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Angela M. Oliverio
Smith College

Laura A. Katz
Smith College, lkatz@smith.edu

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The Dynamic Nature of Genomes across the Tree of Life

Angela M. Oliverio¹ and Laura A. Katz^{1,2,*}

¹Department of Biological Sciences, Smith College

²Graduate Program in Organismic and Evolutionary Biology, University of Massachusetts, Amherst

*Corresponding author: E-mail: lkatz@smith.edu.

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Abstract

Genomes are dynamic in lineages across the tree of life. Among bacteria and archaea, for example, DNA content varies throughout life cycles, and nonbinary cell division in diverse lineages indicates the need for coordination of the inheritance of genomes. These observations contrast with the textbook view that bacterial and archaeal genomes are monoploid (i.e., single copied) and fixed both within species and throughout an individual's lifetime. Here, we synthesize information on three aspects of dynamic genomes from exemplars representing a diverse array of bacterial and archaeal lineages: 1) ploidy level variation, 2) epigenetic mechanisms, and 3) life cycle variation. For example, the Euryarchaeota analyzed to date are all polyploid, as is the bacterium *Epulopiscium* that contains up to tens of thousands of copies of its genome and reproduces by viviparity. The bacterium *Deinococcus radiodurans* and the archaeon *Halobacterium* sp. NRC-1 can repair a highly fragmented genome within a few hours. Moreover, bacterial genera such as *Dermocarpella* and *Planctomyces* reproduce by fission (i.e., generating many cells from one cell) and budding, respectively, highlighting the need for regulation of genome inheritance in these lineages. Combining these data with our previous work on widespread genome dynamics among eukaryotes, we hypothesize that dynamic genomes are a rule rather than the exception across the tree of life. Further, we speculate that all domains may have the ability to distinguish germline from somatic DNA and that this ability may have been present the last universal common ancestor.

Key words: LUCA, life cycle variation, polyploidy, epigenetics, genome.

Introduction

Although recent work has highlighted the diversity in genome structures and processes among eukaryotes (McGrath and Katz 2004; Parfrey et al. 2008; Parfrey and Katz 2010), archaeal and bacterial genomes are generally still thought of as static and relatively stable throughout life cycles; for example, bacteria are described in many biology textbooks as monoploid and dividing by simple binary division. As discussed below, this textbook depiction of bacteria and archaea is being challenged by numerous studies on dynamic genomes from diverse lineages within both domains. These observations impact how we view genome evolution since the time of the last universal common ancestor (LUCA) as they suggest either multiple origins of dynamic features or greater complexity within LUCA.

We recognize that claims about LUCA come with many caveats including that inferences on ancestry at this scale are challenging to make given the preponderance of nonvertical events among lineages and particularly among microorganisms (Mirkin et al. 2003; e.g., Dagan and Martin 2006;

Martin 2011). Lateral gene transfer (LGT) is well recognized as widespread among bacteria and archaea (Doolittle 2000; Ragan et al. 2009; Martin 2011) and to a lesser extent among eukaryotes (Andersson 2005; Hotopp et al. 2007; Katz 2012). Given the caveat of LGT, we proceed to describe the distribution of dynamic genomes across the tree of life while being cautious when making inferences about any single pattern or mechanism being present in LUCA.

To illuminate the dynamics of archaeal and bacterial genomes, we focus on variation in genome content during life cycles. We have chosen exemplar lineages to emphasize the tremendous diversity of dynamic features and the broad distribution of these features across the tree of life. There is extensive coverage of the diversity of genome rearrangements among strains and between species (Mazur et al. 2011; Bertelli and Greub 2012; Mann et al. 2013). Here, we focus on three characteristics of dynamic genomes in archaea and bacteria: 1) ploidy level variation, 2) epigenetics underlying genome rearrangements, and (3) nonbinary life cycles.

Extensive Polyploid Lineages

Although polyploidy—the existence of multiple copies of a chromosome or set of chromosomes—is widely distributed among eukaryotes, archaeal and bacterial lineages are generally thought of as monoploid (i.e., having one copy of a chromosome; Breuert et al. 2006). Although there are some monoploid lineages, the number of polyploid “exceptions” may exceed the number that follows the “rule” of monoploidy for bacteria (Hildenbrand et al. 2011) and perhaps also for the less well-studied archaea (Breuert et al. 2006).

