sense, μ should be considered as an average rate of growth. According to the population at a given time varies from experiment to experiment even though N_0 and μ remain constant.

There are two viewpoints from which to investigate the motion of populations, the Lagrangian viewpoint involves

Since the probability density function is given by eq.(3) can calculate the expected value, probability average of population, N_{avg},

$$N_{avg} = \sum_{N=0}^{\infty} Np(N,t) = N_0 e^{\mu t} \qquad (4)$$

and this coincides with the deterministic values. In other words, the deterministic methodexpresses the average state of the actual stochastic process. this statement is true in the case of exponential growth, but is not necessarily true in general.

One then may inquire as to what extent this average state represents reality. i.e. actual experimental results . To answer this question, need to calculate the standard deviation of N about its average value:

$$\sigma = (e^{\mu t} - 1)^{1/2} N_{avg}^{1/2} = N_0^{1/2} e^{\mu t}(1 - e^{\mu t})^{1/2}. \qquad (5)$$

Taking the ratio of the standard deviation σ with the average value,

$$\sigma / N_{avg} = (1 - e^{-\mu t})^{1/2} / N_0^{1/2} \to 1/N_0^{1/2} (t \to \infty) \qquad (6)$$

That is, the relative error of the deterministic method varies inversely with $N_0^{1/2}$ after a sufficient amount of time has passed. The larger the initial population, the better is agreement between experimental values and value obtained from the deterministic method. this result
applies not only to simple exponential growth but also to the general case.

However, cases exist where a critical difference arises between the two methods. Consider simple birth and death processes occuring simultaneously, with the birt rate μ excceding to the death rate λ. According to the deterministic theory,

$$N = N_0 e^{(\mu - \lambda)t}, \qquad (7)$$

so that the population must always increase. According to the stochastic theory , on the other hand, the possibility that the population becomes extinct also exists. the probability of extinction after sufficient time has elapsed is given by $(\lambda/\mu)^{N_0}$. Since $\mu > \lambda$, when N_0 is sufficiently large, this probability is extremly small, but isit is not zero. The existence of the possibility of extinction can in no way be obtained from the deterministic theory. Here the basic difference between the two methods appears, and in certain cases the deterministic method must be discarded. Clearly the stochastic method is considerably less tractable.

Diffusion is also a stochastic process and thus the above discussion must be generalized to consider the probability density function p(x,t) of finding the population density at time t and space x.

In the present consideration of the deterministic population method, tacitly it is assumed that population growth is a continuous process and generations overlap. For

many species such as certain insects, population growth takes place at discrete intervals of time, and generations are completely nonoverlapping, the appropriate mathematical description for this growth process is in terms of nonlinear difference equations. Such nonlinear difference equations, even if simple and deterministic with respect to their characteristic parameters, can exibits a remarkable spectrum of dynamic behavior including apparent random fluctuations. Thus arbitrarily close initial population sizes can lead entirely different patterns of population growth as time progresses. In fact the dynamical fluctuations of the system are in many respects in distinguishable from the sample realizations of a random process.

In the life time of most individuals there occurs a time when the site of inhabitation is abandoned in favor of migration. Thus, in an environment changing through space and time , the most probable strategy for a new individual to adapt to survive and reproduce may not necessarily consist of remaining to complete with its parents or congeners, but may rather consist of migrating elsewhere to find an empty niche to inhabit. As a results the spread of population dispersal take place. Such population movement includes nomadism, whereby individuals wander with no particular direction in search of sustenance, in a manner that resembles the random walk , and migration which may be either periodic as individuals move from one habitatto another in a repetitive cycle, or nonperiodic implying a certain degree of permanence to the move.

The migration and dispersal of individuals, while containing subjective elements that may not be totally controlled by idividuals, by and large constitute a ceaseless, active effort on the part of the animal to put itself in advantageous circumstances. However, the movemnt two individuals placed in the same environment is not identical. It is necessary to consider individual motion as a random variable. Nevtherless, the random motion of individuals in general cannot be considered to be that of a "simpler diffuser " such as the random walker.

