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Lamarck and Panspermia - On the Efficient Spread of Living Systems Throughout the Cosmos

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ABSTRACT

We review the main lines of evidence (molecular, cellular and whole organism) published since the 1970s demonstrating Lamarckian Inheritance in animals, plants and microorganisms viz. the trans-generational inheritance of environmentally-induced acquired characteristics. The studies in animals demonstrate the genetic permeability of the soma-germline *Weismann Barrier*. The widespread nature of environmentally-directed inheritance phenomena reviewed here contradicts a key pillar of neo-Darwinism which affirms the rigidity of the *Weismann Barrier*. These developments suggest that neo-Darwinian evolutionary theory is in need of significant revision. We argue that Lamarckian inheritance strategies involving environmentally-induced rapid directional genetic adaptations make biological sense in the context of cosmic Panspermia allowing the efficient spread of living systems and genetic innovation throughout the Universe. The Hoyle-Wickramasinghe Panspermia paradigm also developed since the 1970s, unlike strictly geocentric neo-Darwinism provides a cogent biological rationale for the *actual widespread existence* of Lamarckian modes of inheritance - it provides its *raison d'être*. Under a terrestrially confined neo-Darwinian viewpoint such an association may have been thought spurious in the past. Our aim is to outline the conceptual links between rapid Lamarckian-based evolutionary hypermutation processes dependent on reverse transcription-coupled mechanisms among others and the effective cosmic spread of living systems. For example, a viable, or cryo-preserved, living system travelling through space in a protective matrix will need of necessity to *rapidly adapt and proliferate* on landing in a new cosmic niche. Lamarckian mechanisms thus come to the fore and supersede the slow (blind and random) genetic processes expected under a traditional neo-Darwinian evolutionary paradigm.

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Preamble - purpose of this article

All of us have contributed these past 50 years to the assembly of biological, biophysical and astrophysical data consistent with both Lamarckian modes of evolution and the conclusion that life itself is not specifically restricted to Earth but is a cosmic phenomenon (Panspermia). Our purpose then in writing this speculative review is to assemble the relevant molecular, cellular, evolutionary and astrobiological data in a coherent new evolutionary synthesis. We make the scientific case for the efficient spread and further evolution of *pre-existing* diverse living systems, unicellular or multicellular, prokaryote, archaea and eukaryote, throughout the observable universe. While we discuss the problems of the odds against the emergence of life from non-living chemistry on Earth our pragmatic position leaves the mechanisms for the ultimate cosmological origin of life in the Universe an open question. We make this clear at the outset - this article is *not* about the origin of life *per se*. However our article is concerned with how life has been continuously seeded to Earth from the Cosmos, and how terrestrial life has evolved as we recently discussed in this journal (Steele et al., 2018, 2019). Obviously, all our discussions on Lamarckian modes of inheritance are derived from observations and experiments about living systems in habitats here on Earth. This provides valuable insight, in our opinion, of how life can spread throughout the Cosmos and literally infect and colonize every available niche in which evolution proceeds as a cosmologically defined and connected process. The whole universe is thus a single connected biosphere.

1. Summary of terrestrial neo-Darwinism

The widely accepted traditional view of the origin of Life and its further evolution on Earth, in the period after the Hadean Epoch (~4 billion years ago) can be summarised by the following dot-points:

- Life emerged as the first free-living cell on Earth from non-living chemistry (Abiogenesis), perhaps via an RNA World, 3–4 billion years ago in one of Darwin's hypothetical "warm little ponds" or the canonical "primordial soup." The current consensus is that hydrothermal deep sea vents are a plausible location for the origin of terrestrial life (Martin et al., 2008; Baross, 2018; Ménez et al., 2018).
- The first primitive free-living cells then replicated and flourished by Darwinian evolution.
- These early cells repeatedly duplicated their genomes and genes, slowly mutating their DNA sequences and further rearranging their genomes. This allowed progression from the archaeal and prokaryotic bacterial worlds, thence to diversify into a vast range of new and diverse cellular species. At the inception the multiplication and production of viruses by most cells further aided cell-cell genetic communication.
- All these evolutionary genetic steps arose by random events which were then preserved by natural selection.
- The emergence of the first free-living eukaryotic cells occurred by cell-cell fusions and symbiosis events providing the evolutionary path prior to the emergence of the metazoans, multicellular plant and animal life.
- Many of these evolutionary phases were ponderously slow, taking millions if not hundreds of millions of years. However the fossil record, as well as phylogenetic nucleic acid and protein sequence analyses, show that most novel species and life forms emerge suddenly in a "punctuated" way either persisting to the present or going to extinction (termed "punctuated equilibrium" by Eldridge and Gould).
- Since the explosive events of the Cambrian adaptive radiation (~542 million years ago), two further major extinctions and adaptive radiations have been recorded in the fossil record, at the Permian/Triassic (P/T) boundary (~252 million years ago) and the Cretaceous/Paleocene (K/T) boundary (~65.5 million years ago).
- The time intervals between such apocalyptic events, roughly about every 200–300 hundred million years, suggests a cosmic orbiting cycle of our Sun and Solar System around the galactic centre of the Milky Way; and shorter 30 million year cycles as our star system oscillates through the galactic plane (Clube et al., 1996, Wickramasinghe, J.T. et a., 2010).

This dot-point summary accurately describes the widely held scientific view of Life under the umbrella term "neo-Darwinism", on which the analytical discipline of "Population Genetics" is firmly based. This conventional schema is scientifically valuable because its "big data" statistical methods have allowed the navigation of the genomes of thousands of diverse organisms made possible by next generation sequencing. However, we ourselves and many others over the years have considered neo-Darwinism itself as being in need of major conceptual reform. While it unquestionably deserves respect as the over-arching foundation theory of biology it no longer reflects the actual state of affairs concerning the totality of life, its history and how it may have emerged and evolved both on Earth and throughout the Cosmos (Steele, 1979; Hoyle and Wickramasinghe, 1981, 1982; Bateson et al., 2017; Noble, 2013, 2017, 2019).

Since the 1970s many key lines of scientific investigation have produced evidence contradicting this comfortable view of Life on Earth. We shall discuss some of that key evidence below as it pertains to inheritance and genetic mechanisms (Sections 2 and 3). Recently we ourselves and many colleagues have reviewed most of this salient contradictory evidence in the context of the data supporting Panspermia (Steele et al., 2018, 2019). The clear conclusion is that the restricted neo-Darwinian view of terrestrial evolution is untenable and no longer scientifically credible. It is not denied that evolutionary developments have occurred in the terrestrial setting. However at key junctures widely accepted observations do not fit the actually observed data which allows the plausible conclusion that " … living organisms such as space-resistant and space-hardy bacteria, viruses, more complex eukaryotic cells, and on very rare occasions, even fertilized ova and seeds have been continuously delivered … to Earth so being one important driver of further terrestrial evolution which has resulted in considerable genetic diversity and which has led to the emergence of mankind" (Steele et al., 2018). Thus life on Earth in all its astonishing variety appears to have been seeded from the wider Cosmos with the further terrestrial evolution of these space-derived "varieties" occurring over hundreds of millions and billions of years on Earth (marked, as it were, by major cosmic bolide "seeding" events caused by passing star systems and the passage of our solar system through giant molecular clouds (e.g. see Hoyle and Wickramasinghe, 1993, Wickramasinghe, J.T. et al., 2010). We will return to this evidence and the critical arguments in Sections 4,5 and 6.

2. The evidence for Lamarck

2.1. The rise of neo-Lamarckian acquired inheritance and the collapse of traditional neo-Darwinian thinking on evolution

A simplified overview of the main evidence gathered since the 1970s is summarised in Table 1. This will be expanded on further in Section 3. The data collected in this period have firmly established the validity of the neo-Lamarckian evolutionary paradigm. This 50 year period documents the rise of neo-Lamarckian acquired inheritance and the collapse of traditional neo-Darwinian thinking on evolution. These environmentally-induced cellular and molecular processes can now be considered the *primary evolutionary driver mechanisms* for the evolution and ongoing diversification of life on Earth. We then further argue the case (Section 5) that these DNA and RNA inheritance mechanisms are likely to be general throughout the Cosmos (e.g. see Wickramasinghe et al., 2018a) and will likely operate in the efficient Panspermic dispersal of living systems throughout the Universe. That is, they allow the immediate proliferation, rapid adaptation and genetic diversification on landing of the cosmically-derived organisms surviving impact in their new cosmic niche.

2.2. Environmental stimulation as the directional mutational driver

Tangible signals from the environment in their broadest sense, play the key driving role in the origins of "directed" physiological adaptations and mutations which emerge in the "somatic" body of the organism. For example, by induced stresses such as pathogen-inducing innate and adaptive immune responses (deaminase-mediated mutagenesis at Transcription Bubbles, Fig. 1) but there are others as discussed in Section 3.

Table 1
Evidence consistent with Lamarckian evolutionary processes.

1	Environmental Stimulation as the Directional Mutational Driver
2	Role of Epigenetic Gene Targeting
3	Rapid Genetic Adaptation
4	Penetration of the *Weismann Barrier*
5	Horizontal Gene Transfer (HGT)
6	Central Role of Reverse Transcription

The summaries of evidence for Horizontal Gene Transfer phenomena are well covered at the Wikipedia site https://en.wikipedia.org/wiki/Horizontal_gene_transfer.

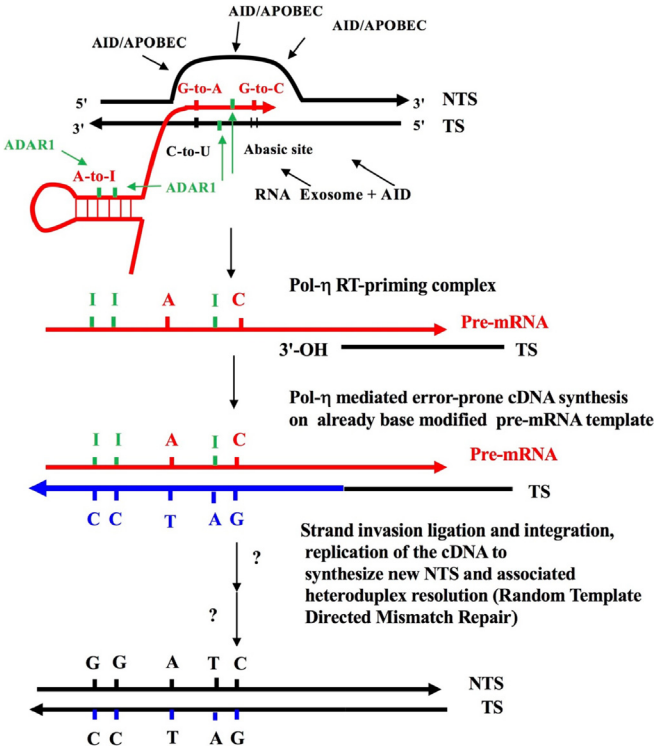

Fig. 1. The key features of the reverse transcriptase mechanism of somatic hypermutation (SHM) at Transcription Bubbles - a type of representation of the deaminase-based "Universal Mutator" likely to operate in many kingdoms of life (Lindley, 2018; Krishnan et al., 2018). Some elements of this figure have appeared before, and this figure is a modified combination of parts from (Steele, 2017), Lindley and Steele (2013), as well as from mechanism figures in Steele (2009, 2016a) and Steele and Lindley (2017). This is also an adaptation of the target site reverse transcription process reported in Luan et al. (1993). Shown is an RNA Polymerase II-generated Transcription Bubble with C-site and A-site substrate deamination events by AID, APOBEC and ADAR deaminase enzymes, which generates the strand-biased transition mutation signatures - A-to-G, G-to-A, G-to-T, and G-to-C. DNA strands shown by **black lines**; pre-mRNA as **red lines**; cDNA strands as thick **blue lines** due to DNA polymerase η acting in its reverse transcriptase mode (Franklin et al., 2004; the RT activity of DNA Polymerase η has been independently confirmed recently by Su et al., 2019). **Green bars** are Inosines. Shown also is the action of the RNA exosome (Basu et al., 2011) allowing access of AID deaminase to cytosines on the transcribed strand (TS). The ssDNA regions on the displaced non-transcribed strand (NTS) are established targets of AID action. Note that DNA mutations are first introduced as AID/APOBEC-mediated C-to-U, followed by excision of uracils by DNA glycosylase (UNG), which creates Abasic sites in the TS (these can mature into single strand nicks with 3′-OH ends via the action of AP endonuclease, Zanotti et al., 2019). These template Uracil and Abasic sites can be copied into pre-mRNA by RNA Pol II generating G-to-A and G-to-C modifications as shown (Kuraoka et al., 2003). Following target site reverse transcription (Luan et al., 1993), this results in G-to-A and G-to-C mutations in the NTS, in a strand biased manner. Separately at WA targets in nascent dsRNA substrates, adenosine-to-inosine (A-to-I) RNA editing events, mediated by ADAR1 deaminase, are copied back into DNA by reverse transcription via Pol-η (Franklin et al., 2004; Steele et al., 2006). In theory, ADARs can also deaminate the RNA and DNA moieties in the RNA: DNA hybrid (Zheng et al., 2017; Steele and Lindley, 2017). The strand invasion and integration of the newly synthesized cDNA transcribed strand, as well as random-template mismatch repair (MacPhee, 1995) are hypothesized additional steps (not shown here). In short, RNA Pol II introduces modifications in the Ig pre-mRNA as it copies the TS DNA with AID/APOBEC lesions (Uracils, Abasic sites) and this is coupled to A-to-I editing in dsRNA stem-loops near the transcription bubble (Steele et al., 2006) as well as in RNA:DNA hybrids within the bubble (Steele and Lindley, 2017). Next, a RT-priming substrate is formed when the nicked TS strand with an exposed 3′-OH end anneals with the base modified pre-mRNA copying template allowing cDNA synthesis by Y Family translesion DNA polymerase-η, now acting in its reverse transcriptase mode (Franklin et al., 2004). These 3′-OH annealed priming sites could arise due to excisions at previous AID/APOBEC-mediated Abasic sites. Alternatively, they could arise due to an endonuclease excision associated with the MSH2-MSH6 heterodimer engaging a U:G mispaired lesion (Wilson et al., 2005; Zanotti et al., 2019). Shown is an A-to-T transversion generated at the RT step at a template Inosine. ADAR, Adenosine Deaminase that acts on RNA; AP, an Abasic, or apurinic/apyrimidinic, site; APOBEC family, generic abbreviation for the C-to-U DNA/RNA deaminase family of which AID is a member (e.g., APOBEC1; APOBEC3 A, B, C, D, F, G, H); AID, activation induced cytidine deaminase causing C-to-U lesions at WRCY/RGYW C-site motifs in ssDNA; W, A, or U/T; WA-site, target motif for ADAR deaminase including DNA polymerase-η error prone incorporation *in vitro* (Rogozin et al., 2001); Y, pyrimidines T/U or C.; R, purine A or G.