In bacteria, there are numerous well-documented polyploid lineages (table 1), including *Escherichia coli* where genome copy number changes with growth rate and can be 6–7 copies (Pecoraro et al. 2011). Other examples of polyploidy in bacteria include *Thermus thermophilus* (Ohtani et al. 2010), *Deinococcus radiodurans* (Hansen 1978), and many cyanobacteria genera including *Synechocystis* (Griese et al. 2011). In *Synechocystis* PCC 6803, the motile wild-type strain has 218 genome copies in the exponential phase and 58 genome copies in the linear/stationary phase (Griese et al. 2011). In an extreme example, *Epulopiscium* are large (up to 600 μm), cigar-shaped endosymbionts of surgeonfish that contain tens of thousands of copies of their genomes (Pecoraro et al. 2011).

There are also multiple polyploid archaeal lineages (table 1). In one review, none of the four Crenarchaeota examined were polyploid, whereas all six Euryarchaeota genera examined are polyploid (Mendell et al. 2008). Polyploids also include methanogenic archaea *Methanocaldococcus* and *Methanosarcina* (Hildenbrand et al. 2011; Soppa 2011) and *Halobacterium*. In *Halobacterium salinarum*, 25 genome copies were found in the exponential growth phase (Breuert et al. 2006).

There are many possible advantages of polyploidy including providing resistance to DNA damage conditions, supporting a large cell size, and/or allowing for global regulation of gene expression (reviewed in: Kondrashov 1997; Comai 2005; Breuert et al. 2006; Mendell et al. 2008). Additionally,

polyploidy may allow for maintenance of integrity for inheritance and simultaneous experimentation with other genome copies leading to novel “somatic” combinations.

Epigenetics and Extensive Genome Repair

Epigenetic phenomena are well documented in eukaryotes (e.g., Bond and Finnegan 2007; Henderson and Jacobsen 2007; Mohn and Schubeler 2009; Bonduriansky 2012; Katz 2012) and more recently in bacteria and archaea (table 1, Wisniewski-Dye and Vial 2008; Soppa 2011; Terns MP and Terns RM 2011). We define epigenetics broadly, following Denise Barlow, discoverer of the first imprinted gene, who is quoted as arguing that “Epigenetics has always been all the weird and wonderful things that can’t be explained by genetics” (McVittie 2006). Hence, epigenetics includes heritable changes in genomes beyond substitutions in DNA sequences such as chromatin modification, integration of foreign material, and developmentally regulated rearrangements within a genome. At least three categories of epigenetics have been documented in bacteria and, to a lesser extent, archaea: 1) phase variation (variation due to genetic recombination), 2) targeted genome rearrangements via CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) defense systems, and 3) the repair of highly fragmented genomes.

There are several comprehensive reviews covering the epigenetic mechanisms of phase variation in bacteria (e.g., Wisniewski-Dye and Vial 2008; Slade et al. 2009), though little is known about analogous processes in the less well-studied archaea. In phase variation in some pathogens, bacteria generate diversity of antigens on cell surfaces that enable cells to escape host immune systems and perhaps to explore new ecological niches. Phase variation also occurs in free-living bacteria, for instance, to escape bacteriophage infection (Bikard and Marraffini 2012). Phase variation can occur due to a variety mechanisms including gene conversion (fig. 1a),

Table 1

Summary of Genome Dynamics in Bacteria and Archaea

Category	Clade(s)	Description	Exemplars	Major References
Ploidy levels	Archaea and bacteria	Multiple copies of genome in a single cell	<i>Epulopiscium</i> ; <i>Escherichia coli</i> ; and <i>Halobacterium</i>	Breuert et al. (2006), Griese et al. (2011), Hildenbrand et al. (2011), Pecoraro et al. (2011)
Epigenetic inheritance	Archaea and bacteria	Heritable changes not underlain by substitutions in DNA sequence	<i>Borrelia burgdorferi</i> ; <i>Pyrococcus furiosus</i> ; <i>Deinococcus radiodurans</i> ; <i>Halobacterium</i> ; and <i>Sulfolobus</i>	Grissa et al. (2007), Wisniewski-Dye and Vial (2008), Coker et al. (2009), Slade et al. (2009), Terns and Terns (2011)
Alternative life cycles	Bacteria	Deviations from binary fission	<i>Epulopiscium</i> ; <i>Dermocarpella</i> ; and <i>Planctomyces</i>	Waterbury and Stanier (1978), Angert and Losick (1998), Angert and Clements (2004), Angert (2005), Ward et al. (2009)

site-specific inversions, insertion-excisions, slip-strand mispairing, and diversity-generating retroelements (Wisniewski-Dye and Vial 2008; Jayaraman 2011).

