Do Bacteria Age?

A Contemporary Controversy in Biology

Souvik Bhattacharyya

Aging, a progressive deterioration of the physical functions necessary for survival and fertility, resulting from deleterious changes, is one of the most fundamental features of Eukaryotes. Bacteria are thought to be examples of organisms that do not age. They divide by binary fission, which is assumed to be a symmetrical division, such that both daughter cells produced from the parent bacterium have the same constituents with no obvious deterioration. The two daughter cells can continue the process apparently indefinitely giving an impression of immortality. But this thinking has come under scanner in recent years. The following new observations argue that bacteria do age: occurrence of morphologically asymmetric cell division; differential cell behavior during the stationary phase of bacterial growth; and asymmetric inheritance of an older pole by one of the daughter cells during cytokinesis. Is there a loss of fitness when a bacterium eventually divides into two daughter cells? Do they initiate ageing to increase fitness under special circumstances? These issues will be the focus of this article which attempts to resolve this controversy based on current evidence.

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Why is the Question Important?

According to Ernst Mayr[1] (1904–2005), an eminent evolutionary biologist, there are two basic differences between living and non-living which can be claimed as universal. First is the property of self-reproduction of living organisms; a car cannot make a copy of itself on its own, but an organism can do that in favourable conditions. Secondly, property of evolution of organisms over time (which is a result of adaptation in varying environmental conditions) makes them unique. These two differences, as argued by Mayr, are indirect products of biological hierarchy. If a

[1] Ernst Walter Mayr, *Resonance*, Vol.10, No.7, 2005.

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hierarchical system X has four components A, B, C, and D, the number of properties of the system X will be greater than the sum of its individual components, i.e., X > (A + B + C + D). Hierarchy exists not only in the living world, but also in the non-living world (quarks, atomic particles, atoms, molecules, gas/liquid/crystal, and so on). But they differ in their characteristics. Biological hierarchy consists of the following components from lower to higher order: biological macromolecules, organelles, cells, tissues, organs, organ systems, organism, population, species, and ecosystem. This biological hierarchy has given rise to many features exclusively present in an organism: response to stimuli, sustenance, phenotypic plasticity, adaptability, aging, and death.

Apart from aging, all other characters mentioned above are universal among organisms. It was previously thought that aging does not occur in bacteria. This thinking arose from the fact that bacteria divide symmetrically so that two identical daughter cells are produced. Thus, there is no chance of degeneration of cell components. The individuality of the parent bacterium is lost as two daughter cells are produced. So, it was argued that bacteria are immortal and they do not age. If this is true, then the following question is relevant; why was biological hierarchy unable to program aging in bacteria? If the answer to the question of bacterial aging is yes, bacteria can serve as a great model system for studies related to the aging process and aging-related diseases in higher organisms. So, it is important that this question is addressed.

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History of Studies on Aging

Throughout history, humans have taken death as the tragic end or an ultimate fate of a struggle against adversity. If not by accident or disease, all humans and other living beings will have to embrace death by aging. But scientific study and understanding of aging surfaced only in the late 19th century. In 1891, August Wiesmann (1834–1914) was able to phrase questions related to the mechanism of aging and its evolution. These questions were reformulated through experimental efforts of various investiga-

tors such as Élie Metchnikoff (1845–1916) in Russia and Raymond Pearl (1879–1940) in the United States. Together, Metchnikoff and Pearl demonstrated that aging or senescence processes are almost similar among all species, and they hypothesized mechanisms by which aging is acquired in an organism's lifetime. But the aging process is complex and with the experimental tools available at that time, it was difficult to address the issue. Also, as new fields of research were coming up in biology at that time, research on aging took a back seat. In 1956, Alex Comfort's book *The Biology of Senescence* resurrected the topic and its importance in biology. In 1966, William D Hamilton[2] (British Evolutionary Biolgist, 1936–2000) proposed that aging is inevitable because the force of selection declines with age, making later ages unimportant to evolution. Survival and reproduction are the key players in evolution and they are the traits that are negatively affected when selection force is weak. After his theory, many decades have passed and much information related to molecular mechanisms underlying aging has been revealed. It is now thought that aging is a default and natural process which has been coded in all organisms. The definition of aging has also changed with time.