2.3. Role of epigenetic gene targeting

This environmentally-induced phase "lights up" or "targets" expressed genes for the adaptive regulation of gene expression in progeny cells and organisms (Fig. 2). The main epigenetic modifications are the methylation of targeted cytosines (at CpG sites) via methyltransferases and their subsequent demethylation of such sites by AID/APOBEC deaminases and/or TET oxidase enzymes (reviewed in Guo et al., 2011a,b; Nabel et al., 2012). Demethylations of this type can thus allow reactivation of gene expression in previously suppressed genes. During the demethylation process such genes are vulnerable to cytosine to uracil and 5me cytosine to thymine deaminase mutations via the AID/APOBEC family of deaminases causing C-to-U and 5MeC-to-T primary somatic mutations (at DNA and RNA substrates generated at Transcription Bubbles (Steele and Lindley, 2017, Fig. 1). This first phase of an induced adaptive response thus involves "soft" Lamarckian inheritance, popularly known as "epigenetic inheritance" as it is reversible, see Skinner 2015, Skinner et al., 2015 for a recent comprehensive view (and Fig. 2).

2.4. Rapid genetic adaptation

Evolutionary adaptive change can be very fast and directional - immediately adaptive to a changing environment within one or two progeny generations. There is rapid genetic update of genomic DNA sequences being passed on to progeny organisms. Matic (2019) has recently reviewed these hypermutation rate strategies allowing survival of populations of living systems in unpredictable environments.

2.5. Penetration of the Weismann Barrier

There are numerous instances showing the genetic permeability of the Soma-Germline *Weismann Barrier* in higher animals. This actually requires the resurrection (Liu, 2008; Liu and Li, 2016) of the ancient idea of Pangenesis employed by Charles Darwin, to paraphrase Democritus " …. that the seed is formed continuously from all parts of the body". The published work now describes the molecular-vesicle variety of Darwin's "gemmules". There is now a solid foundation for the concept of Pangenesis as a molecular, cellular and physiological explanation for the inheritance of environmentally-induced acquired characters in higher animals (with a *Weismann Barrier*) and plants (with no traditional *Weismann Barrier*), see Fig. 2 and legend, and the review by Noble (2019).

2.6. Horizontal gene transfer (HGT)

Facilitating these genetic diversification and adaptation processes are the ubiquitous phenomena associated with horizontal gene transfer (HGT) involving genetic exchanges between cells (and their viruses) involving all levels of life, prokaryote, archaea, eukaryote.

2.7. Central role of reverse transcription

Apart from horizontal gene transfer, the next widespread and mutagenic phase is the *vertical transmissions of Lamarckian acquired adaptations* which involves somatic mutation, somatic selection

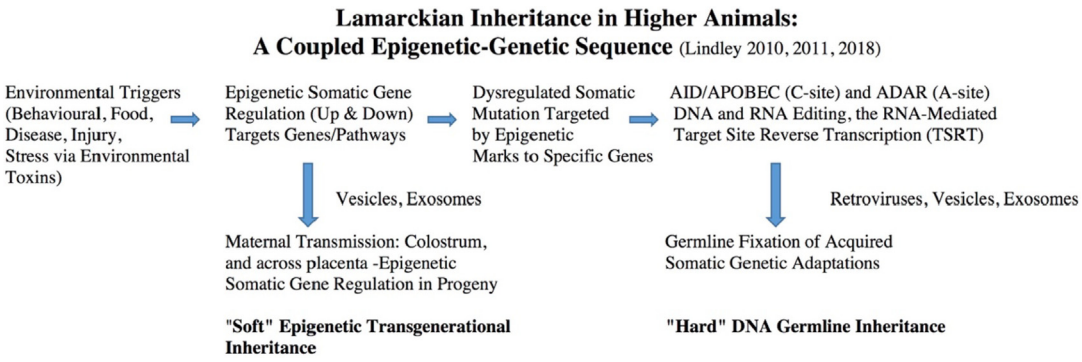

Fig. 2. Coupled Epigenetic-Genetic Mechanisms of Lamarckian Inheritance with the Penetration of the *Weismann Barrier* in Higher Animals. The point of the sequence is to show that genes targeted first for epigenetic transgenerational regulation can mature via a reverse transcription step targeting the same genes causing hard genetic (DNA) inheritance. The key epigenetic-genetic concepts are discussed at length in Lindley (2010, 2011) and specifically in Lindley (2018). The properties of cytosine modifications play a key role in the plasticity of the Epigenetic-Genetic coupling (see Guo et al., 2011a,b, Nabel et al., 2012). The distinction between "soft" and "hard" Lamarckian inheritance is discussed explicitly in Steele (2016b). The often confused distinction between the *Central Dogma of Molecular Biology* and the *Weismann Barrier* (Steele, 1979; 2016b) is discussed and further clarified in Noble (2018). In the first phase after stimulation, the environmentally-induced "epigenetic" gene regulatory factors (e.g. methylation-demethylation at CpG sites and other modifications at cytosines; synthesis of small 21 nt-24nt sRNAs such as miRNAs etc. and guided by other non-coding regulatory RNAs) light up and target specific genes and gene pathways for regulated gene expression. The epigenetic role of long non-coding RNAs (>200 nt) targeting regulatory portions flanking protein-coding genes is covered in conceptual detail by Mattick (2003, 2018). The recent review by Kulski (2019) shows the functional importance of locus-wide lncRNAs in conserving long ancestral haplotypes at the human Major Histocompatibility Complex locus - where they act as genomic anchor points for binding transcription factors, enhancers, and chromatin remodeling enzymes thus regulating transcription and chromatin folding. LncRNAs specifically target DNA sequences usually via RNA-DNA triple helix interactions involving the weaker yet biologically significant Hoogsteen hydrogen bonding. Hoogsteen base pairing, considerably weaker than Watson-Crick base pairing is varied, in both parallel and anti-parallel configurations with the RNA sequence aligned in the major groove of the DNA duplex (Li et al., 2016). These allow multiple points of hydrogen bonding over significant sequence lengths (e.g. Enhancer or Promoter regions) thus allowing gene-specific recognition. RNA-DNA triple helix interactions thus allow targeted delivery of chromatin modifications resulting in either active transcription (activation via acetyltransferase-associated complexes) or gene silencing (chromatin compaction via methyltransferase -associated complexes). These data and the analytical methodology are reviewed in detail in Smith et al. (2013, 2017), Buske et al., (2011, 2012) and in Li et al. (2016). Such lncRNA epigenetic regulators are ubiquitously found in secreted extracellular vesicles and exosomes, particularly in tumours and tumour cell microenvironments (Xie et al., 2019; Chen et al., 2019). Epigenetically "marked" genes can become targets for AID/APOBEC-deaminase mediated cytosine to uracil (C-to-U) and cytosine to thymine (C-to-T) mutations (at 5Me CpG sites, Morgan et al., 2004), which result in G•U and G•T mispairs. Then as shown in part in Fig. 1 these can progress through further error-prone steps of DNA repair following base excision resulting in Abasic sites and then single stranded DNA nicks in the transcribed strand with 3′OH ends that can prime both DNA and RNA-dependent cDNA synthesis (off homologous newly transcribed RNA sequence templates). These downstream nicks resulting from ncRNA regulatory targeting therefore "open" the DNA in that genomic region to invasion and targeting of previously base-modified and mutated mRNA sequence templates which can be reverse transcribed and their specific cDNA fragments integrated at these C-sites (and surrounding sequence) into the genomic DNA, by target site reverse transcription,TSRT (Luan et al., 1993) as discussed at length elsewhere (e.g. Steele, 2016a. Steele and Lindley, 2017) and shown in Fig. 1. This is a variant of AID/APOBEC deaminase-mediated dysregulated immunoglobulin somatic hypermutation-like responses initiated at C-sites across the cancer genome (Lindley, 2013; Lindley and Steele, 2013; Lindley et al., 2016). ADAR deaminases causing adenosine to inosine modifications in RNA and DNA are also part of this dysregulated Ig SHM-like response scheme (A-to-I, read out as A-to-G transitions, Lindley, 2013; Lindley and Steele, 2013; Steele and Lindley, 2017). The enzymatic deaminase targeting specific C-sites and A-sites in DNA and RNA substrates occurs in protein-coding regions in codon context (Lindley, 2013) most plausibly in the 3D environment of stalled Transcription Bubbles (Lindley, 2013; Steele and Lindley, 2017). There is evidence that deamination of 5-methylcytosine (5 mC) and 5-hydroxymethylcytosine (5hmC) and generation of mutagenic C-to-T mutations directly by the activity of AID/APOBEC complexes is an alternative path to successive oxidation reactions by TET enzymes for the initiation and regulation of DNA demethylation (Guo et al., 2011a,b, Nabel et al., 2012, Pastor et al., 2013, Scourzic et al., 2015). The role of extracellular secreted vesicles and exosomes is discussed in Fig. 1 of Steele and Lloyd (2015) based on the seminal vesicle/exosome data published in Cossetti et al. (2014) (mice) and later in Sharma et al. (2016) (humans). B lymphocytes themselves when activated by mitogens secrete large numbers of endogenous retroviruses (Moroni and Schumann, 1975; Moroni et al., 1980). The significance of the very high concentrations ($>10^{11}$ per ml) of endogenous retroviruses in seminal fluid, surrounding the placenta and actually bound to the heads of spermatozoa (Keissling et al., 1987) challenges the widely held belief *that only one successful sperm* affects the internalized genetic cargo at fertilization. The questioning of this commonly held belief is justified given the huge number of spermatozoa attached to a given ovum. Finally, apoptotic vesicles have also been invoked as DNA/RNA soma-to-germline transmission vehicles (Steele et al., 2002). Indeed there are many formal similarities between retroviruses and secreted extracellular vesicles (Hoena et al., 2016). The properties of extracellular extruded vesicles and exosomes has been extensively reviewed (van der Pol et al., 2012) and extracellular membrane vesicles with exported cargos appear across the three domains of life and form a intercellular communication system (Gill et al., 2018). All this has been recently highlighted by Noble (2019) in the context of Darwin's Pangenesis.

and then reverse transcription at the RNA level into germline genomes of multicellular animals and plants (Steele, 1979). In many cases this begins via cytosine and adenosine deaminase action during gene expression - as represented by the key mutagenic events at Transcription Bubbles as shown in Fig. 1.Thus RNA modifications brought about by deaminase action are locked into the genomic DNA by the process of Target Site Reverse Transcription, TSRT (Fig. 1 and see specifically Luan et al., 1993). The coupling of the "soft" inheritance of the "epigenetic" first phase with the second "hard" germline or DNA inheritance phase, leads to the stable transmission of the acquired character(s) to cells and progeny organisms. Lamarckian inheritance can be envisaged therefore as a two-step process involving Epigenetic-Genetic coupling (Fig. 2).

In Section 3 we select representative examples where each one is a type of conceptual and/or evidential 'Demarcation Data' point in its own right - forcing us to choose between the traditional "slow, random and blind " neo-Darwinian view of Life to the now rapid, directional and far more accurate Lamarckian-Panspermic coupled paradigm of biological evolution.

3. Acquired inheritance phenomena

The development of the main conceptual and experimental steps are outlined here more or less in chronological order as the field(s) infolded since 1970 when Temin and Baltimore first reported the discovery of reverse transcriptase in RNA tumour viruses (Temin and Mizutani, 1970; Baltimore, 1970). The implications of reverse transcriptase for the inheritance of some acquired characters was made explicit by Howard Temin at this time if not earlier (Temin, 1970, 1971). These examples are selective and illustrative of the diversity and thus generality of Lamarckian acquired inheritance phenomena. More detailed technical information and references are confined to figure legends for the interested reader to further explore in depth.

3.1. Somatic Selection Hypothesis (1979): origin, maintenance, diversification of antibody V genes

The variable (V) genes of higher vertebrate antibodies, or

immunoglobulins (Ig), exist as large arrays in the germline DNA of very similar V sequences (≥50–100 V gene segments). In the germline they are inactive V segments (coding for about 100 amino acids) but in a mature somatic B lymphocyte in the lymphoid and blood circulation they rearrange at the DNA level to join with shorter D and J elements forming transcriptionally active somatic genes encoding rearranged heavy (VDJ) and light (VJ) chains of the HL heterodimers of antibody proteins. A viable antigen combining site is formed from a heterodimer of one heavy (H)) and one light (L) chain, essentially by a combinatorial protein association sorting process in any given B cell. In this "somatic configuration" the V[D]J genes hypermutate following antigenic stimulation. This is a typical "Darwinian" process of rapid mutation, proliferation of antigen-selected B cell survivors with large cellular apoptotic death factors (in so called "Germinal Centres" in peripheral lymphoid organs, such as spleen, lymph nodes).

Thus many B cells are destined to die (>90%) in Germinal Centres. The successful antigen-selected mutants, bearing an antigen-specific receptor on their surface membrane survive to become affinity-improved, clonally expanded, memory B lymphocytes (clonal selection). The daughter cells then enter the vascular circulation and seed other lymphoid organs. All the extant *in vivo* molecular and cellular evidence indicates the mechanism of Ig somatic hypermutation (SHM) is driven by antigenic stimulation via an AID (APOBEC) and ADAR deaminase-coupled Reverse Transcription process (RNA/RT), as shown in outline in Fig. 1 (Steele et al., 2006; Steele 2016a, 2017; Steele and Lindley, 2017). The first iteration of the RNA/RT-Ig SHM model was by Steele and Pollard (1987), and the demonstration that the key error-prone DNA polymerase-Eta (η) involved in Ig SHM is a very efficient reverse transcriptase was first demonstrated by Franklin et al. (2004) and independently confirmed recently by Su et al. (2019).