The parasitic bacterium *Borrelia burgdorferi*, the causative agent of Lyme disease, provides an example of phase variation through gene conversion (fig. 1a: Liveris et al. 2004; Wisniewski-Dye and Vial 2008). *Borrelia burgdorferi* generates different genetic forms of surface proteins through recombination between an expressed and silent copy using *vsI* cassettes (fig. 1a: Liveris et al. 2004; Wisniewski-Dye and Vial 2008).

Another mechanism that both bacteria and archaea use to generate different forms is rearrangements in the genes encoding S-layer (surface layer) proteins (Sleytr and Beveridge 1999). S-layers are arrangements of proteinaceous units on the cell envelope with a diversity of functions and are present in most bacteria and many archaea

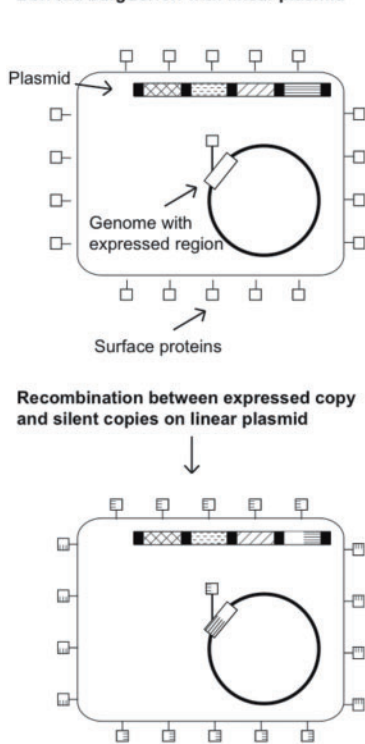
(e.g., *Methanococcus*, *Methanosarcina*, *Sulfolobus*, and *Thermoproteus*; Mayerhofer et al. 1998; Sleytr and Beveridge 1999). The bacterium *Campylobacter fetus*, for example, avoids activating a host immune response with recombination as 8–9 different S-layer cassettes can be expressed when a DNA inversion occurs that rearranges the location of the promoter (Sleytr and Beveridge 1999).

A particularly interesting example of genome dynamics in archaea and bacteria is targeted genome rearrangement via CRISPR/Cas defense systems (fig. 1b). The CRISPR/Cas system is a defense mechanism that relies on the ability to integrate foreign DNA into genomes, so that future invaders can be recognized and silenced or degraded (Grissa et al. 2007; Terns MP and Terns RM 2011). Though there is variation among the specific details of CRISPR in different lineages, cells generally capture and incorporate pieces of foreign DNA into their genomes to eventually make small RNAs that

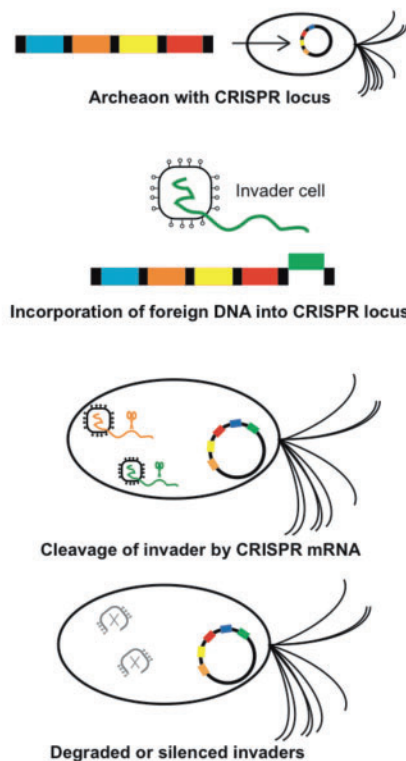
Epigenetic phenomena in Bacteria and Archaea