A degree of success has been achieved in the analysis of dispersal of populations by starting with a direct analogy to the random walk or physical diffusion, with an additional consideration of intra and interspecific population interaction. However, a more realistic model of biological diffusion must be built properly combining the following concepts: correlated random walks, diffusion incorporating spce –time variation of parameters and nonuniformities, tratment of individual interaction after the fashion of the many body problem and statistical treatment using computer simulation. The formulation of such models alone necessitates a better grasp of the natural occurance of movements of animal individuals and populations.

Let consider the random walk the equation goverenig the statistics of population. Let define the probability that a individuals rlesed from the origin at t=0 reaches point x by time t to be p(x,t). At one time interval earlier ,i.e. at time t-τ, the individual was at either of points x-δ or x+ δ . If call ά the probability that a individual will move to the right in time unit τ, and β the probability that the individuals will move to the left and ά + β=1,

$$p(x,t) = \alpha p(x-\delta, t-\tau) + \beta p(x+\delta, t-\tau). \qquad (8)$$

Let consider the case that ά = β=1/2. A random walk in which the probabilities of movement to the right and left are equal is called a simple, or isotropic random walk.

To obtain a diffusion equation it is assumed that δ and τ are small compared to respectively, x and t and that each term on the right hand side of the equation can be expanded in a Taylor series in x and t,

$$p(x-\delta,t-\tau) = p(x,t) - \delta\partial p/\partial x - \tau\ \partial p/\partial t + \partial^2/2\ \partial^2 p/\partial x^2 + \delta\tau\ \partial^2 p/\partial x\partial\tau + \tau^2/2\partial^2 p/\partial t^2 \ldots \qquad (9)$$

$$p(x+\delta,t-\tau) = p(x,t) + \delta\partial p/\partial x - \tau\ \partial p/\partial t + \partial^2/2\ \partial^2 p/\partial x^2 - \delta\tau\ \partial^2 p/\partial x\partial\tau + \tau^2/2\partial^2 p/\partial t^2 \ldots \qquad (10)$$

All of the right hand derivatives are evaluated at (x,t). If eq.(9) is substituted into eq.(10) and the relations ά + β=1 and ά - β=ε is obtained,

$$\frac{\partial p}{\partial t} = -\frac{\delta\varepsilon}{\tau}\frac{\partial p}{\partial x} + \frac{\delta^2}{2\tau}\frac{\partial^2 p}{\partial x^2} + \delta\varepsilon\frac{\partial^2 p}{\partial x\partial t} + \frac{\tau}{2}\frac{\partial^2 p}{\partial t^2} + \ldots \qquad (11)$$

where the parameters δ, τ and ε are ssumed to be constant.

Now let consider the limit as these parameters go to zero. It shall not do this indisriminately, rather it shall suppose that as τ becomes small, δ and ε decrease so as to be of the same order of magnitude of $\tau^{1/2}$. In other words, in this first and second terms on the right hand side of eq.(11),

$$\lim_{\delta,\varepsilon,\tau\to 0} \delta\varepsilon/\tau = v, \quad \lim_{\delta,\tau\to 0} \delta^2/2\tau = D. \qquad (12)$$

Since the other right hand terms converge to zero, the following equation is obtained,

$$\frac{\partial p}{\partial t} = -v\frac{\partial p}{\partial x} + D\frac{\partial^2 p}{\partial x^2}. \qquad (13)$$

This is the equation of diffusion for the random walk that results from the limiting process. If p is multiplied by the total number of the released entities, the entity concentration c is obtained, so that

$$\frac{\partial c}{\partial t} = -v\frac{\partial c}{\partial x} + D\frac{\partial^2 c}{\partial x^2} \qquad (14)$$

IV. MICROBIAL POPULATION MODEL

Let consider entity distribution in space,

$$\psi\ (x, y, z, t, \xi_1, \xi_2, .. \xi_m) \tag{15}$$

and for arbitrary selected spatial region:

$$\int \psi\ (x, y, z, t, \xi_1, \xi_2, .. \xi_m)\, dx dy dz dt d\xi_1 d\xi_2 .. d\xi_m = 1 \tag{16}$$