The Somatic Selection Hypothesis (Steele, 1979) was created to explain the origin, maintenance and diversification of the germline V gene arrays via the agency of somatic mutation and clonal selection (Burnet, 1957, 1959) utilizing Temin's harmless endogenous retroviruses acting as somatic gene vectors transducing somatic V mutant sequences at the mRNA level and shuttling them into the germline of immunized animals. Rothenfluh (1995) vastly improved the model by invoking mobile mutant B lymphocytes interpenetrating reproductive tissue and delivering the endogenous V-transducing vectors more or less directly to germ cells (later apoptotic B cell-derived vesicles were also invoked as transport vehicles, Steele et al., 2002). Rothenfluh (1995) also reviewed the evidence that endogenous retroviruses are secreted in large numbers from B lymphocytes stimulated by antigens and mitogens of foreign pathogens (Moroni and Schumann. 1975; Moroni et al., 1980).

The Somatic Selection Hypothesis was the first attempt, post the Lysenko era, to build a viable Lamarckian genetic model for the penetration of the *Weismann Barrier* - that was at the same time consistent with all the known facts of development, molecular genetics, virology and Mendelian inheritance. As far as the genetic structure of higher vertebrate germline V gene arrays are concerned it is still the most economical explanation for the origin, maintenance and further diversification of all the current published germline V segment data (Steele and Lindley, 2018) which always bear the hallmark signatures of intense somatic mutation and selection implying regular soma-to- germline V gene feedback during life and across generations (Blanden et al., 1998; Steele et al., 1998; Steele and Lloyd, 2015).

3.2. Inheritance of acquired neonatal tolerance to foreign histocompatibility antigens in mice

These experiments showed that the deep tolerance of immune reactivity at the level of cytotoxic T lymphocytes (CTL) measured in *in vitro* assay systems which was induced in neonatal male mice, could, after mating those males as adults to females of the same inbred stain, be passed on to first and second generation progeny (appearing in the second generation without exposure to the foreign histocompatibility (H-2) antigens used to set up specific tolerance in the original father (Gorczynski and Steele 1980, 1981). In later experiments the specific H-2 tolerance in progeny generations correlated with specific delayed skin graft rejection (Gorczynski et al., 1983). Experiments in the Brent-Medawar laboratory claimed these acquired paternal transmission experiments could not be repeated (Brent et al., 1981). The controversy surrounding these differences in the two studies initially focused on significant differences in the way the CTL assay was performed in the Toronto/Canada and Harrow/UK laboratories. However, the Brent et al. (1981) progeny clearly showed significant numbers of delayed skin graft rejectors (Steele, 1981) later confirmed by Gorczynski et al. (1983). In subsequent follow-up studies the same group again claimed negative paternal transmission results (Brent et al., 1982) when they set up a smaller number of breeding males than the original experiments - four neonatally treated males, down from ten in the original protocols (Gorczynski and Steele, 1980; Brent et al., 1981). This exposed this work to the further criticism that these investigators had reduced the odds of observing paternal transmission given that previous observations had shown that only ~ two out of ten neonatally H-2 tolerant males routinely documented high transmission of H-2 specific hyporesponsiveness (Gorczynski and Steele, 1980). Indeed, Mullbacher and colleagues, conducting breeding experiments at the same time and in the same laboratory as Brent et al., with inactive *Bebaru* virus antigens, demonstrated a positive non-antigen specific paternal transmission of induced neonatal hyporesponsiveness at the CTL level with *in vitro* cytotoxicity assays (Mullbacher et al. (1983). Later, positive paternal transmission was demonstrated in experiments in inbred mice to foreign (rat) erythrocytes, using both repeated high dose neonatal male tolerance (Steele et al., 1984) or single shot immunity to the erythrocytes in adult males prior to breeding to normal females (Steele, 1984). So these acquired inheritance immune system effects induced in male inbred mice were certainly controversial 30–40 years ago, but they were real, yet complex with respect to mechanism, involving most likely, in retrospect, all the epigenetic and genetic dimensions summarised in Fig. 2.

3.3. The sire effect, telegony and subsequent maternal influence

The acquired inheritance phenomena and history associated with what is called the "Sire Effect" have been reviewed (Lindley, 2010 pp. 22–29). The phenomenon was reported by Gorczynski et al. (1983) when they tested the normal inbred female mice who had raised offspring to male mice of the same inbred strain made neonatally tolerant to repeated doses of foreign lymphoid cells expressing specific H-2 histocompatibility antigens as just described (Gorczynski and Steele, 1980, 1981). When these mothers were bred to normal males of the same inbred strain they produced tolerant or hyporesponsive progeny to the *same H-2 antigens* as used in the original neonatal tolerance regime in the original breeding male.

This was a surprising result. Such mothers also passed on the effect when fostering normal pups, identifying causal factors in the colostrum and milk (Gorczynski et al., 1983). This is a striking and important result with implications resurrecting the old observations surrounding the non-Mendelian breeding results caused by male sperm and thus phenomena associated with "Telegony" (Watson et al., 1983). The "Sire Effect" thus opens a Pandora's Box with wide implications for pure-line animal breeding and wider societal implications (Lindley, 2010 pp. 22).

The "Sire Effect", whatever the detailed transmission mechanism, has real-world practical implications (Lindley, 2010 pp.26–27). Wild rabbits in rural Australia were in plague proportions in the 1940s and 1950s causing great damage to agriculture, particularly the sheep and cattle industries. To control these wild rabbit populations the Commonwealth Scientific and Industrial Research Organization (CSIRO) released rabbits infected with lethal *Myxomatosis* virus. The virus was very effective initially in controlling wild rabbit numbers. But the speed with which immunological resistance developed caused further investigations. At first sight it seemed much faster than simple "Darwinian" recovery of a resistant residual population after such a large kill (≥90%). Indeed careful follow up controlled breeding experimental work by Bill Sobey and Dorothy Conolly discovered a significant factor in the rapid spread of resistance (Sobey and Conolly, 1986): bucks which had recovered from *Myxomatosis* virus when mated to a doe who had not previously been exposed to *Myxomatosis* virus produced litters that were resistant to the lethal effects of the virus- a clear paternal transmission or "Sire Effect" as described by Gorczynski et al. (1983). Thus when a non-immune buck was mated with a doe that had previously been mated to an immune buck a significant number of progeny were born with immunity to *Myxomatosis* virus. Sobey and Conolly concluded that an unknown factor transmitted via the semen of the *Myxomatosis* virus recovered bucks to the normal females which could be further transferred in other matings to normal non-exposed males.

The molecular-cellular mechanisms of the *Myxomatosis* virus sire effect in rabbits, as well as the H-2 antigen-specific maternal influence in the mother's milk acquired by the mother from the original neonatally tolerant male have not been analysed. However obvious candidates for study can be drawn from an array of epigenetic and genetic transmission effects discussed above and in Fig. 2. For example they could be related to the small regulatory RNA-mediated spermatozoa non-Mendelian inheritance effects described by Rassoulzadegan and colleagues (Rassoulzadegan et al., 2006; Kiani et al., 2013; Liebers et al., 2014) and other foreign RNA and DNA in semen and associated with spermatozoa reported by Spadafora and colleagues (Lavitrano et al., 1989, Zoraqi and Spadafora, 1997, Cossetti et al., 2014, Smith and Spadafora, 2005, Spadafora, 1998, 2008, 2018). These effects are also consistent with the functional role of sperm-associated RNA reviewed in Ostermeier et al. (2004). Indeed the oocyte during the fertilization process has many attached spermatozoa, and it is difficult not to believe that all the unsuccessful non-fertilizing sperm cells have not left a functional nucleic acid signature behind in the oocyte. These could be small regulatory RNAs, specific mRNAs as discussed, or via genetic information in endogenous somatic retroviruses (Steele, 1979) attached to sperm heads (Keissling et al., 1987; Rothenfluh, 1995). Indeed it is hard not to think that the specific nucleic acid cargoes in the seminal fluid vesicles described by Cossetti et al. (2014) and Sharma et al. (2016) are also not playing a functional inheritance role.

3.4. Pavlovian conditioning, coupled maternal influence: brain, behaviour, immunity

There have been numerous studies published on behavioural traits associated with Pavlovian conditioned immune phenomena (Ader and Cohen, 1982, 1993; Moynihan and Ader, 1996). The implications of these experiments and observations are far reaching for understanding the emergence of specific instincts in higher animals. In some specific conditioning experiments in mice, in which cyclophosphamide induced immune suppression was coupled with saccharin in the drinking water as the conditioning regime, Gorczynski and colleagues subsequently showed not merely a saccharin-mediated conditioned recall of immune suppression, as initially described by Ader and Cohen (1982) but the propagation to progeny through several breeding generations of that conditioned immunosuppression. Gorczynski and colleagues localised the transmissible entity by a maternal cross-fostering design to characteristics of the nursing mother (Gorczynski and Kennedy, 1987). In other experiments they localised these causal effects to regulation by factors in the colostrum/foetal-placental unit modified by conditioning phenomena (Gorczynski, 1992). This conclusion is the same as the maternal immune factors transferred in the acquired sire effect described earlier by Gorczynski et al. (1983).

In a subsequent review Gorczynski et al. (2011) argued "there is now compelling evidence to suggest that a variety of perceived environmental "insults" to pregnant females, and even to nursing females in the post delivery period, in the form of physical, pathogen-related or emotional stressors, can produce significant perturbations in the immune responses seen in their offspring." The mechanisms involved are ill-understood, but at least in part may depend upon altered activation of the HPA axis, and of altered cytokine, neurohormone and neutrotransmitter production within the CNS. Other data imply an evolutionary balance is struck between changes in maternal behaviour sacrificing some aspects of maternal innate immunity at the expense of improved immunity in offspring. It is now acknowledged that even effects as subtle as an altered dietary behaviour change in the mother can itself produce profound changes in the microbiome of both mother and offspring, and this also can potentially have important implications for subsequent immune development. Since these interactions between behaviour and immune response potential in mothers and their offspring are reciprocal in nature, an altered immune activation in the mother may in turn thus evoke altered behaviour in the offspring, the "loop" essentially becoming closed.

Indeed at this juncture we can ask: How do instincts arise in evolution? If one studies the range of these strong and lifesaving reflex actions in humans and animals, logic implies an ultimate adaptive Lamarckian cause in ancestors. Strong survival instincts based on prior learnt fear responses must have arisen in our ancestors not by random chance events that were selected, but in a Lamarckian manner, which were then passed on to their progeny *en masse* providing a survival value to the small familial and interbreeding groups of mammals in the wild. The recent report by Dias and Ressler (2014) shows that parental mice subjected to Pavlovian odour fear conditioning before conception produced progeny generations with specific behavioural sensitivity to the specific chemical odour used to condition the parents. Unrelated chemical odours did not trigger a conditioned fear response. Other breeding experiments established that these specific acquired transgenerational effects are indeed inherited via parental gametes. Thus, both direct genomic and indirect epigenetic odorant receptor gene targeting appear to act together to establish what we now recognize as specific instinctual responses involving odorant receptor genes and behaviour. This is consistent with a coupling of both "soft" and "hard" inheritance schemes summarised in Fig. 2.

3.5. Transgenerational "epigenetic" experiments in endocrine metabolic systems in rodents

The maternally-mediated transgenerational effects just described in the immune and behavioural systems have traditionally been interpreted under the general "Above the Genes" or "Soft" acquired inheritance or "Epigenetics" paradigm (Jablonka and Lamb, 1995; Lindley, 2010; Skinner, 2015). This is indeed the first phase of environmental stimulation as summarised in Fig. 2. Definitive induced-transgenerational effects have been described

in the endocrine and metabolic physiological systems as reviewed by Campbell and Perkins (1988). The most well known are the studies showing the paternal and maternal transmission of chemically-induced acquired diabetes in rodents (Okamoto, 1965; Goldner and Spergel, 1972; Steele, 1988), passed down many breeding generations via male and female parents without any further exposure to the diabetogenic inducing agent (Goldner and Spergel, 1972). Clearly we are dealing here with a complex interactive epigenetic and genetic transmission system. In these studies the strategies described above (Gorczynski et al., 1983) of testing the potential of mothers mated to affected males for *in utero*/foetal effects by subsequent mating of such mothers to normal males or cross fostering effects via the colostrum and milk were not conducted.

3.6. The Dutch Famine

The epigenetic transgenerational phenomena described are not just of academic interest but impact human health. The famous after effects of the extreme starvation episodes at the end of World War II, the "Dutch Famine", underscore the long term inherited effects (Painter et al., 2008). Indeed Pembrey and colleagues have reviewed the induction by environmental conditions of grand parents and parents, such as nutritional deprivation, exposure to endocrine disruptors, and traumatic stresses, which can lead to disease susceptibility and altered immunity in the progeny and descendants (Pembrey et al., 2014).

Isabell Mansuy and colleagues have shown in mouse models of maternally-induced stress that unpredictable maternal separation combined with unpredictable maternal stress (MSUS) can lead to multiple effects in offspring transmitted via the male line up to three generations. The progeny phenotypes include depressive-like syndromes, aberrant social recognition, glucose (insulin) dysregulation and deficits in memory. In recent studies their results demonstrate both metabolic and behavioural symptoms in progeny mice into the 4th generation. They conclude that their MSUS induced transgenerational model produces solid and reproducible transmission effects initiated in the mother of early life adversity of male offspring (van Steenwyk et al., 2018).

In all these cases in humans and rodents the phenomena are interpreted as phase 1 "soft" epigenetic effects (Fig. 2) and thus potentially reversible via epigenetic reprogramming effects. It is difficult not to think, given the transmission through to four generations, that there are no associated "hard" DNA changes, related to the regulated expression of the relevant targeted gene pathways as outlined and predicted in phase 2 in Fig. 2. It has not escaped our notice that the phase 1 to phase 2 or soft-to-hard" acquired inheritance outlined in Fig. 2 has similarities to the simulated Lamarckian process described earlier (in 1896) referred to as the "Baldwin Effect" (Simpson, 1953).