Related articles from Resonance:

1. Nand K Shah, Tarvinder K Taneja and Seyed E Hasnain, Mitochondria can Power Cells to Life and Death: Role of Mitochondria in Apoptosis, *Resonance*, Vol.5, No.4, 2000.

2. Anthony Deepak D'souza and Ramesh Maheshwari, Senescence in Fungi, *Resonance*, Vol.7, No.3, 2002.

3. Ramesh Maheshwari, The Largest and Oldest Living Organism, *Resonance*, Vol.10, No.4, 2005.

Definition of Aging

In 1962, Maynard Smith[3] (1920–2004) defined the processes associated with aging as "those that render individuals more susceptible as they grow older to the various factors, intrinsic or extrinsic, which may cause death." In 1978, Robert R Kohn, in his book *Principles of Mammalian Aging*, commented: "By teleological criteria, development can be viewed as consisting of early processes that enhance the functional capacities of a system, whereas aging consists of later processes that diminish or have no effects on ability to function." In 1995, Paul T Costa (USA) and Robert R MaCrae (USA) tried to simplify and defined aging as "what happens to an organism over time". In 1982, V V Frolkis, a famous Russian gerontologist, took an ecological approach and stated: "aging is a naturally developing biological process which limits the adaptive possibilities of an organism, increases the

[2] Bill Hamilton – The Greatest Darwinian Since Darwin, *Resonance*, Vol.6, No.4, 2001.

[3] John Maynard Smith, *Resonance*, Vol.10, No.11, 2005.

Aging has four properties: it is deleterious, progressive, intrinsic, and universal.

likelihood of death, reduces the lifespan and promotes age pathology." But, the most accepted definition came from Bernard Louis Strehler (1925–2001) in 1982. He proposed that aging has four properties: it is deleterious, progressive, intrinsic, and universal. Aging is deleterious, i.e., it must reduce function of an individual; it is progressive, i.e., it must take place gradually; it is intrinsic, i.e., aging must not be a result of a modifiable environmental agent; it must be universal, i.e., all members of the species should have that property.

Aging in Different Organisms

The process of aging is obviously present in most organisms. The pets we have and the cattle we breed all show aging. Humans inevitably grow old through aging. All vertebrates show physical manifestations of aging somewhat similar to humans (other than white hair!). Aging is also seen in plants. The yellowing, withering, and falling of leaves and other plant parts are age-old observations. The most striking symptom of plant senescence is the yellowing of green tissues, which in turn signifies radical alterations in the plastids of green cells. Aging is present in invertebrates too. *Caenorhabditis elegans* is a terrestrial free-living nematode feeding primarily on bacteria. This nematode is already a huge success as a model organism for gerontology, the science of aging. Aging has been reported in yeast (*Saccharomyces*), fungi (*Podospora*), and many other simple organisms with lower complexity. But, until recently, aging was thought to be absent from bacteria.

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Things that go Against the Concept of Bacterial Aging

There are several prerequisites for a cell to undergo aging: 1) damage of cellular components; 2) cells in a population having differential damages, i.e., one set of cells having more damage than the other (this is essentially called age-structured population); and 3) partial or complete loss of cellular functions. If one cell has more damage than another, the former has more chances of death than the latter. A bacterial cell was thought to have none of them.

If favourable conditions are present, bacteria divide fast and there is little time between divisions. Because of the near absence of somatic life, it was thought that daughter cells do not get time to acquire much of damaged cellular components. Cell division in bacteria, known as binary fission, was thought to be symmetrical; the components of cytoplasm are divided equally so that each daughter inherits the same proportion of damaged and undamaged components. Hence, a bacterial population seemed to be 'clones' of the parent cell which started the population, without any apparent difference among the progeny. After a single parent cell divides into two daughter cells, the identity of the parent cell is lost. So, for a bacterium, death does not occur.

Cell division in bacteria, known as binary fission, was thought to be symmetrical; the components of cytoplasm are divided equally.

Eukaryotic cells in culture show a phenomenon called 'Hayflick's limit', which refers to a limitation in the number of divisions that an individual cell can undergo. If a eukaryotic cell divides for the first time, it will produce two cells. If those cells continue to divide, the resultant number of cells would be four after the second round, eight after the third round, sixteen after the fourth round and so on. Hayflick's limitation theory states that after a certain number of divisions, all the cells in that lineage will lose their ability to divide and eventually die. This is because of the aging process in those cells. For example, in the case of a normal skin cell, this limit is approximately 50. For bacteria, there is no such limit known. If a cell or its daughter cells do not die by processes that apply to eukaryotic cells, then naturally it comes to mind that bacterial cells do not age.