Such as there are 3+n independent variables plus time which can be developed as 3+n dimension space. For arbitrary small space for considered entity is obtained [10],[11].

$$\frac{\partial}{\partial x}(v_x\psi_c) + \frac{\partial}{\partial y}(v_y\psi_c) + \frac{\partial}{\partial z}(v_z\psi_c) + \sum_1^n \frac{\partial}{\partial \xi_i}(v_i\psi_c\ ) - \frac{\partial}{\partial x}\ (D_{ix}\frac{\partial}{\partial x}\frac{\psi_c}{}) + \frac{\partial}{\partial y}(D_{ix}\frac{\partial}{\partial y}\frac{\psi_c}{}) + \frac{\partial}{\partial z}(D_{ix}\frac{\partial}{\partial z}\frac{\psi_c}{}) = \frac{\partial \psi_c}{\partial t} \tag{17}$$

where v geometrical velocity, ψ_c is entity distribution concentration, D is diffusivity, and t is time.

Assuming effective diffusivity coefficient can be written:

$$\frac{\partial \psi_c}{\partial t} + v_x\frac{\partial \psi_c}{\partial x} + v_y\frac{\partial \psi_c}{\partial y} + v_z\frac{\partial \psi_c}{\partial z} + \sum_1^n \frac{\partial}{\partial \xi_i}(v_i\psi_c) = D(\frac{\partial^2 \psi_c}{\partial x^2} + \frac{\partial^2 \psi_c}{\partial y^2} + \frac{\partial^2 \psi_c}{\partial z^2}) \tag{18}$$

It is assumed that two properties is needed to described the state of a cell the mass m *and* cell age. In well mixed and constant fermentation volume the macroscopic population balance can be derived and biodiffusion and bioconvection can be neglected.

$$\frac{\partial \psi}{\partial t} + \frac{\partial}{\partial \xi_1}(v_1\psi) + \frac{\partial}{\partial \xi_2}(v_2\psi) - (B - D) = -\frac{1}{\bar{t}}\psi \tag{19}$$

for $\xi_i = m$, t_{age} it is obtained,

$$\frac{\partial \psi}{\partial t} + \frac{\partial}{\partial m}(v_1\psi) + \frac{\partial}{\partial t_{age}}(v_2\psi) - (B - D) = -\frac{1}{\bar{t}}\psi \tag{20}$$

where D means death, B is birth, m means mass of cells, ψ is a distribution function and $\bar{t}$ = v/Q means holding time.

The function $\psi(m,t,,t_{age})dm$ is representative of number of cells per volume at time t with mass between m and $m+dm$ and can be further broken down into:

$$\psi(m,t,t_{age}) = N(t)f(m,t,t_{age})dm \tag{21}$$

where $N(t)$ total number of cells per volume at time t, and $f(m,t,t_{age})$ fraction of cells at time t with mass between m and $m + dm$.

The various birth and death processes were considered. Birth occurs by division of larger cells and can be formulated as follows. Let, $\gamma(m,c)dt$ defines fraction of cells of mass m at time t that divide in time t to time $t + dt$, where c is concentration substrate (nutrient in the vessel environment), and $p(m,m')\,dm$ is fraction of daughter cells of mass m to $m + dm$ obtained from a cell of mass m' at fission. Thus, the rate at which daughter cell of mass *m to m+dm* are obtained per mass of cells at age *m'* (one generation) is

$$Popul\ \_trans\ \_fun = 2\gamma(m', t, t_{age})p(m, m') \tag{22}$$

where the factor 2 results from the assumption that only binary fission takes place. The total number of cells of mass m obtained from fission is then found by multiplying Eq.(22) by the number of cells of age m', ψ *(m',t)dm'* and then integrating for all values *m' > m.*

$$B = 2\int_m^\infty \psi(m',t,t_{age})\gamma(m',t,t_{age})p(m,m')dm' \tag{23}$$

which daughter cells of mass *m* to *m+dm* are obtained per mass of cells at age m' is multiplied by factor 2 results from the assumption that only binary fission takes place. The various death processes was determined. The rate of fission of cells of mass m to smaller cells is

$$\gamma\ (m\ , t, t_{age}\ )\psi\ (m\ , t, t_{age}\ ) \tag{24}$$

A certain number of cells die without fission (true biological death) and if we define $T\ (m\ , t, t_{age}\ )dt$ as fraction of cells of mass m at time t that die in time t to time $t + dt$ then biological death is

$$D_{\substack{Bio\log ical \\ death}} = T(m,c,t_{age})\psi(m,c,t_{age}) \tag{25}$$