3.7. Uptake of foreign DNA by spermatozoa and inherited effects in progeny

Corrado Spadafora and colleagues in Rome from the late 1980s (Lavitrano et al., 1989) to the present have published a series of important papers showing sperm uptake of foreign nucleic acid molecules and transmission of the genetic information to progeny organisms. Thus mouse spermatozoa clearly can take up foreign DNA/RNA molecules and express the genetic information in their progeny organisms. In some cases they show that a LINE-1-derived reverse transcription step can execute the copying of the RNA into DNA. In $\leq$ 10% of cases the DNA sequences are integrated into the germline genome. In most cases the sperm-absorbed DNA/RNA exists as extrachromosomal episomes which replicate along with the host somatic cells during development displaying mosaic tissue expression (see reviews in Smith and Spadafora, 2005; Spadafora, 2008). Recent work in mice by Cossetti et al. (2014) suggests a role for exosomes vesicles released into the bloodstream from human tumour xenografts transferring somatic RNA to spermatozoa.

This work clearly shows there is no physical barrier in spermatozoa to the uptake of DNA or RNA, although developmental stages in spermatogenesis may be more susceptible to foreign nucleic acid uptake (Zoraqi and Spadafora, 1997).

In his most recent review of all his group's data Spadafora (2018) has arrived at an important generalisation:

" I propose that RNA-containing nanovesicles, predominantly small regulatory RNAs, are released from somatic tissues in the bloodstream, cross the *Weismann Barrier*, reach the epididymis, and are eventually taken up by spermatozoa; henceforth the information is delivered to oocytes at fertilization. In the model, a LINE-1-encoded reverse transcriptase activity, present in spermatozoa and early embryos, plays a key role in amplifying and propagating these RNAs as extrachromosomal structures. ".

This is among the most precise descriptions of Darwin's "gemmules" in animals published, and is a mode of transfer which is also utilised in genetic information transfer in plant graft-hybridization, described below (Liu, 2018) and consistent with the current way we now view Lamarckian inheritance, Fig. 2.

Finally in 2002 Patrick Fogarty reported a striking result of simple intraperitoneal injection of DNA into adult male or female mice. Employing a technique based on P-element transposons and delivering DNA transgenes intravenously in simple vesicles, Fogarty has shown that 50% of progeny from such male mice inherit the gene sequence (Fogarty, 2002). The critical integration event requires a transposase enzyme. Thus non-cellular DNA can readily transverse the testes tissue barriers, that normally quarantine the production of sperm, be integrated into the germline and be transmitted to progeny. This was a clear demonstration of the genetic penetration of the *Weismann Barrier* in mammals in a Lamarckian mode typical of what may take place in the wild in a now familiar Horizontal Gene Transfer event.

3.8. Adaptive mutations in bacteria and other micro-organisms

Somewhat separate from the above developments involving the *Weismann Barrier* in multi-cellular sexually differentiated vertebrates, the work in bacteria and other rapidly multiplying unicellular organisms (such as yeast) are less definitive conceptually. This is because simple Darwinian selection of rare population variants could never be ruled out. However very challenging demonstrations of substrate-induced adaptive evolution phenomena in bacteria and yeast have been described (Cairns et al., 1988; Hall, 1988; Rosenberg, 2001). The data focus thinking on the possibility of rapid mutator mechanisms in microorganisms during the stationary phase (slower replication) and this somehow increases the odds of 'selecting' an adaptive mutant. Thus Cairns et al. (1988) published data suggesting "directional" mutation phenomena in bacteria. Mutants of *E. coli* requiring lactose for growth (lac-) can be "directed" under certain conditions to produce lac+ (wild-type) revertants if cultured in the presence of lactose. They interpreted this phenomenon as being consistent with a Lamarckian process of adaptive evolutionary genetic change and they provided a reverse transcriptase-coupled mechanism for the inheritance of acquired characteristics, much like that proposed earlier (Steele and Pollard, 1987) for the somatic hypermutation process summarised and now updated in Fig. 1.

So their work then raised the unexpected and exciting possibility that environmentally induced, non-random mutator processes dependent on a reverse transcriptase step also occur in

bacteria. This was rapidly confirmed a few months later by the timely report of Lampson et al. (1989) demonstrating reverse transcriptase activity in *E. coli*. Temin dubbed them all "retrons" in bacteria (Temin, 1989) and many different reverse transcriptase activities have now been described throughout prokaryotes and archaea (Liu et al., 2002; Guo H et al., 2011, 2014; Paul et al., 2015). Indeed Radman (1999) had earlier predicted such polymerase enzymes of evolutionary change (Radman, 1974) as part of the now familiar adaptive "SOS response" in bacteria to a range of environmental stress signals (Tippin et al., 2004). What is very intriguing about all these developments is that the Y family DNA Polymerases that figure prominently in the SOS response are all error-prone polymerases and are indeed related by their DNA encoded sequence to the human Y family DNA repair polymerases eta, kappa, iota (Ohmori et al., 2001) all of which have been shown to be efficient reverse transcriptases (Franklin et al., 2004). However none of the other bacterial Y family DNA polymerase members have yet to be examined for their RT activity.

So all these different RT activities in bacteria associated with adaptive mutator responses such as the diversity-generating retroelements (DGR) (Guo H et al., 2011, Guo H et al., 2014; Paul et al., 2015) in bacteriophage, bacterial and archaeal genomes provide a unity with the RNA/RT process developed for the Ig SHM in the higher vertebrate and mammalian immune system. Mammalian systems seem to be employing an ancient hypermutation strategy - a targeted RNA template-directed and reverse transcriptase-mediated hypermutation process (estimated minimum age given archaeal systems - 3–4 billion years on Earth). Guo et al. (2014) also comment on the conserved protein folds of Ig domains in the DGR reverse transcriptases: "These observations suggest that DGR target proteins and antigen receptors may have evolved different solutions to accommodate sequence diversity in the context of Ig folds."

3.9. Deaminases, cancer progression and next generation sequencing analyses

The summary in Fig. 1 showing deaminase-mediated attack on DNA and RNA substrates in the context of the Transcription Bubble (ssDNA, RNA:DNA hybrids and nascent dsRNA stem loops) is very relevant to understanding the somatic mutator processes in progressing cancer genomes (Lindley, 2013; Lindley et al., 2016; Steele and Lindley, 2017). What is intriguing is the deaminase substrate analysis of the clinically relevant single nucleotide polymorphisms (SNPs) in the human germline - the OMIM data base (Online Mendelian Inheritance in Man) - and in the wider dbSNP itself (Lindley and Hall, 2018). The first point to note is that 30–40% of all the SNPs occur at deaminase sequence motifs typical of AID, APOBEC3G, APOBEC3B and ADAR deaminase action in somatic cells during Innate and Adaptive Immunity to pathogens (see glossary legend Fig. 1). The next points are that >99% of the far larger number of millions of SNPs in the NCBI dbSNP are mild or benign (not associated with overt inherited diseases) and in the protein-coding regions are in typical C-sites and A-sites specifically targeted in codon-context as observed in somatic cancer genomes (Lindley, 2013; Lindley et al., 2016). Thus deaminase -mediated non-random mutation patterns appear written into human germlines over evolutionary time. Given the specificity of the targeted somatic mutation (TSM) signatures of the deaminases, and their coincidence with many common established C-site and A-site deamination motifs this suggests a causal direct role for the AID/APOBEC and ADAR deaminases mutating human germlines, triggered perhaps by innate immune responses to viral infections. But this speculation implies that human germline DNA is not quarantined from such pathogen-driven SHM-like processes. Currently some APOBEC deaminases are known to have low level expression in normal human ovary but not testes (Refsland et al., 2010), and some ADAR isoforms are significantly expressed in normal human testes (Picardi et al., 2015). The deaminases could be acting directly on transcribed regions of the human germline; alternatively they act first in the tissues which are somatically selected and thus become physiologically "benign" (somatic polymorphic variant), then followed up by a soma-to-germline feedback step to deliver portions of the mutated somatic sequences into their homologous genomic sites in germline loci. It seems most unlikely that viral pathogens would be allowed, under normal circumstances, to stimulate dysregulated AID/APOBEC and ADAR deaminases to go on a "mutator spree" in oocytes or during spermatogenesis. Clearly future human studies should focus on these questions. The point of discussing all this is to raise the possibility that the current DNA sequencing and Bioinformatics technologies will soon provide definitive answers to a more accurate understanding of the true origins of human genetic variation.

3.10. Inheritance of characters acquired by plant grafting

Plant grafting is an ancient agricultural and horticultural practice that combines the shoot (scion) of one plant with the root system (stock) of another. Historically graft-induced variations were recorded to occur in ancient China. Charles Darwin (1868) however was the first to use the term "graft hybridization". He noted that the formation of breeding hybrids through plant grafting between distinct species or varieties (without the intervention of the sexual organs). Many such cases of "graft hybrids" were described by Darwin where shoots produced from grafted plants exhibited a combination of characters of both stock and scion. It was understandable that he would explain their formation by his theory of Pangenesis involving transmissible and transported "gemmules" in the phloem. Darwin's concept of graft hybridization was supported by Ivan Michurin, Lucien Daniel, Luther Burbank and many practical breeders. But there has been a reluctance to accept the existence of graft hybrids among some geneticists (Liu, 2018).

Trofim Lysenko was a keen supporter of the Lamarckian inheritance of acquired characters, and demonstrated experimentally the conversion of spring wheat into winter wheat and *vice versa*. He also accepted the existence of graft hybrids, and led large-scale experiments on graft-induced heritable changes. A German geneticist, Hans Stubbe, failed to confirm Lysenko's results, thus he regarded graft hybridization as part of Lysenko's fraud (Hagemann, 2002). However many epigenetic phenomena are now recognized in plants (reviewed in Sano, 2010) which would be equivalent to the first "Soft" inheritance phase in Fig. 2. Yet other studies in flax demonstrate "hard" inheritance following environmentally induced adaptive DNA changes (Cullis, 1984).

Over the past few decades, the existence of graft hybrids has been widely documented, and the results are clear and striking and regularly reproduced by many plant breeders and horticulturists. For example, Yosita Shinoto, the former president of the Genetics Society of Japan, a serious scientist and a man of the highest integrity, claimed to have obtained graft hybrids in eggplant and confirmed Lysenko's results (Shinoto, 1955). A similar example of such a graft hybrid is shown in eggplant by Zu and Zhao (1957) (see Fig. 3). There has also been increasing evidence for graft-induced heritable changes in pepper and other plants (Ohta, 1991; Taller et al., 1998). The key to success is the use of the so-called "mentor-grafting" method invented by Michurin.

Graft hybridization is now mainly explained by horizontal gene transfer and genetic transformation (Ohta, 1991). This is supported by recent experimental evidence that DNA and entire nuclear genomes can be transferred between plant cells (Fuentes et al., 2014;

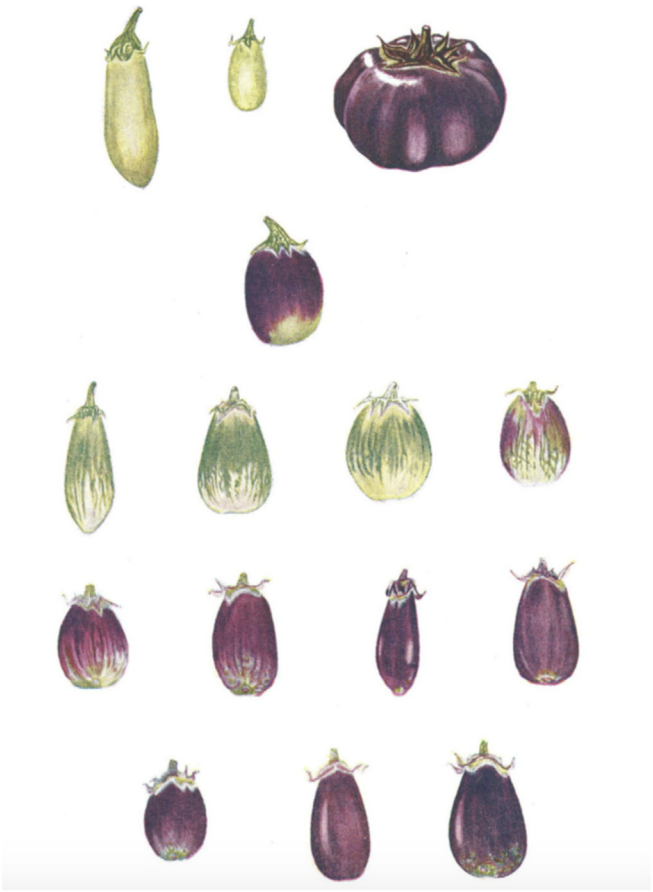

Fig. 3. Graft-induced variations in eggplant, in which 9-leaf eggplant was grafted onto white eggplant. **First row**: left: fruit of white eggplant; Right: fruit of 9-leaf eggplant; Middle: fruit in the stock of the immediate generation. **Second row**: Variant fruit in F1 generation. **Third-Fifth row**: Variant fruits in the F2 generation. Reproduced with permission from Zu, D.-M., Zhao, Y.-S. (1957) A study on the vegetative hybridization of some Solanaceous plants. Scientia Sinica, 6, 889–903. From Fig. 5 in Liu (2018).

Gurdon et al., 2016). In addition, the long-distance transport of mRNA and small RNAs is also considered to be involved in the formation of graft hybrids. Indeed plant hybrid transmission of small regulatory RNAs, mRNAs and other reporter sequences are standard experimental tools in plant molecular genetics and development (Ham and Lucas, 2017). We should now add a reverse transcription step to lock in such transported RNA phloem information into the hybrid seed genomes. Liu (2006) proposed that "the stock (or scion) mRNA molecules being transferred into the scion (or stock) – then reverse-transcribed into cDNA that can be integrated into the genome of the scion's (or stock's) germ cells, embryonic cells, callus cells, as well as the somatic cells of juvenile plants – and thus may be the main mechanism for graft hybridization".