This opinion was developed by evolutionary biologists who argued that biological aging is only applicable to organisms with a soma distinct from germline. Germline refers to cells which carry genetic material to the next generation through the process of reproduction; they are also called gametes. Soma refers to all the cells other than the germ cells which constitute the body; they are also known as somatic cells. In bacteria the same cell serves the purpose of both somatic and gamatic cells. Aging, to these evolutionary biologists, is a compromise to pass on undamaged genetic material and other cellular components to the next gen-

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eration. To keep germ cells undamaged, somatic cells make a trade-off with Nature and start aging. So, from this perspective, bacteria do not age.

Recent Studies Indicating Bacterial Aging

Asymmetric Cell Division in Caulobacter cresentus

Caulobacter cresentus was the first bacterium that is reported to have morphologically asymmetric cell division. It is a Gram-negative bacterium found in oligotrophic aquatic environments (i.e., environments with very low nutrient levels). *C. cresentus* has two morphological types. The first one is the planktonic 'swarmer cell' which has one flagellum and multiple pili at one cell pole. The second type is the sessile 'stalked cell' where the flagellum is absent and a thick extension known as 'prostheca' or stalk is present. At the tip of the stalked cell, an adhesive organelle called 'holdfast' is present. Only a stalked cell can divide and it divides asymmetrically to give rise to a swarmer cell and another stalked cell. As the stalked cell elongates, a flagellum emerges on the pole opposite to the stalk. It then again divides to give rise to two morphologically asymmetrical cells and the process goes on (*Figure* 1). Swarmer cells cannot divide as they

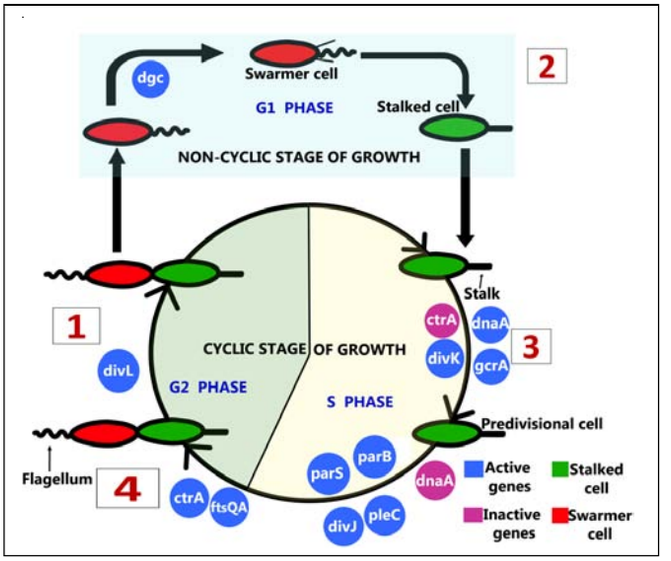

Figure 1. Life cycle of *Caulobacter cresentus* showing 1) morphological asymmetry between two daughter cells after cell division, 2) transition of swarmer cell into stalked cell, 3) DNA replication stage in stalked cell to produce predivisional cell, and 4) flagellum formation in swarmer cell.

are unable to replicate their DNA. They can only divide when they get converted to stalked cells over a certain period of time. In a typical eukaryotic cell division cycle, there are usually four major stages: G1, S, G2, and M, in that order. G1 is a preparatory phase for DNA synthesis and growth. DNA is replicated during the S phase. G2 is again a preparatory phase for division. M phase is where actual cell division occurs. Thus, the swarmer cell of *C. cresentus* is a prokaryotic equivalent of the G1 cell that is in pre-synthetic phase whereas the stalked cell is equivalent to the S-phase cell of eukaryotes. After DNA replication the stalked cell becomes incompetent for DNA replication, and the M phase, i.e., the divisional phase, takes place.