Also, the rate of increase of cells of mass m is a function of m an substrate concentration in the environment $v_1(m,c)$. Thus, substituting eqs.(23), (24) and (25) into Eq.(19) obtains:

$$\frac{\partial \psi}{\partial t}+\frac{\partial}{\partial m}(v_1\psi)+\frac{\partial}{\partial t_{age}}(v_2\psi)=2\int_m^\infty \psi(m',t)\gamma(m',t)$$

$$p(m,m')dm'-\{\frac{1}{t}+\gamma+T(m,t,t_{age})\}\psi(m,t,t_{age}) \quad (26)$$

If separate macroscopic population balance is made on the total number of cells present $N(t)$ it would have the form

$$\frac{\partial N}{\partial t}+D-B=-\frac{1}{t}N \quad (27)$$

where

$$N(t)=\int_0^\infty \psi(m,t,t_{age})dm \quad (28)$$

The birth term includes all fissions and has the form

$$B=\int_0^\infty \gamma(m,c)\psi(m,t,t_{age})dm \quad (29)$$

Also, the death term only includes all actual biological deaths since cells fission are still somewhere in the total system:

$$D=\int_0^\infty T(m,c)\psi(m,t,t_{age})dm \quad (30)$$

Substituting eq.(29) and eq.(30) into eq.(19) gives

$$\frac{\partial N}{\partial t}=\int_0^\infty \gamma(m,c)\psi(m,t)-\frac{N}{t}- \int_0^\infty T(m,c)\psi(m,t,t_{age})dm \quad (31)$$

Equation (31) is also can obtain by integrating equation (26) over all m which can be demonstrated as follows. two relationships that are of use in this integration are:

$$\int_0^\infty f(t,t_{age},m)=1 \quad (32)$$

Since no cells have mass less than zero, thus

$$\int_0^\infty \psi(m,t,t_{age})dm=\int_0^\infty N(t)f(m,t,t_{age})dm=(1)N(t) \quad (33)$$

Also,

$$\int_0^{m'} p(m,m')dm=1 \quad (34)$$

since any daughter cell at division will have a mass between zero and the mass of its parent cell.

V. MICROORGANISMS GROWTH KINETICS

In treating microbial growth kinetics as a practical matter process analysis can extend to the determination of the moments.The zero-th moment N, "segregated unstructured" models, has given in Eq.(13). The first moments are termed "distributed"

$$\mu_c \equiv C_m=\int_0^\infty m\psi(m,t)dm \quad (31)$$

where m is cell mass. C_m can be found from Eq.(8) using the definition Eq.(2).

$$\frac{dC_m}{dt}=\int_0^\infty v_1(m,c)\psi(m)dm-\frac{C_m}{t}-\int_0^\infty mT(m,c)\psi(m)dm \quad (32)$$

where $T(m,c)$ is true biological death function.
The relation

$$\int_0^{m'} mp(m,m')dm=\frac{m'}{2} \quad (33)$$

where $p(m,m')$ is defined in Eq.(4), representing the fact that for binary fission the mean daughter cell size must be one half of the original, was used to derive Eq.(15). The growth function was obtained from the postulate that for single cells the rate of cell mass increase is proportional to the surface area and the rate of decrease to the cell as:

$$net\_rate=\phi S-\mu_c m \quad (34)$$

where S is cell surface area/unit volume, ϕ is cell surface flux,

$$\phi=(\frac{\mu C}{K+C}),$$

is commonly used Michaelis-Menton form and μ_c,μ,K are constants. The surface area for rod –shaped cells (neglected ends) is $S=2m/R\rho$ where R is radius of cell and ρ is density of cell.
Thus,

$$v_1(m,c)=(\frac{2}{Rp}\frac{\mu C}{K+C}-\mu_0)m \quad (35)$$

VI. EXPERIMENTAL DATA

Experimental data for fermentation broth have been taken from Cooney and Swartz. The Hansenula Polymorpha DL-1 was growing up limited with ethanol [12].