3.11. Complexity of epigenetic and induced transgenerational inheritance

Despite more than several decades of studying induced epigenetic effects in animals and plants there are large areas of ignorance due to the complexity and variety of the phenomena. A recent balanced and sceptical review of the field by Panzeri et al. (2016) of non-coding RNA directed epigenetic regulation of gene expression is necessary corrective reading, despite the considerable molecular detail on non-coding RNAs short and long now accrued (see legend Fig. 2). The large number of "above the genes" biochemical modifications to various regulated chromatin states justifies their conclusion: " Histone modifications comprise methylation, acetylation, acylation, phosphorylation, ubiquitination, sumoylation, proline isomerization, citrullination, and ADP ribosilation, but also more recently identified (and less represented) crotonylation, butyrylation, propionylation, succinylation, malonylation, hydroxylation, formylation, O-GlcNAcylation, and likely many others yet to be discovered". Furthermore, while gene silencing by methylation at CpGs and the actions of small regulatory 21 nt-24nt RNAs are the best studied transgenerational modes (e.g. see Kiani et al., 2013; Liebers et al., 2014) there are also clear cases of active gene *upregulation* by small RNAs (Portnoy et al., 2011). All these varied findings that are ongoing suggest that protein-coding genes and intervening genomic regions are targeted first by base sequence homologies (e.g. in the small miRNA stem loop structures, and see Fig. 2 legend) which then direct the epigenetic methylation and demethylation mechanisms (e.g. Bayne and Allshire, 2005; Molnar et al., 2010; He et al., 2011; Matzke and Mosher, 2014). It is our considered view, following Panzeri et al. (2016), that current investigations on the plethora of epigenetic-genetic couplings as summarised in Fig. 2 are just the tip of the iceberg, and that many genetic surprizes will be revealed in the research of coming years.

3.12. 100 years ago? - Experiments of Paul Kammerer, Guyer and Smith

One hundred years ago, both before, during and after the first world war there were serious attempts to demonstrate Lamarckian inheritance in higher animals by Paul Kammerer (Koestler, 1971; Vargas, 2009; Vargas et al., 2017) and by Michael Guyer and Elizabeth Smith at the University of Wisconsin (one of their key papers is republished with a modern interpretation in Steele, 2016c). In our view the definitive Lamarckian inheritance experiments in rabbits by Guyer and Smith in 1918–1924 on the transmission via the male line (up to 9 breeding generations) of maternal autoantibody-induced eye defects are on a level with the foundation work in genetics by Gregor Mendel. Yet these experiments were performed and reported in an earlier age antithetical to Lamarck. This was the time of the emergence of Mendel's rediscovery, and the rolling destructive controversies (Koestler, 1971) around the mid-wife toad and salamander experiments of Paul Kammerer – now given a modern interpretation in terms of current epigenetic concepts (Vargas, 2009; Vargas et al., 2017).

This period also heralded the birth of modern neo-Darwinism which became, with RA Fisher's statistical-based 'Population Genetics' with free recombination at and between all loci across the higher plant and animal genome (Hill, 2014), the dominant genetic paradigm for biology in the 20th century. We do not have space to deal fully with the RA Fisher paradigm which tacitly guides all Population Genetics thinking and analysis (Hill, 2014). However we point out that the prominent and genome-wide existence of long "ancestral haplotypes" in man and domestic livestock both structurally and functionally, are *profoundly non-Darwinian genetic phenomena*, in contradiction of the main assumptions of RA Fisher's free-recombination paradigm (Dawkins et al., 1999; Williamson et al., 2011; Dawkins, 2015; Steele, 2014; Steele and Lloyd, 2015). The existence of numerous and diverse functional long non-coding RNAs which display functional conservation (Mattick, 2003, 2018; Smith et al., 2013, 2017; Li et al., 2016) is consistent with the prior ancestral haplotype concepts (Steele, 2014) discovered by Roger Dawkins and colleagues at the Major Histocompatibility Complex (MHC). Indeed Yurek Kulski, who has spent many years working on the long MHC haplotypes described by Dawkins et al.

(1999), recently reviewed the evidence for involvement of evolutionary conserved lncRNAs in the ancestral haplotype phenomena associated with the MHC region (Kulski, 2019). Indeed some of us have also published the possibility of reverse transcriptase-coupled generation of lncRNAs defining the origin and regulatory integration of long ancestral haplotypes (Steele et al., 2011).

3.13. Summary and conclusion- Definition of a "gemmule"

The general conclusion from our review of some of the main extant relevant data seems clear: the traditional *Weismann Barrier*, assumed for many years as the bedrock and protective foundation pillar of modern neo-Darwinism (the past 100 years at least) is *very permeable* to somatic DNAs and RNAs with inherited influences on subsequent generations. Thus a Darwinian "gemmule" or "pangene" can be defined as a somatically-derived vesicle loaded with a functional cargo - amongst other molecules (proteins, lipids, transcription factors) - of specific regulatory or specific coding nucleic acid information (small regulatory RNAs, mRNAs, lncRNAs and even DNAs). It is satisfying that the conceptual wheel has now come full circle (Noble, 2019) such that we are now able to coolly accept such an important conclusion on how extant life may be evolving on Earth (Fig. 2).

4. Pragmatic position: Demarcation Data and the statistical odds of abiogenesis

There are now solid grounds for believing in the reality of the inheritance of acquired characters as a widespread biological process, albeit with different molecular and cellular details in different living systems, whether unicellular or multicellular. There are also now good scientific grounds for believing in the in-fall of living systems from space continuously "seeding" various life forms on Earth over the past 4 billion years (Steele et al., 2018, 2019) and Section 5. However the question of the *actual* of origins of life whether on Earth or the wider Universe is clouded in mystery – with roots stretching into the deepest depths of cosmic antiquity. Here we outline, as we have done before (Hoyle and Wickramasinghe, 1981, 1993, 1999a, Steele et al., 2018), our philosophical or, if you will, our pragmatic position.

4.1. Eukaryotic and prokaryotic microfossils in carbonaceous meteorites dated at > 4.5 billions years

In our view the hard evidence *already exists* distinguishing terrestrial neo-Darwinism from the evidence for Cosmic Panspermia (Steele et al., 2019). We refer to this key evidence as the "Demarcation Data".The accrual of this and other multifactorial evidence has been comprehensively covered in successive books since the 1970s as the data and observations unfolded by Fred Hoyle and N. Chandra Wickramasinghe (1978a, 1979, 1981, 1985, 1991, 1993, 2000 with references to all peer-reviewed papers). A recent detailed summary of all the key evidence covering the terrestrial atmosphere, bacteria and other micro-organisms, the comets as protective incubators and amplifiers of living systems, the infra-red (IR) analyses of interstellar dust and cometary ejecta among other central issues can be found in Wickramasinghe (2015a, 2015b, 2018).

The "Demarcation Data", or data that has a defining interpretation, distinguishing neo-Darwinism from Cosmic Panspermia have been recently highlighted by us (Steele et al., 2019).

A key focus is on the internal structure of carbonaceous meteorites showing clear microfossils of both eukaryotic and prokaryotic organisms. These published observations have been secured from *independently curated and examined* carbonaceous meteorites, dated at > 4.5 billion years old. The data have been confirmed by experts in four well curated and characterised carbonaceous meteorites: Murchison (Pflug and Heinz, 1997; Hoover, 2005, 2011), Murchison, Orgueil, Mighei (Rozanov and Hoover, 2013), Polonnaruwa (Wallis et al., 2013; Wickramasinghe et al., 2013). Terrestrial contamination has been ruled out e.g. the scanning analytical EM technology now allows confirmation that the mineralised fossil has the same chemical composition as the surrounding matrix in which it is embedded.

As scientists we must critically evaluate these four different and independent "experiments of nature "on their own terms. Eukaryotic fossils with silica-based hard shells, are prominent in these fossils. Certainly in the Polonnaruwa meteorite (Wickramasinghe et al., 2013) the frustules of clear diatoms are evident and not considered to be contaminants (Fig. 4). Striking eukaryotic microfossils like this are also evident in the other carbonaceous meteorites (Rozanov and Hoover, 2013). Clearly these are features of mature cell biology in astrophysical phenomena that require a coherent explanation. "They strongly imply that complex cell-based life, now immortalised as fossils in carbonaceous meteorites, pre-dates the age of the Earth (and solar system). An explanation based on Panspermia seems unavoidable to us." (Steele et al., 2019).

4.2. Abiogenesis: life arose from non-living chemistry on earth - what are the statistical odds ?

The question of the actual origins of life should, in our view, be considered in terms of the information content of life as we know it and thus in terms of pragmatic statistical probabilities. Thus the actual origins of Life with its near infinite information content, enshrouded in the deep recesses of Cosmic antiquity are, for all practical purposes, scientifically unknowable. Our view on this is unabashedly pragmatic, which forces a philosophical position on priorities on where research funds should be deployed in the scientific investigation of both the origins of life, e.g. laboratory 'abiogenetic' experiments, and in searches where it might exist or arise across the Universe.

What are the main claims of Abiogenesis? What are their weaknesses in supporting a localised chemical origin of life? The summary in the excellent and comprehensive Wikipedia article

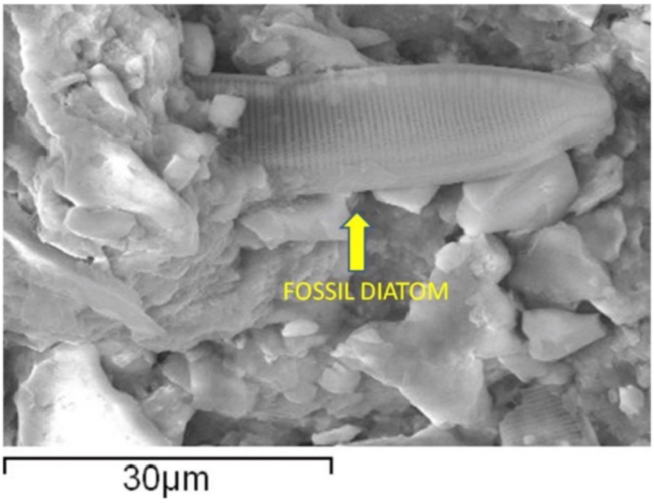

Fig. 4. Eukaryotic microfossil in Carbonaceous meterorite. voidal-shaped ribbed structure embedded in the rock matrix of the Polonnaruwa carbonaceous meteorite, Wickramasinghe et al. (2013), see also other chemical analyses in Wallis et al. (2013).

needs to be read in association with our analysis here (https://en.wikipedia.org/wiki/Abiogenesis) – it clearly shows that apart from the type of laboratory experiments in the Miller-Urey tradition of the 1950s (showing that many organic molecules can be created by electrical discharge processes that may have existed on the early Earth) the whole discussion in this area is built entirely on hypothesis, assumption and speculation with *no evidence* anywhere documenting the emergence of a living cell from non-living chemistry. This is not surprizing on reflection –the scientific enterprise investigating Abiogenesis is built (to quote the Wikipedia article) on "the prevailing scientific hypothesis … that the transition from non-living to living entities was not a single event, but an evolutionary process of increasing complexity that involved molecular self replication, self assembly, autocatalysis, and the emergence of cell membranes." There is a great enthusiasm (Martin et al., 2008; Lane, 2015) and much inspired laboratory and theoretical research for the first RNA replicator (Szostak et al., 2001; McFadden, 2016) that would have flourished in the hypothesized RNA world some 3–4 billion years ago. Such a brief summary is not to downgrade the importance of the question of the likelihood of Abiogenesis. We have to be cautious, re. contaminations by all pervasive living systems here on Earth (cf. observations on tryptophan abiosynthesis at shallow subterranean levels at deep sea hydrothermal vents as in Menez et al., 2018 – which need critical evaluation given the known all pervasive existence of the deep hot microbiological biosphere, Gold, 1992, 1999). And we need to be aware there have also been some spectacular claims (RNA self replicators) that turned out to be based on experimental artifacts,so skepticism and caution are warranted (Litovchick and Szostak, 2008, retracted 2017; and see https://retractionwatch.com/2017/12/05/definitely-embarrassing-nobel-laureate-retracts-non-reproducible-paper-nature-journal/).

Omission of key information in science is not helpful in any investigation. Nor should we turn a blind eye to certain overriding philosophical and epistemological difficulties that have been recognized. The philosopher of science Karl Popper (1974) expressed a huge problem for abiogenesis theories thus:

"What makes the origin of life and of the genetic code a disturbing riddle is this: the genetic code is without any biological function unless it is translated; that is, unless it leads to the synthesis of the proteins whose structure is laid out by the code. But …. the machinery by which the cell (or at least the non-primitive cell, which is the only one we know) translates the code consists of at least fifty macromolecular components which are themselves coded in the DNA. This constitutes a baffling cycle; a really vicious circle, it seems, for any attempt to form a model or theory of the genesis of the genetic code … …Thus we may be faced with the possibility that the origin of life (like the origin of physics) becomes an impenetrable barrier to science … …"

Certainly the 'sin' of omission applies to the Abiogenesis field. Thus the pragmatic statistical probabilities we discuss below are rarely mentioned at all in the Abiogenesis research literature nor at the Abiogenesis Wikipedia site (but see the interesting work by McFadden, 2016, below).

The paucity of supportive direct scientific evidence for Abiogenesis is in stark contrast with our own efforts to review here all the extant concrete and positive evidence demonstrating the reality of Lamarckian modes of inheritance in nature (Sections 2, 3) and the direct positive biophysical and astrobiological evidence (Fig. 4, Section 5) consistent with the extraterrestrial origins of life on Earth (Steele et al., 2018, 2019).

As indicated in our Preamble we are not at all pretending to provide an explanation for the *actual origins of life* in the Universe. We have discussed this again recently (Steele et al., 2018 and Appendix A in that paper). Many commentators, public and private, consider we are just shifting the problem – "kicking the can down the road"- and not solving the actual origin of life itself. However our pragmatic view is that conventional hypothetical explanations for Abiogenesis - as an explanation for the emergence of life on Earth - are mathematically and statistically improbable. Indeed the odds against successful "Abiogenesis" events popping up all the time around the Cosmos as implied by regular NASA Press releases and fuelled by conventional thinking (Walker, 2017) are also not scientifically supported in any way, and are moreover super-astronomically improbable. This is based on what we know of the information content of the simplest minimal cell capable of an independent self-replicating existence. The odds of bootstrap self-assembly are formidable (despite the argument that the odds are sequentially reduced by the emergence of "self replication, self assembly, autocatalysis, and the emergence of cell membranes."