Substantial research has gone into understanding the molecular mechanism of the asymmetric cell division in *C. cresentus*

Substantial research has gone into understanding the molecular mechanism of the asymmetric cell division in *C. cresentus*. The genes identified to be involved in DNA replication and stalked-cell division include *divK, gcrA, podJ, divL,* and *dnaA*. The genes involved in 'swarmer cell to stalked cell' transition are *pleC, pleD, dgc, divJ, divK, dgrA, and dgrB*. These gene products ensure that the flagellum with pili is destroyed, the stalk is produced, and the ability to replicate DNA is again generated in the stalked cell. If the stalked pole or any structures segregating with it deteriorates after many divisions, it can be considered as aged. In 2003, Ackerman *et al*. reported that the time a stalked cell takes to produce a new swarmer cell (i.e., generation time) steadily increases with the increasing number of divisions. Using flow chamber microscopy, they observed the stalked cells attached to the walls of the chamber with their holdfast and tested them for signs of senescence. In three independent experiments, a group of cells of the same age were followed for about 300 hours, their reproductive events were monitored and the number of progeny produced per individual as a function of its age was calculated. This quantity represents the age-specific reproductive output, combining both survival and division. Although some cells produced up to 130 progeny in 300 hours, many stopped dividing or divided more slowly with increasing age, resulting in a decrease in reproductive output with age. This may reflect a

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kind of *bacterial replicative aging*. It is similar to the loss of reproductive fitness after the reproductive age for multicellular organisms. Thus aging can be present in bacteria if there are systematic differences present between the two cells emerging after cell division. This was the first report that morphologically asymmetric cell division in bacteria can lead to its own kind of aging. It led to intense investigation on those bacteria that divide by apparent symmetrical division.

Functionally Asymmetric Cell Division in E. coli

Bacteria can divide by binary fission where daughter cells are apparently morphologically identical. Can there be an asymmetry sufficient for aging that may not necessarily be apparent during cell division? Stewart *et al*. in 2005 reported functional asymmetry in *E. coli* cells during division. This bacterium grows in the form of a rod, which reproduces by dividing in the middle. One new end per progeny cell is produced during this division event (*Figure* 2). Therefore, one of the ends of each daughter cell is newly created (new pole) and the other end is pre-existing from the mother cell (old pole). Old poles can exist for many divisions. While experiments following the partitioning of cell constituents have found uniform distributions of DNA and lipids in daughter cells, it was known that components of the cell wall undergo slow turnover and are conserved in the same position where they are

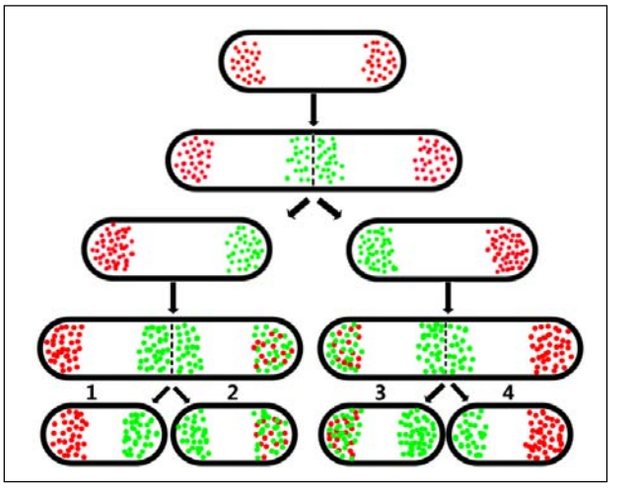

Figure 2. Functionally asymmetric division in *Escherichia coli*. Red dots indicate the old pole. Green dots indicate new pole, which subsequently become 'old' as a result of cell aging in successive divisions (as shown by a mix of red and green dots). Old elements (red dots) will increase over time in all the cells leading to their aging and death. Note that cells marked as '1' and '4' are older than cells marked '2' and '3'. Even in '2' and '3' cells, there is an older pole and a newer pole.

formed. More generally, any cell constituent with limited diffusion and a long half-life may be expected to accumulate at the old pole. Thus, a physiological, rather than morphological, asymmetry between the old and new poles may exist during cell division. In other words, there are cellular components that may not change position from the poles during division. Thus, after successive divisions, their functionality will reduce over time.