VII. COMPUTATIONAL PROCEDURE

Partial differential equations solution was performed by software package PDES [13]. Microbial growth was simulated for different contour conditions. Some of these results are shown in Figure1 -Figure5.

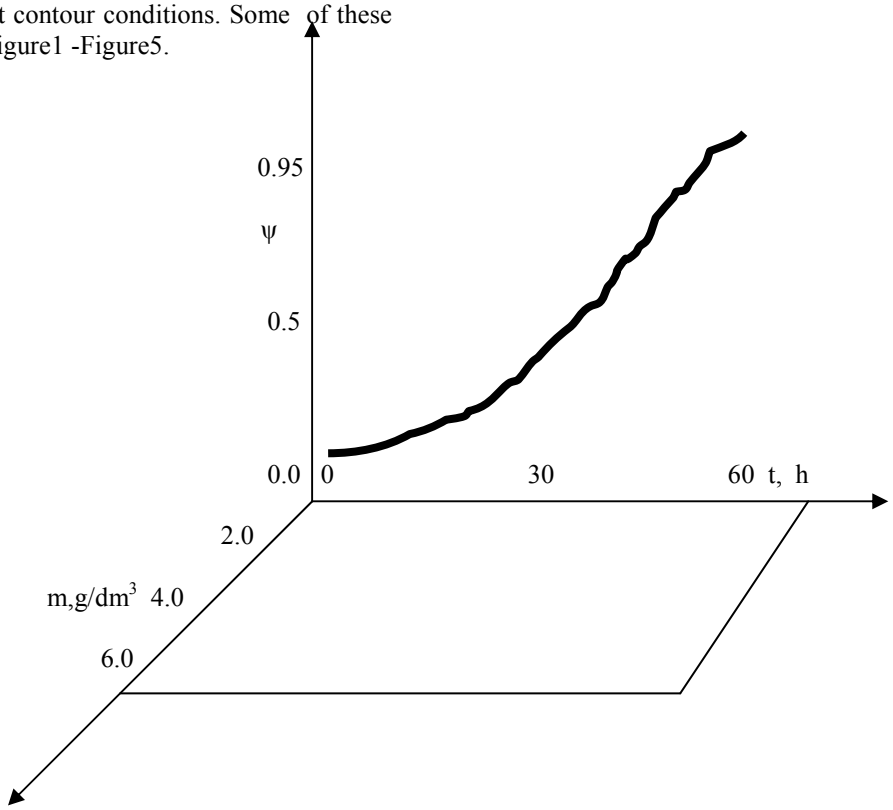

Fig.1 Population distribution function vs. cell mass and time for D=0.5g/dm^3 and B=0.3 g/dm^3