(a) Antigenic variation

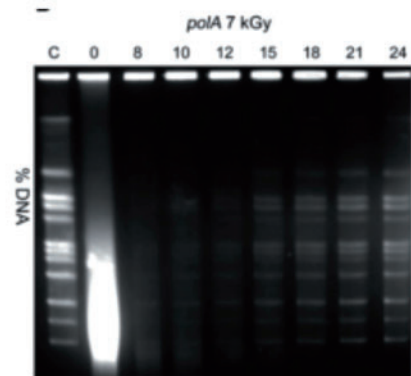
Borrelia burgdorferi with linear plasmid



(b) CRISPR defense system



(c) Repair fragmented genomes



DNA repair in *D. radiodurans* after irradiation of enzyme-digested cells

FIG. 1.—Epigenetic phenomena in bacteria and archaea. (a) Phase variation: genome rearrangements generating diversity of surface proteins in *Borrelia burgdorferi*, causative agent of Lyme's disease (Wisniewski-Dye and Vial 2008). (b) Targeted genome rearrangements: CRISPR/Cas defense system in *Pyrococcus*, an archaeon with CRISPR defense mechanism (modified from Terns MP and Terns RM 2011). (c) Repair of highly fragmented genomes in *Deinococcus radiodurans*: gel shows restriction digest of unirradiated cells in lane C, and from time 0–24 h later in consecutive lanes (modified from Slade et al. 2009, with permission from Elsevier).