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To determine if *E. coli* cells experience aging related to the inheritance of the old pole, Stewart *et al*. followed individual exponentially-growing cells upto nine generations in an automated fluorescence microscopy system (individual cell tracking) measuring the physical parameters of each cell over time. They provided conclusive evidence for aging in the old pole cell, including cumulatively slowed growth or decreased metabolic efficiency, less offspring biomass production, and an increased probability of death. It has been recorded that the reproductive lifespan of the old pole bearing cells ultimately terminates upon reaching about 100 divisions. Although the exact nature of the old-pole elements is still not completely clear, it is likely that they may include fragments of cell wall, harmful/damaged DNA molecules, and modified proteins. This report revealed that aging might exist in all bacteria and provided the impetus for further research.

Bacterial Aging in the Stationary Phase: *Conditional Senescence*

The normal growth curve of bacteria shows four phases: the initial lag phase in preparation for divisions, the log phase related to growth and quick rounds of division, the stationary phase as the growth medium gets saturated with bacterial cells and death phase where many bacteria die due to starvation and toxicity. The best recognized mode by which bacteria confront adverse, oligotrophic environments is by entry into stationary (stasis) phase. In the laboratory, this stationary phase can easily be achieved by growing bacteria in a closed (batch) culture system, without adding fresh nutrients. Here, as a result of vigorous growth in the

In stationary phase, bacteria undergo various degenerative changes which ultimately lead to reduction of cell division capacity, increased susceptibility to environmental changes and antibiotics, etc.

log phase, nutrients become limiting and toxic metabolic by-products accumulate. This propels bacteria to go into a steady-state equilibrium between cell division and cell death.

It has been shown that in stationary phase, bacteria undergo various degenerative changes which ultimately lead to reduction of cell division capacity, increased susceptibility to environmental changes and antibiotics, reduced metabolic processes, decrease in cell mass, and change in cell shape. These changes are attributed to aging in those cells. The molecular changes that take place in these aged, stationary phase cells have been characterized. These changes are used as measures of their ability to survive under such conditions and are listed below:

1. Nucleoid gets condensed.
2. Ribosomes get dimerized.
3. Decreased cell size and sphereication of cells.
4. Osmolarity response regulator (OmpR) protein activates antidote/toxin systems which leads to increased cell death.
5. Protein content in the outer cell membrane is decreased.
6. There is an increased production of certain proteases and peptidases.
7. There is an increase in the production of secondary metabolites such as microcins (a type of bacterial toxin composed of very small peptides) McjA and MccA which act as bacteriocins (kills other bacteria).

These are phenotypic manifestations of aging in bacteria in stationary phase. This kind of aging is, however, not a consequence of a natural program or genetic circuitry and protein interaction networks that are present in eukaryotes. This aging is induced under certain conditions which occur only in stationary phase. In the case of eukaryotes, aging is inevitable irrespective of the conditions as it is genetically programmed. Thus, this kind of bacterial aging in stationary phase is called 'conditional senescence'. Some pathogenic bacteria go into a dormant state when they encounter unfavourable conditions inside the host. It has been proposed, but yet to be established, that these dormant states

Bacterial aging in stationary phase is called 'conditional senescence'.

can also manifest conditional senescence. If that is indeed the case, then the study of aging in stationary phase will be of clinical importance. Some of the causal factors involved in conditional senescence have been identified and are listed below:

Ageing in eukaryotes is inevitable as it is genetically programmed.

1. Due to nutritional stress and competition, there is an altered expression of genes controlling cell growth, energy generation and macromolecule synthesis such that these activities get reduced to minimal level. Some of the genes which get down-regulated are: *sdhA* (encodes a component of succinate dehydrogenase), *cydA* and *cydB* (encode subunits of cytochrome bd-I terminal oxidase), and *murI* (encodes glutamate racemase).
2. Due to the presence of increased reactive oxygen species (ROS), there is increased oxidative damage to proteins involved in vital cellular processes. Some proteins which undergo ROS-mediated carbonylation are: DnaK (required for protein folding and reconstruction), Ef-Tu (required for protein synthesis), H-NS (required for DNA organization), and Mdh (required for carbon catabolism).
3. There is an increased accumulation of structurally abnormal proteins.
4. Translational defects increase due to increased susceptibility of aberrant proteins to oxidation.