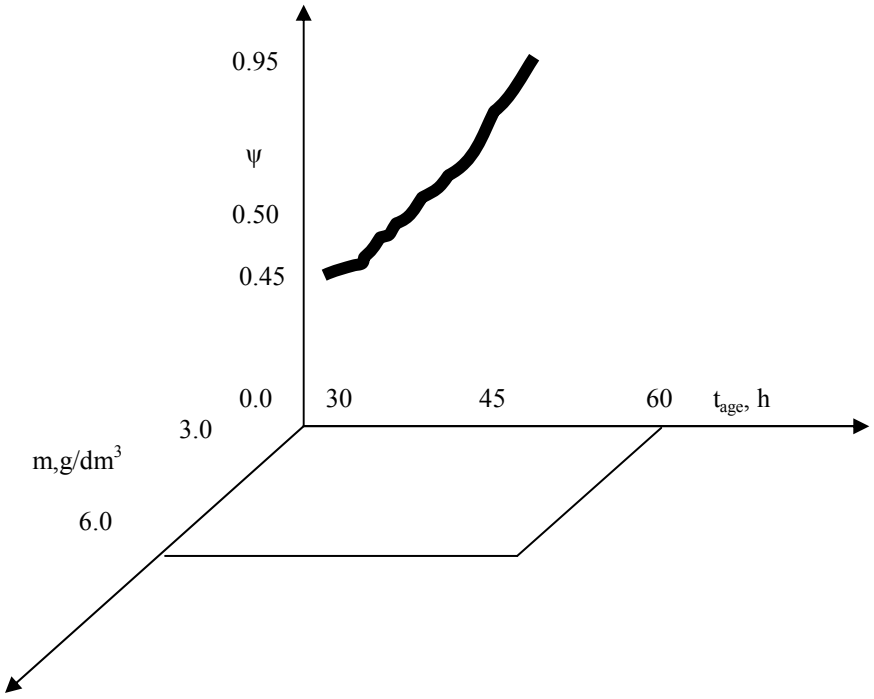

Fig.2 Population distribution function vs. cell age and cell mass for D=0.5g/dm^3 and B=0.3 g/dm^3

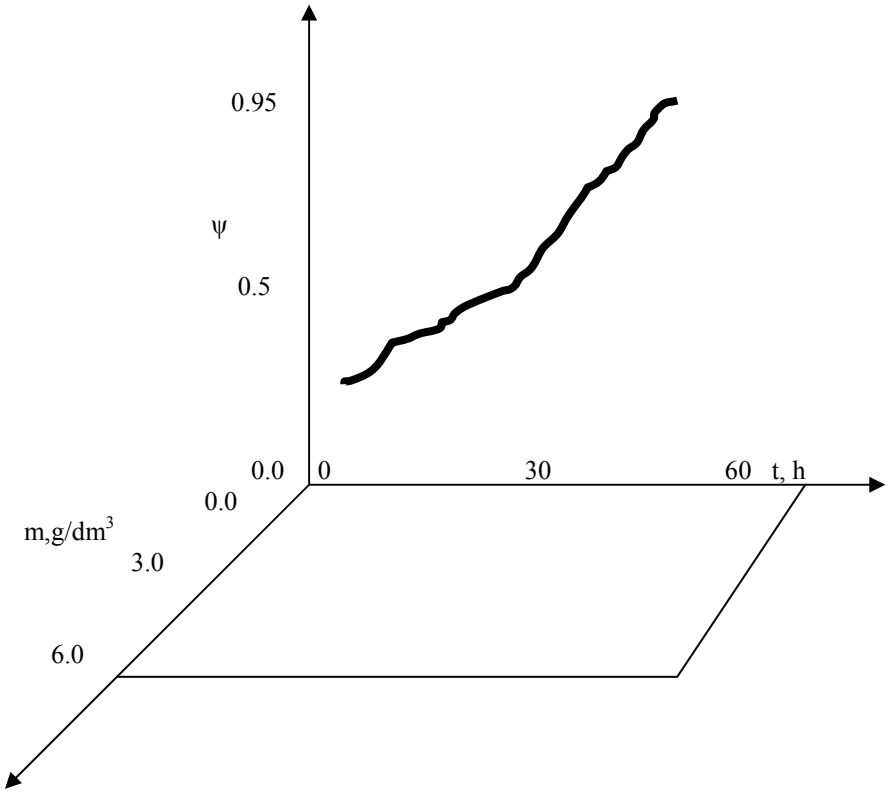

Fig.3 Population distribution function vs. cell mass and time for D=0.7g/dm^3 and B=0.2 g/dm^3