Thus the odds against a successful Abiogenesis event are formidable. For the emergence of the first independent free living bacterial-like cell using a minimal number of essential 256 protein-coding genes (Mushegian and Koonin, 1996), we can expect one successful abiogenic trial in $10^{5,120}$ trials (Hoyle and Wickramasinghe, 1999a) an improbable event anywhere in the currently known universe, as this number far exceeds by many orders of magnitude the known atomic and molecular resources of the observable universe (below). It is thus baffling to continue with the insistence that this event took place in the infinitesimal locales that could ever have become available on a primitive Earth. If we invoke an intermediary RNA world hypothesis as a way of reducing the odds, then the advocation of a successful "first RNA self-replicator" is also highly improbable at 4^{100} (McFadden, 2016). McFadden is an expert and concedes the improbabilities as advanced by Hoyle and Wickramasinghe based on the "Koonin" number of minimal essential genes. Thus he considers that 4^{100} is an impossible number. He tries to reduce the odds by his Quantum computing Life Search model, but he compounds the problem (in our view) by further assuming highly improbable intermediate steps. The invocation of improbable intermediate steps is a common feature of all experimental modelling of Abiogenesis.

The enormity of these super-astronomical numbers we consider is not often fully appreciated (Hoyle and Wickramasinghe, 1999b). They can be made somewhat clearer by reference to other large familiar numbers such as the number electrons, protons, and neutrons in the known Universe, at 10^{80} to 10^{90}. The magnitude of these truly vast improbability factors against abiogenesis is such that their full impact is not being fully appreciated by the mainstream scientific community. To repeat ourselves, the figure of $10^{5,120}$ for a minimal number of trials far exceeds by many orders of magnitude the known molecular as well as probabilistic resources of the observable universe.

So this is our pragmatic and philosophical position, much like the pragmatic Copenhagen interpretation in Quantum Mechanics. Yet we realise that it leads to the following, and to many, unpalatable conclusions: *Abiogenesis is unlikely anywhere in the known Universe but would be possible in an "Infinite" Universe or one approaching infinite size where "Big Bangs" need to be considered as local space-time expansion-contraction phenomena* (which we termed "rolling Big Bangs", in Appendix A in Steele et al. (2018). Indeed a powerful *raison d'etre* for our continuing insistence to present an alternative cosmological/panspermic viewpoint is that every avenue of research in laboratory simulations of localised abiogenesis have led thus far to an impasse.

Craig Venter's recent success in transplanting a synthetically manipulated genome in an existing bacterial cell has been hailed by some as a significant step forward in the quest to create artificial life *de novo* (Gibson et al., 2010). This claim, however, is in our view seriously flawed because what was achieved, using the entire

biochemical machinery of a living cell, was to modify or engineer an *existing* genome in a fully functioning living cell. Manifestly this is a far cry from synthesising life. A digitally modified DNA sequence alone is a world apart from generating a living bacterium.

To move forward scientifically we suggest we adapt and embrace a realistic and pragmatic position in the scientific search for extraterrestrial life. We show below that what is knowable can be gleaned from the evidence already available from Earth-based observation and experiment, as well as careful observation and experiment of relevant astrophysical/biophysical phenomena in our near-Earth neighbourhood (as discussed in Steele et al., 2018, 2019, and see the data of Allen and DT Wickramasinghe, 1981, DT Wickramasinghe and Allen, 1983, 1986, NC Wickramasinghe Hoyle, 1998, Wainwright et al., 2015, Grebennikova et al., 2018, Wickramasinghe et al., 2018b, Shatilovich et al., 2018).

We expand on the implications in Sections 5 and 6 in relation to the spread of pre-existing living systems throughout the cosmos via rapid and directional Lamarckian inheritance.

5. Lamarck and Panspermia

5.1. Panspermia provides the raison d'etre for Lamarckian Inheritance

Here we strengthen the association between Lamarck and Panspermia that we began to assert a few years ago. To us it is plausible to consider a strong conceptual link between rapid Lamarckian-based evolutionary processes dependent on reverse transcription-coupled mechanisms among others (Wickramasinghe and Steele, 2016) and the effective cosmic spread of living systems via Panspermia. Thus our position is embodied in the answer to the following key question:

"Why, in contrast to the erroneous fundamental assumptions of neo-Darwinism, should there be widespread evidence for the existence on Earth for environmentally-driven (non-random, directional) Lamarckian modes of inheritance in all the kingdoms of life?"

Indeed one main purpose in writing this review is to be able to conclude that H–W Panspermia provides the *raison d'etre* for the existence of Lamarckian Inheritance *per se*; a conclusion quite apart from any controversial engagement with the limitations of neo-Darwinism itself. Yet we also agree with the reviewer who made the following important points:

"..In the manuscript, the rapid adaptation processes that are inherent in the Lamarckian view of evolution (Section 2, 3) are the sole conceptual links with Panspermia (Section 5 of the manuscript). The authors provide no additional evidence to strengthen this correlation. This is a critical aspect that requires a more stringent discussion and conceptual justification."

Our re-joiner to this type of criticism is this – we are advancing a conceptual position based on the critical review of the extant evidence from the Lamarckian Evolution and Panspermia scientific fields. The new synthesis thus provides the basis for research programs in space research. Our conceptual position advances a hypothesized causal link between "Lamarck" and "Panspermia" which can advance knowledge in a positive conceptual way, greater than either one alone. As we discuss below, this allows rational evaluation of data and speculations of outcomes from current research programs for the search for extraterrestrial life in the near-Earth neighbourhood. e.g. orbiting biological laboratories on the ISS, or other similar platforms, to detect potential space-derived pathogens, incoming eukaryotic microorganisms, bacteria and viruses (a research program that can be considered part of the "Hoyle Shield", Smith, 2013). .

Further to this, it allows us to understand why adaptive evolution strategies *always involve* hypermutation and clonal diversification (Rosenberg, 2001; Matic, 2019), very much like the antigen-driven somatic hypermutation process in vertebrate immune responses (Steele, 2016a, 2017). We expect this "survival" strategy to be implemented by all surviving incoming living systems from space – so the genetic signature of a surviving population of progeny organisms (after an in-fall) will *always be one of hypermutation and adaptive diversity.* This is an important insight that can be applied to the epidemiological and genetic analyses of all incoming (read "rapidly emerging") diseases from space (Hoyle and Wickramasinghe, 1979). And it is an insight that supports our conclusion that Panspermia provides the *raison d'etre* for Lamarckian evolution which is independent of any other criticism of traditional neo-Darwinian theory.

We also try here to make quantitative estimates and predictions, and discuss how living systems may survive in long term space journeys. Thus on the basis of available evidence *Archaea* enmeshed and protected from lethal radiation in salt crystals may survive space conditions and be revived after at least 100 million years (Vreeland et al., 2007). The revival of a spore-forming bacterium *Virgibacillus sp* from brine inclusions in halite crystals has been discovered after 250 million years during which time exposure to the Earth's natural radioactivity may have delivered radiation doses exceeding those encountered in the typical transit time between two exoplanetary systems in space (Satterfield et al., 2005). Perhaps such long-term survivability of bacteria, their spores and archaea is not surprising. But what about more complex multicellular animals? For example, a viable, or cryo-preserved, complex multicellular living system (fertilized egg or plant seed) travelling through space buried deep within an icy bolide or large meteorite could be transferred to another habitable planet and will need to rapidly adapt and proliferate on a landing and thawing in a new cosmic niche. Within more finely dispersed ejecta arising from an impact of an asteroid on an inhabited planet, DNA from locally evolved life could similarly be transferred to other distant habitable planets. Lamarckian mechanisms of environmentally-driven inherited rapid adaptation discussed above would come to the fore in such situations and supersede the infinitesimally slow (blind and random) genetic processes that are expected under the traditional neo-Darwinian evolutionary paradigm.

5.2. Growing astronomical evidence from interstellar dust and comets

With the advent of infrared and ultraviolet astronomy through the 1970's the evidence for organic molecules existing on a vast galactic scale became incontrovertible (e.g. Hoyle and Wickramasinghe, 2000). There is no easy way by which one could argue that the discovery of vast quantities of complex organic molecules in the universe could be unconnected with life. As in the case of the Earth the overwhelming bulk ($\gg 99.99 \ldots \%$) of organic molecules present on a cosmic scale could most plausibly have a biological connotation. Although a trend emerged to assert without proof that pre-biotic chemistry or even pre-biotic chemical evolution was taking place on an astronomical/cosmological scale, the only correct line of argument in our view is to accept that biology is a galactic, even cosmological, process (see references in Wickramasinghe, 2015a; b, 2018). Biological genetic transfers were clearly taking place over astronomical distance scales. Thus *de novo* origination of improbable events for life (Abiogenesis) on the Earth or on other galactic habitats becomes unnecessary. Panspermia, modulated and augmented by Lamarckian inheritance processes now becomes an inescapable cosmic imperative.

The current biophysical and astrophysical evidence strongly suggests that the dust grains in the interstellar medium have an

infrared (IR) absorption spectrum typical of desiccated (freeze-dried) *E. coli* bacteria (secured in the laboratory by PhD student Shirwan Al-Mufti). These data, following age-old standard procedures in Astronomy, were predicted by Hoyle and Wickramasinghe *in advance* of the interstellar dust observations by DT Wickramasinghe and DA Allen, is shown in Fig. 5 (from Steele et al., 2018 Fig. 1 insert). This figure shows the normalised IR extinction (absorption) flux for two independent data sets. The IR absorption spectrum in the wavelength range 2.9–4.0 (μm) for desiccated (freeze dried) *E. coli* bacterial cells (solid line). This is an intricate and complex IR absorption spectrum of living, albeit dried and dormant, living cells. The observational data points were secured at each wavelength indicated for IR electromagnetic radiation emitted 23,000 light years away near the centre of the Milky Way. As this IR light traverses through clouds of the dust grains it is absorbed in a similar fashion to the IR absorption by dry *E. coli* cells in the laboratory experiment on Earth.

The data shown in Fig. 5, was confirmed independently by the team of Okuda et al. (1990) (and see Fig. 4.3b page 43 in Hoyle and Wickramasinghe, 1993). The Pearson correlation of this paired comparison data gives r as 0.9324 for N = 77 pairs. For Okuda et al. (1990) the r value is 0.9275 for N = 35 pairs. The P values for both are $<10^{-9}$. That is, we would expect to see such an exact spectral match by chance alone in more than one billion similar trials (DT Wickramasinghe, G Briggs, NC Wickramasinghe, EJ Steele unpublished calculations).

The simplest option is to concede that the dust grains in the interstellar medium have infrared absorption properties over the entire continuum from 2.8 to 4.0 μm that are identical to desiccated bacterial cells. After 1983 many other spectral features of interstellar dust over other wavebands have also found ready explanations in terms of dust particles of biological origin. We note in particular the IR absorption spectral matches of larger eukaryotic cells such as diatoms (algae) for the 8–13 μm infrared range (e.g. Hoyle et al., 1982; Hoover et al., 1986; Majeed et al., 1988, and see Wickramasinghe and Hoyle, 1998).

To the best of our knowledge no artificial modelling of compound organic mixtures will produce such invariant and exact matches to astronomical data with any reasonable set of assumptions. It is difficult therefore to provide an interpretation for these data that avoids Panspermia.

The idea of biology connected with comets also moved swiftly from speculation to serious science following the last perihelion passage of Comet P/Halley in 1986. The first investigation of a comet in the Space Age (ESA's Giotto mission) thus marked a turning point in the history of cometary science. A dark organic comet surface (darker than the darkest coal) was vindicated by the Giotto photometry. More importantly, in our view, D.T. Wickramasinghe and D.A. Allen obtained the first 2–4 μm spectrum of the dust from an outburst of the comet on 31st March 1986 (D.T. Wickramasinghe and Allen, 1986), Fig. 6. This spectrum showed unequivocal evidence of C–H rotational/vibrational stretching indicating complex aromatic/aliphatic hydrocarbon structures, which moreover was consistent with a calculated spectrum for bacterial dust. Similar data have been published since by others (e.g. Capaccione et al., 2015).

Another significant correspondence with a putative biology emerged in the *Stardust Mission* which captured high speed cometary dust in blocks of aerogel that were later brought back to laboratories on the Earth. Amongst the minute fraction of surviving molecular residues found was the most common of amino acids Glycine together with a complex mixture of hydrocarbons (Elsila et al., 2009).

The most recent Rosetta Mission to comet 67P/C-G yielded data that satisfy consistency checks for biology. Fig. 7 shows a close consistency between the surface properties of the comet and the spectrum of a desiccated bacterial sample.

The presence of complex organic molecules including the building blocks of life in comets is amply confirmed, suggesting fully-fledged microbial life in comets, or the chemical components of life (Altwegg et al., 2016) that through coincidence match exactly the spectra of bacteria. The latter more "conservative" view is that such molecules could be formed by ion-molecule reactions including surface chemistry on the surfaces of pre-solar or interstellar grains.

Biological catalytic transformations are of course the most efficient processes by which simple organic and inorganic molecules can be turned into complex biochemistry of the type seen in astrophysical phenomena (Steele et al., 2019). Once biology gets started the conversion of non-biological molecules to biomolecules (Figs. 5–7) proceeds with an unparalleled efficiency as is indeed evident from our terrestrial experience. Over 99.9 percent of all the organic material found on Earth is biologically produced. If biology is permitted to exist and spread on a galactic/intergalactic scale a

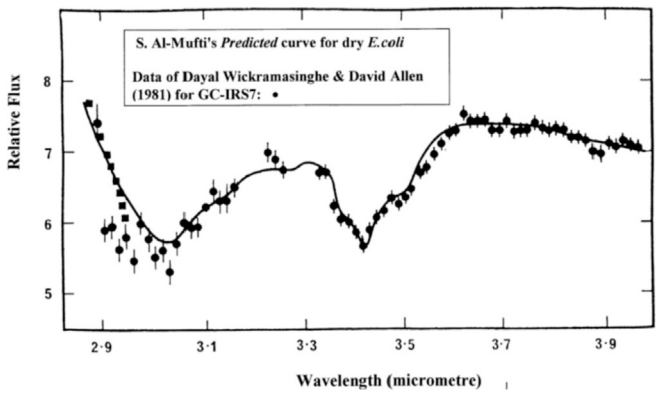

Fig. 5. Comparison of the infrared flux (arbitrary units) from the astronomical source GC-IRS7 near the galactic centre, with the curve predicted for freeze dried *E. coli* cells (Allen D.A. and D T Wickramasinghe, 1981). Also see Wickramasinghe, D.T. and Allen, D.A. (1983). This is a blow up of the inset in Fig. 1 Steele et al., 2018.