This kind of conditional senescence is not seen in eukaryotes.

The Free Radical Hypothesis

The free radical hypothesis (D Harman, USA, 1956) for aging in all organisms states that aging results from random deleterious events; oxidative damage by reactive oxygen species (ROS) which is generated due to normal energy metabolism, is the primary contributor to such a stochastic degeneration of organisms. The hypothesis has been proven in different multicellular organisms including humans, fruit flies, nematodes, and fungi. Experiments show that steady-state levels of oxidation-damaged macromolecules increase with age of an organism. Presence of

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oxidative stress defense system in multicellular organisms enables redox homeostasis of the cell and this system includes enzymes such as catalases, peroxidases, superoxide dismutase, and glutathione peroxidase. ROS induces oxidative damage to almost all the cellular components including DNA and proteins. In multicellular organisms, activity and levels of the anti-oxidant enzymes become reduced during aging. By contrast, in the case of bacterial cells that have stopped dividing, these enzymes have increased levels and activity. Yet, the levels of damaged proteins increase markedly in these cells. The answer to this paradox has been obtained to some extent in recent years. Translational errors are shown to be one of the factors involved in increased protein oxidation. Due to increased mistranslation, aberrant proteins and their isoforms accumulate with age. These proteins escape the anti-oxidant pathway and increase oxidative damage. The whole translation machinery shows increased error rate (reduced fidelity) due to this oxidative damage making a positive feedback loop. Thus, bacteria too face a problem of free radicals just as multicellular organisms have!

Infinite Resource?

If bacteria are grown in a hypothetical medium that has no limitation of nutrients, will they be immortal? This was thought to be the case till the 1990's. But, to prove it experimentally, Ackermann *et al*. continuously subcultured *C. cresentus* so that they could grow through 2000 generations and observed the aging status of those cells. There were two classes of cells present, a predominant young age group and a few old-aged bacteria (depending upon how many times they have divided). They showed that aging can be present on bacteria due to a higher mutation load as observed in other organisms. They also showed how aging and lifespan evolve in response to external conditions in the case of bacteria.

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Role of Aging in Bacterial Life History

What exactly is aging in relation to an organism? Is aging a part of survival strategy, a way to increase fitness, or is it merely the

inevitable failure of an organism to survive? If we can find some answers in the case of bacteria, it would be easier to address these questions in the case of more complex organisms. Studies on aging have led to two closely related hypotheses described below.

In the lifetime of an organism, there is a trade-off between the resources it devotes for growth and reproduction and those devoted to cellular maintenance and repair.

Trade-off between Maintenance and Growth

This hypothesis states that in the lifetime of an organism, there is a trade-off between the resources it devotes for growth and reproduction and those devoted to cellular maintenance and repair. For a major part of its lifetime, an organism can do both and survive. But, during the later part of life the latter continues and the former stops. Finally maintenance and repair also stop when the organism encounters death. This trade-off does not apply to bacteria when it is rapidly dividing; it applies only when it enters the stationary phase, stops growth, and survives without death.

A model to explain aging at the molecular level has been proposed (*Figure* 3). The model is based on the argument that RNA polymerase (RNAP) available for transcription is limiting and transcription factors such as $ó^{70}$ and $ó^{S}$ compete for binding to RNAP. This competition is regulated by the nucleotide ppGpp which accumulates during starvation conditions, causing growth arrest. Thus ppGpp primes the RNAP in accordance with environmental signals. As a result, the transcriptional apparatus is

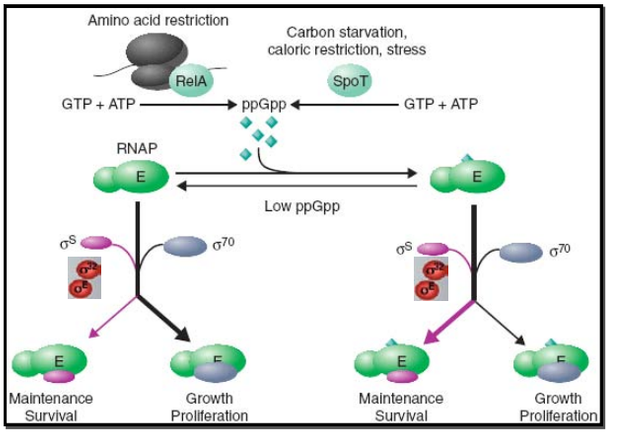

Figure 3. A model for the trade-off between reproduction and survival.
Reprinted with permission from T Nystrom, Aging in Bacteria, *Current Opinion in Microbiology*, Vol.5, pp.596–601, 2002.