Binary fission and alternative life cycles in bacteria

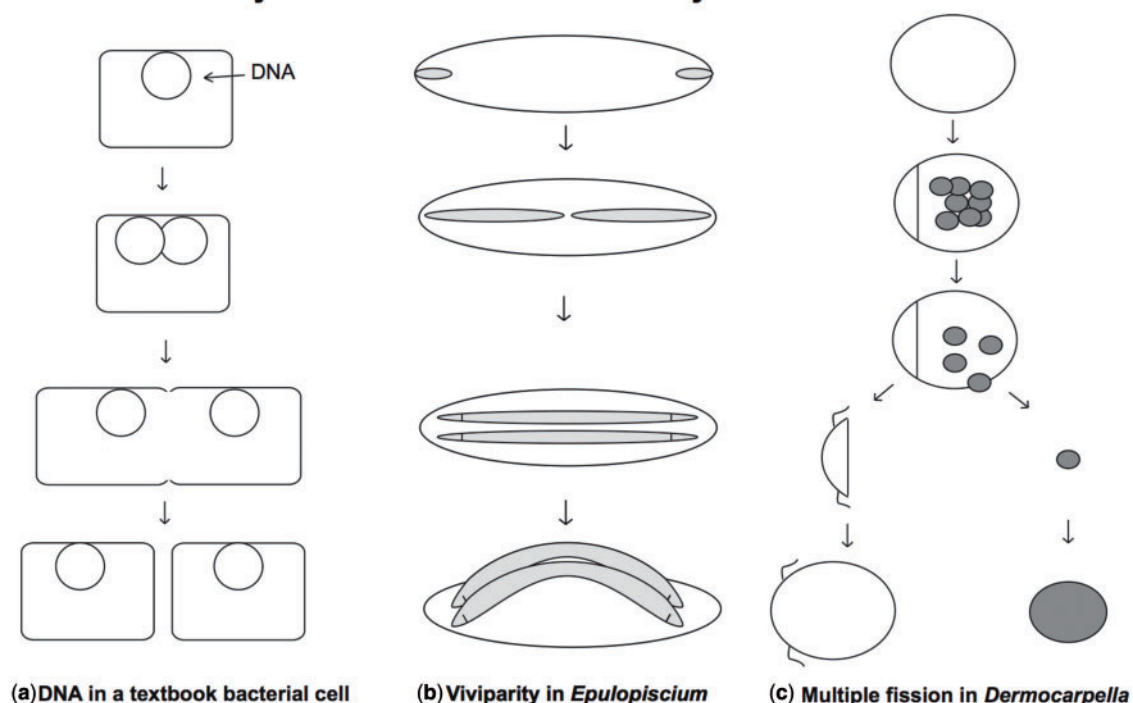


Fig. 2.—Binary fission and alternative life cycles in bacteria. (a) Binary fission (from top to bottom) DNA in a “standard bacteria cell”; chromosomal DNA replicates and cell grows; DNAs separate and cell starts to divide in half; and cell division occurs. (b) Alternative life cycles of bacteria (from top to bottom) viviparity in *Epulopiscium*; offspring grow in cell; offspring almost fill mother cell; and mature offspring emerge from mother cell. (c) Multiple fission in *Dermocarpella*. The mother cell divides asymmetrically, and then one of the resulting cells goes through multiple fission, with each daughter cell having the potential to grow into a new mother cell, whereas the larger cell regenerating into a mother cell again (adapted from Angert 2005).

are able to give heritable immunity against invaders (fig. 2b; Terns MP and Terns RM 2011). CRISPR/Cas systems have been identified in diverse lineages including the archaea *Pyrococcus* (Horvath and Barrangou 2010; Westra et al. 2012), *Sulfolobus solfataricus* (Grissa et al. 2007; Terns MP and Terns RM 2011), and the bacteria *E. coli* (Jansen et al. 2002; Terns MP and Terns RM 2011) and *Geobacter sulfurreducens* (Terns MP and Terns RM 2011).

Integrations, another defense mechanism based on genome rearrangements, enable bacteria to accumulate antibiotic resistance genes via site-specific recombination (Hall and Collis 1995; Cambray et al. 2010). Integrations are genetic elements that acquire and reshuffle genes by excision and reintegration of cassettes. This reshuffling allows genes encoding for resistance to specific antibiotics to be near the promoter, which allows for expression of the gene (Hall and Collis 1995; Cambray et al. 2010).

There are also examples of both archaea and bacteria that are able to repair of extensively fragmented chromosomes, including the bacterium *D. radiodurans* and the archaea *Halobacterium* sp. NRC-1 and *Sulfolobus solfataricus* (Dean et al. 1966; Kottmann et al. 2005; Rolfmeier et al. 2010).

Deinococcus radiodurans, for example, is extremely resistant to ionizing radiation and desiccation as this bacterium can reassemble its genome after fragmentation; chromosomes can be broken more than 100 times and efficiently repaired within a few hours through a process that uses overlapping genome fragments as templates for repair (fig. 1c; Slade et al. 2009). Analogous repair systems are present in multiple genera within archaea, including in the genera *Halobacterium* and *Sulfolobus* (Kottmann et al. 2005; Rolfmeier et al. 2010).

Alternative Life Cycles

There are many examples of nonbinary life cycles in bacteria including lineages that produce multiple buds or divide through multiple fissions (see: Waterbury and Stanier 1978; Angert and Losick 1998; Angert and Clements 2004; Angert 2005; Ward et al. 2009), all of which require coordinated regulation of genome inheritance. Yet division by binary fission is still accepted by many as the primary way that bacterial cells divide and carry out their life cycles, yielding daughter cells that are equivalent in size and contain identical copies of

DNA (fig. 2a). There is currently little literature on diversity of life cycles within archaea.

In a comprehensive review of alternative life cycles in bacteria, Angert (2005) groups alternative strategies of offspring production into several categories including 1) multiple internal offspring, 2) intracellular spores, 3) multiple fission, 4) filamentous growth followed by multiple fission, 5) asymmetrical cell division, and 6) bud producing. In each case, we argue that there must be an organizational system behind these divisions that marks complete genomes to be inherited. For example, the large (~600 μm) *Epulopiscium* propagates by viviparity after creating two or more intracellular offspring in a process that is at least analogous to the engulfment of spores in *Bacillus* (fig. 2b; Ward et al. 2009). Here, the forespore is engulfed by the mother cell after chromosome translocation, and then the internalized forespore matures (Angert and Clements 2004). DNA replication within the terminally differentiated mother cell (after daughter cells are fated) suggests that the maternal DNA plays a somatic role in helping maintain metabolic activities through the growth phase of offspring cells, though the maternal DNA will not be inherited by offspring (Ward et al. 2009). The life cycle of this bacterium suggests 1) highly coordinated replication, segregation, and regulation of genome content and 2) an ability to recognize and mark the genome that will be inherited by the offspring.