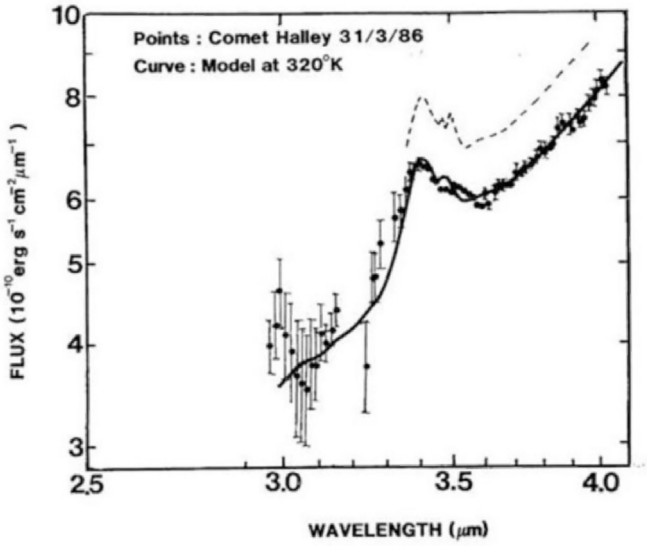

Fig. 6. Comparison of the infrared flux (arbitrary units) from the astronomical source GC-IRS7 near the galactic centre, with the curve predicted for freeze dried *E. coli* cells (Allen D.A. and D T Wickramasinghe 1981). Also see Wickramasinghe, D.T., Allen, D.A., 1983. This is a blow up of the inset in Fig. 1 Steele et al., 2018.

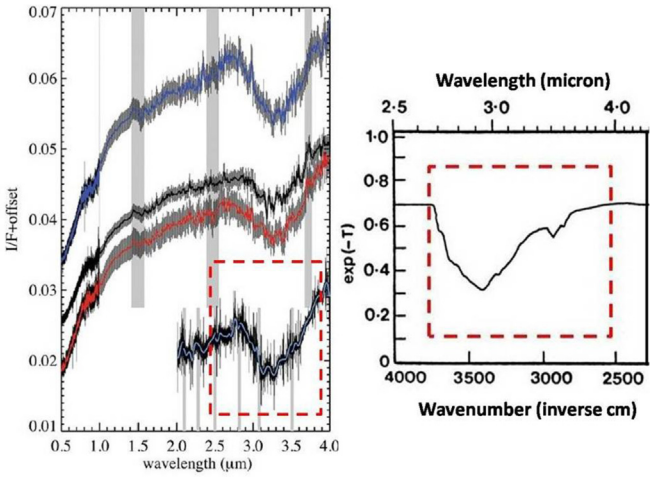

Fig. 7. The surface reflectivity spectra of comet 67P/C-G (left panel, Capaccione et al., 2015; taken at different times) compared with the transmittance spectrum of desiccated E-coli (cf. Figs. 5 and 6) over approximately the same wavelength range for comparison. Also from Wickramasinghe et al., 2018a,b).

similar outcome is to be expected astronomically, consistent with the data in Figs. 5–7. It is useful to point out that the IR and other specific spectral signatures of complex and specific biochemical molecules in the interstellar medium - commonly assumed to be a rich supply of building blocks for cosmic Abiogenesis events - have a simple explanation: they are the molecular detritus of dead, broken and dying cells released into the interstellar medium.

5.3. Space survivability of microbiota, and habitable planets

The requirements for an astronomical source of bacteria-like cosmic dust and complex organic molecules is (a) the operation of biological replication in a large class of astronomical bodies, and (b) the assumption that a non-zero fraction of microbiology so generated survives the transit between such astronomical habitats, at any rate between nearest neighbours. Both these pre-conditions have been established over the past several decades. Survival properties of bacteria under the most hostile space conditions have been amply demonstrated both in the laboratory and by means of direct space experiments. Furthermore, over a hundred billion icy comets that are known to surround our planetary system (the Oort cloud of comets) have been convincingly shown to be likely habitats for microbiology – microbial viability and replication being accomplished within their radioactively heated interiors (Wickramasinghe et al., 2012). A fraction of the microbes amplified in comets are returned into interstellar clouds from which new stars, comets and planets can form. The feedback loop of cosmic biology is schematically shown in Fig. 8. In addition to the well-attested survival attributes of bacteria, particularly of extremophiles (to which we refer later), it should be stressed here that only a minuscule survival fraction of interstellar bacteria, $\ll 10^{-20}$ is required for every circuit in this loop for panspermic transfers to the maintained (Hoyle and Wickramasinghe, 2000).

Evidence of bacteria has also been discovered recently in geological sediments (rocks) that formed 4.1–4.3 by ago during the Hadean Epoch at a time when the Earth suffered an episode of heavy bombardment by comets and asteroids (Bell et al., 2015). This new geological evidence also supports the point of view that impacting comets brought living entities to the Earth, and by extension similar impacts on other planetary bodies could establish life elsewhere in the galaxy.

Perhaps most relevant to the ideas of Panspermia and

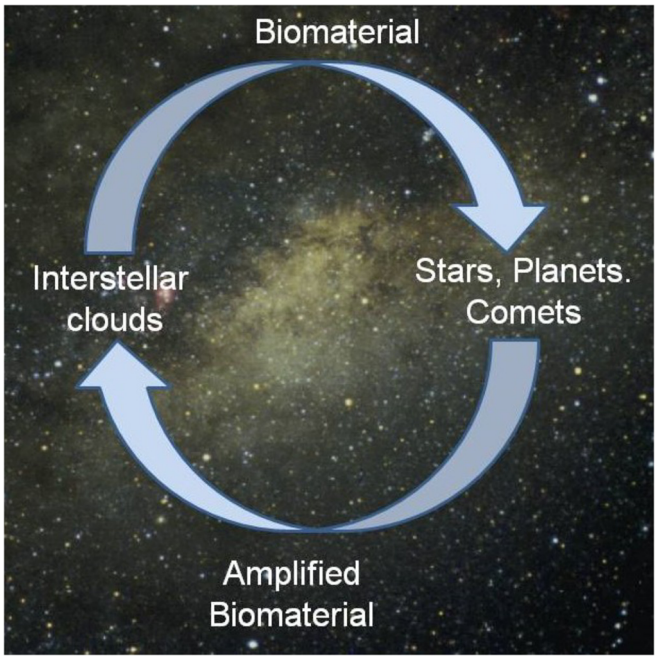

Fig. 8. Amplification cycle of cosmic life. Within our galaxy alone about 100 billion circuits have been completed, one for every sun-like star.

Lamarckian inheritance are the recent discoveries of habitable exoplanets occupying the so-called “Goldilocks zone”. The Orbiting Kepler telescope launched in 2009 has to date reported the discovery of over 3000 exoplanets in a small sampling volume of the galaxy. Extrapolating from these discoveries the current estimate of the total number of habitable planets in the galaxy exceeds 100 billion – approximately one habitable planet for every sun-like star (Kopparapu, 2013). The estimated mean separation between such planets can be estimated to be a few light years. In view of all such recent discoveries it will be foolish to maintain a pre-Copernican idea that biology is necessarily confined to our planet, and more importantly that it originated here against manifestly impossible odds.

5.4. Transfer of evolved living systems across the galaxy

Whilst amplification of microorganisms within primordial comets could supply a steady source of primitive life (archaea, bacteria, unicellular eukaryotes and their viruses) to interstellar clouds and thence to new planetary systems via comets, the genetic products of evolved life could also be disseminated on a galaxy-wide scale. Transportation of entire ecologies of evolved aquatic life on much rarer occasions could also be possible if life-laden watery worlds (or large frozen fragments thereof) could occasionally collide with new habitats in the “Goldilocks zones” of stellar systems. It is tempting to speculate that the Cambrian explosion of “adaptive radiation” on a grand scale was indeed the product of such a cosmic seeding of “life-laden watery worlds (or large frozen planetoid fragments thereof)” as discussed (Steele et al., 2018).

Our present-day solar system with its extended halo of ~100 billion comets (the Oort Cloud) moves around the centre of the galaxy with a period of 240My. Every 40 million years, on the average, this comet cloud becomes perturbed due to the close passage of an interstellar molecular cloud (e.g. the Orion Nebula). Gravitational interaction then leads to hundreds of comets from the Oort Cloud being injected into the inner planetary system, some to collide with the Earth. Such collisions can not only cause

extinctions of species (as one impact surely did 65 million years ago, killing the dinosaurs), but they could also result in the expulsion of surface material back into space. A fraction of the Earth-debris so expelled survives shock-heating and could be laden with viable microbial ecologies of all types as well as genes and viruses of evolved life. Such life-bearing material could reach newly forming planetary systems in the passing molecular cloud within a few hundred million years of the ejection event. A fledgling planetary system thus comes to be infected with terrestrial microbes - terrestrial genes that can contribute, via horizontal gene transfer, to an ongoing process of local biological evolution. If every life-bearing planet transfers genes (bacteria, viruses, somatic cells and in rare instances deep frozen seeds and even fertilized eggs) in this way to more than one other planetary system, life throughout the galaxy on this picture will inevitably constitute a single connected biosphere.

5.5. Some quantitative estimates - cosmic distribution and numbers of living systems

There are thus several key factors to consider in the largely plausible yet speculative scenarios below on the Panspermic dispersal of living systems. All are based on known hard data (Hoyle and Wickramasinghe, 1979; 1981; Wickramasinghe, 2015a,b) that have recently been reviewed (Wickramasinghe, 2018; Steele et al., 2018, 2019).

5.5.1. Space Hardiness

The “space hardy” features of bacteria are legendary, displaying un-Earthly properties unlikely to be selected for survival on Earth but certainly in varied space environments (Hoyle and Wickramasinghe, 1993). A typical example illustrating such resistance properties to radiation, cold, dehydration, vacuum, acid is the extremophile *Deinococcus radiodurans*. Thus bacteria and their spores, other micro-organisms and eukaryotic cells, and some exemplar microscopic animals (Tardigrades) are by now well recognized for these space survival properties. For example the space survival of algae cultures outside the International Space Station (Leya et al., 2017), of plant seeds (Tepfer and Leach, 2017) as well as species of bacteria detected by their DNA sequences in the cosmic dust on the external surface of the ISS (Grebennikova et al., 2018). This is quite apart from the >100 million year survival times of bacteria and archaea in terrestrial salt crystals that we have already discussed (Vreeland et al., 2007; Satterfield et al., 2005).

5.5.2. Effective seeding population sizes

The population size, *N*, of a living system within an impacting bolide that has been ejected from another inhabited planetary or cometary body must be sufficiently large to permit viable transfer. The transfer could take the form of viral particles, bacteria, spores and plant seeds. In some instances even fertilized eggs of insects and higher animals cannot be excluded. When *N* is very large $\geq 10^6$ it is obvious that a 90% or 99% kill on impact still leaves a significant number of survivors to rapidly proliferate in a Lamarckian manner in a congenial niche. This obviously automatically applies to impacting populations of viruses, bacteria, many microorganisms and their spores, large populations of plant seeds, and even the highly contentious suggestion (Steele et al., 2018, 2019) of cryopreserved fertilized Cephalopod eggs which could arrive on impact given large $N \geq 10^6$ (below).

5.5.3. Protection radiation damage

Encasement in a protective matrix or deep burial is important both during space travel and on impact. While many organisms display “space hardy” features, long term survival during space travel (100 million to billions of years) requires a living system to be buried or cryopreserved *within* cometary or planetoid bodies. We have argued elsewhere that such vehicles as comets or larger planetoids may act as both protective incubators (active amplifiers) of living systems and post impact allow significant percentages to survive and proliferate.

5.5.4. Cryopreservation

In this scenario cryopreservation is a key consideration, particularly for mature complex multicellular differentiated organisms. We note the recent observations on the viable recovery of nematode worms from 42,000 year old Late Pleistocene Siberian permafrost (Shatilovich et al., 2018). Such findings need to be replicated at other locations and with other species. The data we have currently available leads to the obvious question: if 42,000 years, why not a billion years of cryopreservation? The discovery relevant to our argument is that soma-to-germline transfer of genetic information (penetration of the *Weisman Barrier*) has been recently demonstrated in *C. elegans*, a nematode (regulatory double stranded RNA triggering RNA interference phenomena Devanapally et al., 2015). This result is of potential importance to the Lamarckian adaptability of thawed nematodes adapting after arrival in a new cosmic niche.

All these discoveries have been of crucial importance for the Hoyle-Wickramasinghe Panspermia paradigm which can include the transportation of cryopreserved plant seeds and animal embryos within protective matrices (e.g. comets, moons and planets) or minimally their genes encoded in viruses via undisturbed space travel extending to hundreds of millions if not billions of years is not just possible but inevitable. Indeed we would not find it beyond the realm of possibility that populations of mature microscopic life forms for example Tardigrades and nematode spp. have a wide cosmic prevalence and can on occasion be transferred between suitable cosmic habitats. This would involve a process that merits being called cosmic Lamarckian evolution. We speculated on such a scenario for the “sudden” emergence of Cephalopods on Earth 275 mya viz. cryopreserved Octopus eggs (Steele et al., 2018). The same scenario could apply to a whole range of populations of fertilized insect eggs of many species as well as plant seeds.

5.5.5. Exoplanets

The number of exoplanetary systems possessing orbiting ecosystems within habitable zones (comets, moons, planets), with available water, surface or subterranean, will determine the total tally of potential cosmic habitats that can be infected. The current estimates of exo-planets in the habitable zones is $> 10^{10}$ (Kopparapu, 2013) and possibly much larger if we consider all types of extreme habits, say, $> 10^{11}$. The range of the types of terrestrial microorganisms existing in the “deep hot biosphere” as first described by Tommy Gold (1992, 1999) is an indication of the extraordinary range of extreme habitats that can support life. Indeed in our Solar System alone there may be an unknown number of extreme habitats in the form of moons and planetoids on which large populations of sub-surface living systems could exist (moons such as Europa, Enceladus, are obvious examples).

We are thus led from many different directions to admit a convergence to the concept of a genuine “Cosmic Gene Pool” based on common DNA/RNA/Protein biochemistry (Wickramasinghe et al., 2018a). Indeed the vast variety of living species on Earth would be a minuscule subset, albeit a significant sub-set, of an almost infinite pool.