When nutrition is aplenty, bacteria undergo growth and proliferation; when nutrition is limiting, they pay more importance to maintenance and survival.

primarily occupied with the transcription of $ó^{70}$-dependent housekeeping genes (proliferation) as long as the ppGpp levels are low, which signals that the nutritional status of the environment is favorable for growth. During growth arrest, elevated ppGpp levels allow the alternative sigma factor $ó^{S}$, required for expression of maintenance genes, to work in concert with $ó^{70}$ by shifting the relative competitiveness of the sigma factors. RelA is ppGpp synthetase I responding to amino acid starvation (uncharged tRNA in the ribosomal A-site), whereas SpoT is ppGpp synthetase II responding to a variety of conditions, including carbon/energy limitation. So, when nutrition is aplenty, bacteria undergo growth and proliferation; when nutrition is limiting, they pay more importance to maintenance and survival.

A Conditional Strategic Choice?

By computer simulation studies, Watve *et al*. modeled growth and propagation of growth-limiting components of a unicellular system using a modified Leslie Matrix framework. They proposed that aging might be a conditional strategy for bacteria to survive even under harsh conditions. They showed that aging and immortality can be selected under different sets of conditions and this selection may also lead to a trade-off between growth rate and growth yield. Here, growth rate refers to increment in population per unit time and growth yield refers to net increase in the number of living cells or components divided by the number of cells or components. This means that during aging, bacteria prefer growth yield (time independent) over growth rate (time dependent). The model points to asymmetrical division favoring rapid growth, whereas symmetry results in slow growth but higher efficiency, i.e., a higher growth yield. This can be true for conditional senescence. It is yet to be experimentally proven for aging as a whole in bacteria.

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Evolutionary Perspective of Bacterial Aging

It appears that asymmetric cell division is absolutely necessary for aging to occur in all organisms. It is also evident that no

organism including bacteria can escape from this asymmetry. This immediately poses two questions: 1) how did asymmetry arise (proximate cause)? and 2) why did asymmetry arise (ultimate cause)? Bacteria can serve as a very good model system for answering these questions. Nystrom in 2007 used bacteria as a model system and made an effort to answer these questions.

Asymmetric cell division in bacteria is an attempt to divide the damaged components unequally between the two daughter cells.

Proximate Causation for Asymmetry

Damage segregation is the most common reason proposed to address the question of how asymmetry arises during division. This theory proposes that asymmetric cell division in bacteria is an attempt to divide the damaged components unequally between the two daughter cells. What are the damaged components? Due to old pole inheritance, one cell will have more damaged cell surface and reduced insulation capacity against environment. There might be segregation of differently damaged DNA strands which could provide one daughter with a less damaged strand (like 'immortal DNA strand' co-segregation mechanism, originally proposed by British Physician John Forster Cairns in 1975, for preserving the integrity of stem cell genomes) and the other with a more damaged DNA. There may be unequal distribution of cytotoxic molecules and oxidative damage too. These factors might produce the necessary asymmetry between daughter cells. This asymmetry is the causal factor for unequal reproductive potential.

Ultimate Causation for Asymmetry

Is it advantageous to produce daughter cells of unequal reproductive potential? Or, is asymmetry caused by accidental, physical, or metabolic constraints that have no obvious bearing on fitness? There are many hypotheses that address this issue: 1) Asymmetric division ensures that at least one daughter cell has less damaged components and thus has a better chance of surviving. If there is equal distribution of damaged components, the chance of death for both the daughter cells will be similar. Thus, this asymmetry might serve the purpose to generate variation. 2) The

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model by Watve *et al*., mentioned earlier, proposed that aging might be a conditional strategic choice and asymmetry leads to faster growth compared to symmetrical division. 3) Asymmetrical segregation of damage that cannot be repaired may be beneficial at high cell densities and slow rates of replication, i.e., during stationary phase. This argument is different from the first argument mentioned here as the former is for all conditions of growth. These hypotheses suggest that asymmetry does confer fitness advantages and so does aging in bacteria.