Asymmetrical cell division occurs in the cyanobacterium *Dermocarpella* spp. where the mother cell produces one smaller cell and one large cell that in turn goes through fission to produce many smaller cells (fig. 2c; Waterbury and Stanier 1978; Angert 2005). The ability to organize and mark inherited genomes in this system can perhaps be best appreciated by examining the rare instance when cell coordination fails and multiple fission is not a success. Waterbury and Stanier (1978) describe two instances of this failure in *Dermocarpa*: the first is when not all the parental cell material is successfully converted into daughter cells and the second is when the number of viable daughter cells produced by the mother cell is larger than the number of genomes in the cell at the start of the multiple fission events. In both cases, some daughter cells are nonviable after being released likely because they lack genetic information (Waterbury and Stanier 1978).

Bacterial species that reproduce by budding likely also have the ability to differentiate “somatic” and “germline” genomes. In many bacteria, budding produces one daughter cell following unequal cell growth and division. In some bacteria such as *Planctomyces* spp., multiple buds grow from a central location and break off to form daughter cells (reviewed in Angert 2005). Angert (2005) noted the complexity of this division and described the process of DNA transport to daughter cells after initial formation of bud membranes from the mother cytoplasm. This suggests the ability of the mother cell to mark what genetic information is to be moved to a specific location for inheritance.

There is also an intimate relation between mother and daughter cell in *Gemmata obscuriglobus* (Planctomycete). Here, cells reproduce by forming a bud at the end of a prosthecum and transporting the genome from the mother cell through the prosthecum into the already formed bud (Lee et al. 2009). The bud is initially without a membrane until it acquires the membranes of the new nucleoid envelope from intracytoplasmic membranes of both the mother cell and bud (Lee et al. 2009). This cell division appears to be a complex process that includes chromosomal transport by currently unknown mechanisms.

Synthesis

Evidence exists for dynamic genome processes within diverse archaeal and bacterial species, with many lineages remaining to be evaluated for these features. The diversity and control over ploidy levels and nonbinary life cycles suggest that perhaps bacteria and archaea have sophisticated mechanisms for regulating genomic inheritance and are able to differentiate between somatic (i.e., not passed down to future generations) and germline DNA in the context of a single cell. Similarly, both bacteria and archaea evade host defense systems by the adaptive CRISPR/Cas defense system that allows integration of foreign DNA as protection against future invaders. We have reviewed analogous, and perhaps even homologous, genome processes among diverse eukaryotes (McGrath and Katz 2004; Parfrey et al. 2008; Parfrey and Katz 2010). Cyclical ploidy cycles and developmentally regulated genome modifications such as extensive processing of somatic chromosomes and generation of extrachromosomal DNAs occur in many lineages across the eukaryotic tree of life (McGrath and Katz 2004; Zufall et al. 2005; Parfrey et al. 2008; Parfrey and Katz 2010; Katz 2012).

Two hypotheses can explain the distribution of dynamic genome features among lineages of eukaryotes, bacteria, and archaea: 1) these features arose independently in each lineage over the vast amount of evolutionary time or 2) these features were inherited from a toolbox of dynamic genome features present in LUCA. Distinguishing between these hypotheses requires both further elaboration of patterns across the tree of life and subsequent reconstruction of the molecular mechanisms underlying these patterns. Nevertheless, there is value in speculating why LUCA may have had a dynamic genome whose inheritance was modulated by epigenetic phenomena. One possibility is that such an arrangement was adaptive in that it enabled LUCA to regulate efficiently chromosome copy number and genome rearrangements while still inheriting full genome complements. Alternatively, LUCA's genome dynamics may have simply been a by-product of early genome evolution in which inheritance and function were not fully separated or coordinated; such a system might even have emerged during (or soon following) a transition from RNA to DNA-based genomes.

Regardless of the timing of the origin of dynamic features in the genomes of bacteria and archaea, it is striking how varied genomes are across the tree of life. This is particularly noteworthy given the typified genomes (i.e., genomes without variation in ploidy, rearrangements, or other dynamic features) represented in most textbooks and assumed in many studies.

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