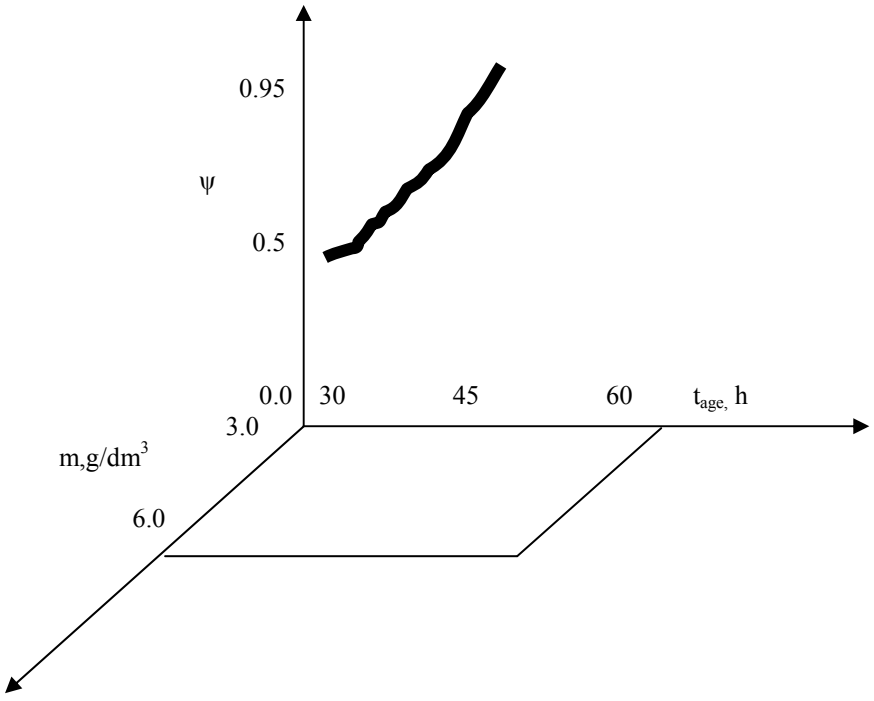

Fig.4 Population distribution function vs. cell age and cell mass for D=0.7g/dm^3 and B=0.2 g/dm^3

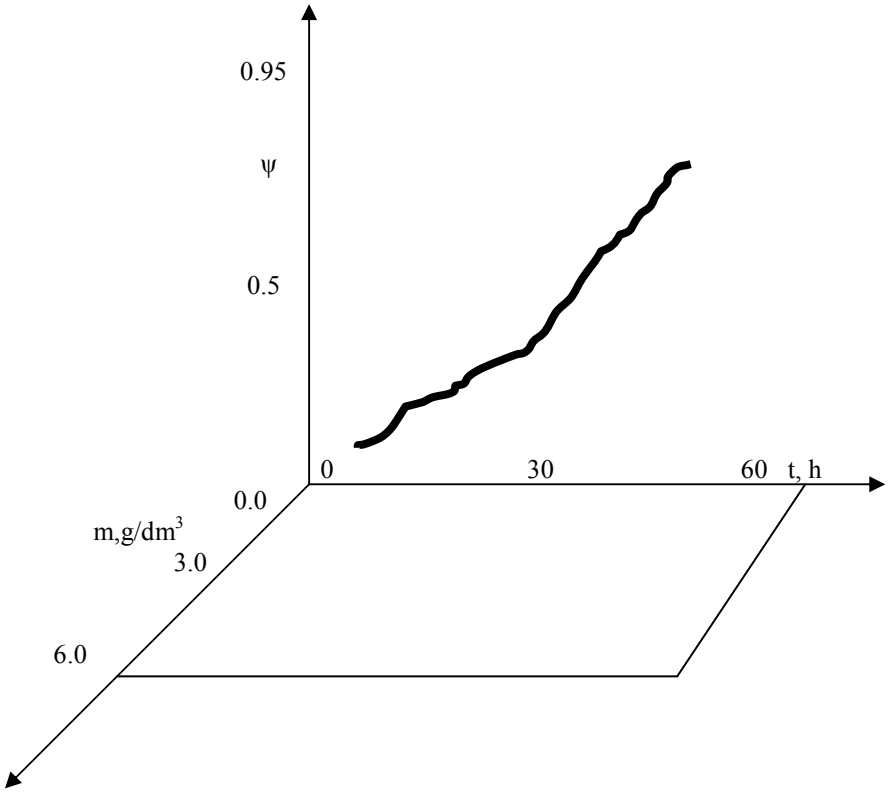

Fig.5 Population distribution function vs. cell mass and time for D=0.4g/dm^3 and B=0.2 g/dm^3