How Does a Finite Reproductive Lifespan Affect Fitness and Resource Allocation?

Aging limits reproductive lifespan in all organisms including bacteria. This finite reproductive lifespan in turn limits fitness. Resource allocation is one of the major factors controlling fitness. It has been proposed (and observed to some extent) that aging affects fitness and resource allocation differentially in different organisms. In the case of simple organisms such as bacteria and yeast, highest fitness can be achieved only when generation time is short and mortality rate is high. This trade-off is an outcome of 'bacterial kind of aging'. In the case of complex multicellular organisms such as birds and mammals, higher fitness can be achieved only when the generation time is long but mortality rate is low. This trade-off is also a result of 'human kind of aging'. So, aging has specific trade-off outputs for specific group of organisms.

In 1977, British biologist Thomas Kirkwood proposed 'disposable soma' theory which states that aging evolved as a consequence of a trade-off between fecundity (reproductive output) and lifespan.

Why Did Aging Evolve in All Organisms?

Does bacterial aging provide any insight into evolution of aging in all organisms? It at least provides clues to the question – when did aging evolve? First, let us look into different theories proposed for evolution of aging. In 1977, British biologist Thomas Kirkwood proposed 'disposable soma' theory which states that aging evolved as a consequence of a trade-off between fecundity (reproductive output) and lifespan. The finite lifespan of an organism, ending in aging and death, is elicited by the limited

energy resources available to allocate to body maintenance/ repair, in order to ensure adequate fecundity. This means that somatic cells selectively undergo more damage so as to protect gametes or germ cells. This theory is similar to bacterial damage segregation. 'Genetic immortality theory' proposes that due to reproduction, the genetic material survives and the body of an organism is merely a vessel for a limited time; this time limit is applied by the aging process to ensure genetic immortality and is carried out by selfish genes. There is another theory called 'viability limitation' which proposes that it is impossible to be immortal due to constant selection pressure and struggle for survival. The body has a natural tendency to lose energy over time. Finally all the energy is lost from the body (death) and recycled within the ecosystem. The validation of these theories is a possibility in bacteria more than in any other organisms as they constitute a relatively simpler system to work with.

It is impossible to be immortal due to constant selection pressure and struggle for survival. The body has a natural tendency to lose energy over time.

Thus, it can be concluded that aging is a trade-off between the biological hierarchical system and the heirarchy that exists in the physical world. Indeed, the physical world hierarchy is already present within a biological hierarchy as all the raw materials for a biological system have their ultimate source in the physical world. Also, biological systems have evolved out of a pre-existing physical world. Thus, during the evolution of biological systems, the genetic circuitry for aging must have got integrated into the system to ensure the maintenance of that biological system for a certain period of time. But why is this so? Any biological system is highly energy rich. For elaboration, let us consider grains of sand as representing energy. The physical world is a flat desert. An organism is like a mountain made up of grains of sand accumulated from the desert. The desert tries to stop this process by erosion or wind flow. First, the height of the mountain increases due to greater accumulation than loss (growth of an organism). Then, the organism tries to build another mountain side by side (reproduction); at that time the height of the first mountain (parent organism) is constant. Finally, the height of the mountain starts to reduce due to greater loss than accumulation of

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sand (aging) and in the end it becomes as flat as the desert (death). This means aging has evolved to ensure death of an organism traded against reproductive fitness.

Aging studies in bacteria show one important development in gerontology: a new focus on single cells. The diseases related to the early onset of aging such as Hutchinson–Gilford progeria syndrome will find a useful model in bacteria and yeast. The evolutionary questions related to aging can be easily modeled and experimentally verified using bacteria as a model system.

Conclusions

There is no denying the fact that bacteria do age and aged bacteria show reduced fecundity. This discovery has led to a lot of controversy among biologists of different fields. There are questions still unanswered. What are the intrinsic factors leading to aging? Does aging occur in all bacteria? Do bacteria age without death? Are the aging mechanisms in simple and complex organisms same? These questions will encourage an increasing number of studies on bacterial aging. Nonetheless, whether aging is present or not, bacteria will continue to be the most successful among organisms as it is postulated that bacteria can even turn aging in their favour in their quest to survive.

Suggested Reading

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