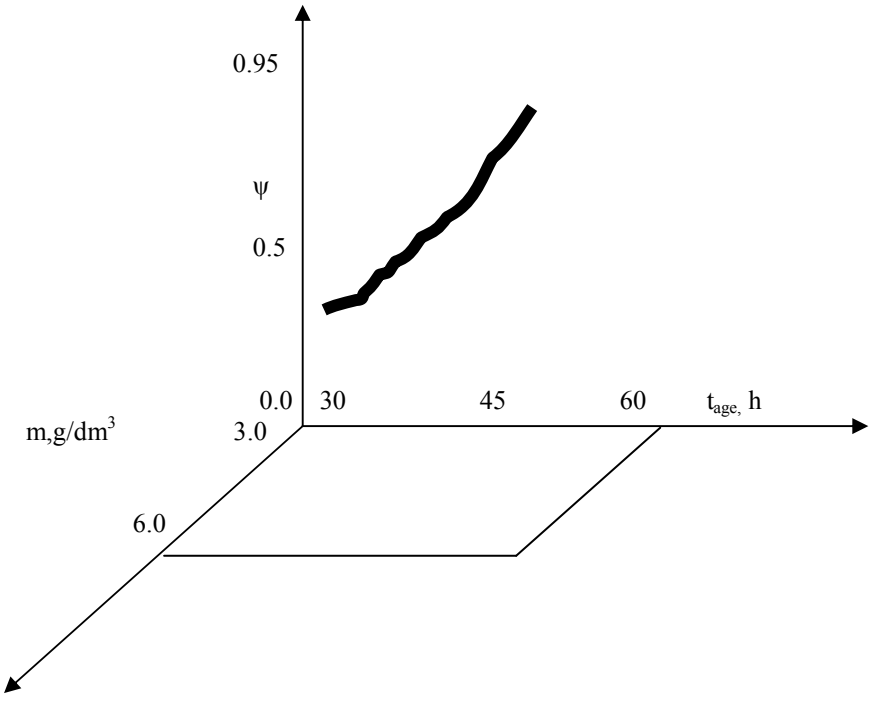

Fig.6 Population distribution function vs. cell age and cell mass for D=0.4/dm^3 and B=0.2 g/dm^3

Function $\psi(m,t,t_{age})$ was calculated by software package PDES for numerical solutions of partial differential equations.

VIII. RESULTS AND DISCUSSION

Various states of microbial media are analysed. Microbial distribution functions vs time for lower cells mass concentration was shown fast growing. Also, distribution function $\psi(m,t,t_{age})$ for middle cells mass concentrations was analysed. Distribution functions vs. time for higher cells mass concentrations has shown slow growing. Distribution function vs. age time of cells prediction was analyse.

IX. CONCLUSION

In this paper the microbial population dynamic model which described the state of a cell mass and cell age was derived. The stochastic partial differential equations were used.

Stochastic and deterministic theories of the biological system were introduced.

This study was illustrated a complex microbial situation modelling where growth as birth and death processes were accounted for. The cells which have various ages of masses and cells age were taken into account. The microbial population transition state was simulated for growing up the Hanseula polymorpha DL-1.

Symbols

B-birth
c-substrate concentration
C_m- mass concentration
D-death
$f(m,t,t_{age})$ - fraction of cell between mass m and m+dm at time t
K-constant
m-mass of cells
N-total number of cells
p(m,m')-fraction of daughter cells from a cell of mass m' at fission
S-surface area /unit volume
t-time
t'-holding time
T(m,c)- true biological death function
v-rate

Greek Symbols

Φ- cells surface flux
ξ-property
μ_c, μ, -specific graw rate
$\psi(m,t,t_{age})$- distribution function
ρ-density of cells
γ- fraction function

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