In terms of magnitudes of incidence of living systems throughout the Cosmos we might be tempted to rank organisms (see Table 2) as follows based on a known “Earth equivalent” multiplied by 10^{22} as an educated guess of the number of Earth-like

habitats in the universe (100 billion in every galaxy and 100 billion galaxies).

Table 2
Cosmic distribution and numbers of living systems.

• Viruses – terrestrial number 10^{31}	10^{53}
• Bacteria/Archaea - terrestrial number $\geq 10^{30}$	10^{52}
• Single cell eukaryotes - terrestrial number 10^{20}-10^{30}	10^{32}–10^{52}
• Complex Metazoans - terrestrial number $\geq 10^{20}$	10^{42}
• Higher plants, terrestrial number $\geq 10^{7}$ species	10^{29}
• Higher animals, terrestrial number $\geq 10^{7}$ species	10^{29}

Thus the *potential* cumulative incidence of complex orbiting ecosystems (on planets, moons, comets) around each observable star in our galaxy alone begins to approach super-astronomical magnitudes when these are multiplied by the estimated number of stars in the observable Universe ~ 10^{22}. We should stress at this point that all the numbers listed above are highly conservative *underestimates* according to current thinking in cosmology. Even within the framework of the currently accepted Big Bang model of the universe (with early inflation), the observable universe would only be a minute fraction of what would be a very much larger, initially causally connected, region that *inflated* and would thus be out there, out of contact, but within which Lamarckian transfers would occur.

5.6. Evidence from the near-earth environment

With some 50–100 tonnes of cometary debris entering the Earth's atmosphere on a daily basis the collection and testing of this material for signs of life should in principle at least be straightforward. Some such projects have been carried out from 2001 onwards. The first serious project was carried out with the support of the Indian Space Research Organisation (ISRO) in partnership with a group of scientists in the UK including one of us (NCW). Samples of stratospheric aerosols collected using balloon-borne cryosamplers were investigated independently in the UK and India and revealed evidence of microbial life (Harris et al., 2002). A particularly interesting component of the collected samples was in the form of 10 μm clumps that were identified by SEM and fluorescence tests as being viable but not culturable microorganisms. Fig. 9 shows putative biological entities discovered in stratospheric samples by electron microscopy; and the left panel of Fig. 9 shows a clump of putative cocci and a bacillus. The right panel of Fig. 9 shows evidence of viable microorganisms which did not prove to be culturable.

Because such large aggregates are virtually impossible to loft to 41 km a *prima facie* case for their extraterrestrial cometary origin has been made. A similar experiment to that conducted in 2001 was repeated by ISRO in 2009 (Shivaji et al., 2009) and 3 new microorganisms were discovered, including one named in honour of Fred Hoyle as *Janibacter hoylei.*

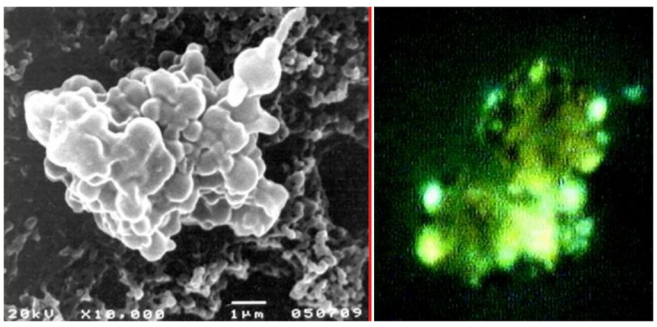

Fig. 9. Left: a clump of carbonacesous particles resembling cocci and a bacillus Right: A clump of viable but non-culturable bacteria fluorescing under the application of a carbocyanine dye which tests for electric potential across cell walls. Harris et al., 2002.

The genetic similarities of the new stratospheric bacteria to existing terrestrial genera have been cited by some as an argument to discount their possible space origin. However, in our view, terrestrial bacterial genera all have a space origin, so homologies of the type found are to be expected and do indeed corroborate a space origin of all bacteria on Earth (Hoyle and Wickramasinghe, 1979; 1981). In order to take the matter further, and hopefully reach a decisive conclusion, further tests of the collected microbial samples would be desirable. One such test involves the deployment of a rather rare laboratory resource – a Nanosims machine. This will determine the isotopic composition of carbon, oxygen and other constituent elements within the individual bacterial cells, and if the composition turns out to be non-terrestrial (Tokoro G, Wickramasinghe NC, Temple R and colleagues, experiments underway).

Experiments can also be conducted on the International Space Station (ISS) to sample the zodiacal cometary dust trails through which the Earth continuously passes in its orbit around the Sun. Such initial experiments are reported (Grebennikova et al., 2018; Wickramasinghe et al., 2018b). Bacteria in the cosmic dust have been detected by standard PCR techniques on the external surface of the ISS. These are ground breaking experiments and contamination has been ruled out. Uplifting of micro-organisms to 360–400 km seem quite improbable on physical grounds (Wickramasinghe and Rycroft, 2018). These data offer the promise that such ISS microbiological phenomena can be confirmed or refuted by independent teams of scientists. We can imagine ISS real-time biological laboratories conducting routine genetic analyses and tissue cultures using the portable Next Generation Sequencing (NGS) machines now available. The range of microbial life, prokaryotic and eukaryotic, in the near Earth cosmic environment can become, as discussed already, part of the proposed "Hoyle Shield", predicting potential pandemics from space (Hoyle and Wickramasinghe, 1979; Smith, 2013).

Such studies may allow confirmation that Darwinian-Lamarckian evolution takes place not just within a closed biosphere on Earth but extends over a large and connected volume of the cosmos (Wickramasinghe et al., 2018a).

5.7. Scientific pragmatism: the near earth neighbourhood?

In our view pragmatic research on extraterrestrial life is now required. The research budgets directed to the search for extant and living extra-terrestrial life needs to be far more focused on the near Earth neighbourhood. The experiments are relatively cheap and can be definitive and unequivocal. They offer real-time experimentation in standard biological laboratories. We have discussed some of the promising data emerging and there are more recent findings.

Microorganisms have been detected by Milton Wainwright and colleagues in-falling from space at 41 Km in the Stratosphere (Wainwright et al., 2015). These data were secured in balloon-lofted experiments and conducted to avoid terrestrial contamination. They were set up technically to establish that the microorganisms and other cellular and viral aggregates *were observed following in-fall not by upwelling*. Critics may conclude it is all due to terrestrial contamination, but the data need to be dispassionately evaluated in their own terms. Many of the eukaryotic species detected can be classed as unassigned Acritarch, and appear viable on impact with the collection medium. The data more readily fit with Panspermia theory (Wainwright et al., 2015).

5.8. Cosmic octopus?

We have tried to discuss throughout this article the "Demarcation Data" which allows distinction between conventional terrestrial neo-Darwinism (Section 1) and the Cosmic Lamarckian - Panspermia paradigm. Thus there are a plethora of multifactorial awkward facts and observations, biological and biophysical, which fit neatly into the Hoyle-Wickramasinghe Panspermia paradigm but are often puzzling or inexplicable under a pure neo-Darwinian terrestrial evolution paradigm - anchored to a super-astronomically improbable and unproven Abiogenesis event producing the first cell here on Earth about 4 billion years ago. Most of the relevant problems and contradictions in this viewpoint are covered in our recent papers (Steele et al., 2018, 2019). In the same vein a similar set of awkward facts and observations fall neatly under a Lamarckian world view but not so easily under neo-Darwinism.

Thus we note again the recent observations on the viable recovery of nematodes from 42,000 year old Late Pleistocene Siberian permafrost (Shatilovich et al., 2018). Such findings need to be replicated at other locations and with other species. Nevertheless the implications under the Hoyle-Wickramasinghe paradigm suggest that the transportation of cryopreserved complex mature animals within protective matrices (e.g. comets, moons and planets) or minimally their genes encoded in viruses via undisturbed space travel extending to hundreds of millions if not billions of years is the favoured" cross infection" mode across the Cosmos. This would remain true even if survival probabilities remain minuscule – with massive death rates during catastrophic ejection events (e.g. comet collisions), followed by further attrition upon re-entry onto receiving host planets. The hundreds of billions of habitable planets in our galaxy alone would make exchanges of mature biological entities a virtual certainty – no matter how ridiculous such a proposition might appear at first sight. The situation is similar to the sowing of seeds in the wind – most of them are lost, but so very many are the seeds that some among them are destined to survive. It is in a similar way that mature animals can albeit exceedingly rarely land, thaw out in a favourable cosmic habitat for growth, and thus undergo further cosmic Lamarckian evolution.

We speculated on precisely such a scenario for the emergence of Cephalopods on Earth 275 mya viz. cryopreserved Octopus eggs (Steele et al., 2018). This possibility has provoked much discussion and some ridicule in our circle of private discussions. However there is no logic whatsoever by which it can be excluded given the current data. The whole point of our discussion was to show a 250 million year gap between nautiloid precursors and squid/octopus. That is the whole point of the discussion in Steele et al., 2018. All the phylogenetic analyses points that out-all experts agree on this gap in the molluscian evolutionary record. But such huge punctuated equilibrium-type gaps permeate the fossil/phylogenetic emergence record, not just the molluscian evolutionary record. That is why Eldridge-Gould is discussed at length – it is a major unexplained conundrum (see Fig. 6 in our paper Steele et al., 2018).

6. Panspermia and Lamarckian inheritance are no longer mere "Hypotheses"

It is reasonable to assert that a scientific theory is a "mature hypothesis" surviving rigorous critical analyses and hard observation and experiment. However, it is still in essence Popperian and thus vulnerable. It can, in principle, be refuted or modified from its original form, as for instance Einstein's modification/generalisation of Newtonian mechanics. On the other hand, a hypothesis is usually the first tentative public utterance of a provisional explanation of a given set of natural phenomena. It will only mature into a "theory" if it survives refutation by severe demarcation tests involving further critical analyses, observation and experiment. By these criteria the modern field of Cosmic Biology/Panspermia, first clearly advanced by Hoyle and Wickramasinghe, can be deemed a mature scientific theory. It provides a coherent explanation for both the origin of life on Earth and its further non-linear progress of terrestrial evolution and adaptation as reviewed recently by Steele et al. (2018).

The H–W thesis has thus survived numerous demarcation tests, and it has offered many predictions that have been subsequently fulfilled and furthermore has strong explanatory and predictive power. For example, a key prediction concerns the distribution and number of living systems in the known Universe. This distribution is dictated *solely by* the "habitability" or otherwise of available viable Cosmic niches (comets, moons, planets - both orbiting or wandering) and the DNA/RNA/Protein paradigm for life will hold across the Cosmos (Wickramasinghe et al., 2018a). This is an important and definite prediction.

H–W Panspermia theory thus brings together a range of multifactorial biological facts and phenomena, at first sight unrelated, providing a coherent explanation for their existence, their biological form and their ongoing evolutionary features (Steele et al., 2018). It therefore provides a general mechanism for the widely accepted evolutionary pattern of "Punctuated Equilibrium" described clearly by Eldredge and Gould (1972), then Gould and Eldredge (1977) but which otherwise remains a semantic description of the known facts. It also predicts and qualifies the 'genetic' boundaries of H–W theory. Thus extraterrestrial life is expected, as just discussed, to possess the same biochemistry, genetic code, the same DNA and RNA as life on Earth. A radically different life form discovered would be significant evidence against a universal Galactic panspermia and the H–W theory would require modification (Wickramasinghe et al., 2018a). Yet Galactic-wide panspermia,as we outline here, is now being widely accepted by the mainstream astronomical community. Thus the Harvard group of Ginsburg et al. (2018) have recently developed a mathematical model of Galactic-wide panspermia in which icy comets or rocky asteroids carrying microbiota could be widely distributed in the galaxy and exchanged between planetary systems. Their calculations lend further support to the H–W model of cosmic biology and our present thesis of Lamarckian transfer in which the galaxy and the wider universe become a single connected biosphere.

We have also discussed above the vast amount of new evidence that has accumulated since the 1970s consistent with Lamarckian Acquired Inheritance phenomena from bacteria through to plants and animals. Indeed the "Hypothesis of Lamarck" has now survived some stringent and severe tests earning recognition as a maturing "Theory" of biological evolution. Our discussion here has focused where possible on the molecular mechanisms which are now much clearer in many cases than they were 40 years ago. And our discussion here has also been on much of the key "Demarcation Evidence" which, as with Cosmic Panspermia, needs to be confronted by the scientific mainstream. Lamarckian inheritance of acquired characteristics, based, at their core, on RNA and reverse transcriptase steps, has successfully run the gauntlet of numerous "Popperian" tests during the past 40 years. In our considered opinion the effective spread of living systems throughout the Cosmos is both by Lamarckian and Darwinian mechanisms - with the emphasis on Lamarckian evolutionary processes as these provide rapid and "directional' adaptations to new Cosmic niches immediately after the organisms have landed.

Authors' Note

In addition to the well attested mechanisms for particle transport discussed it is worth considering other modes assisting the

panspermic dispersal of living systems throughout the Cosmos.

Appendix by Robert Temple: *On the Panspermia of the Ancients, Cosmic Spermata and Speculation on Birkeland Currents and Mechanisms of Space Journeys*

It is a challenging task to write an appendix to the above paper which would meet some of the standards we have set for the wide range of evidence for Lamarckian Panspermia. Although I have some additional scientific observations to make, I will start with an update to the situation regarding the *Prehistory of Panspermia*, which is a scholarly matter relating to early pre-scientific thinking by ancient peoples of panspermic notions.

In 2006 I delivered a paper entitled 'The Prehistory of Panspermia: Astrophysical or Metaphysical?', which was published in 2007 (Temple, 2007). In this paper I surveyed proto-panspermia ideas in a variety of ancient cultures, commencing with the ancient Egyptians. Amongst the ancient Egyptian texts which I discussed were the Pyramid Texts, written in what is known as 'Old Egyptian', and which date from the 5th Dynasty (early 25th century BC to mid 24th century BC) but include much earlier archaic material. During 2018, this paper came to the attention of Professor Joanna Popielska-Grzbowska of the Institute of Mediterranean and Oriental Cultures, Polish Academy of Sciences, in Warsaw. She is an expert in Old Egyptian and she informed me that in her studies of the terminology and concepts embodied in the Pyramid Texts my comments about them had been confirmed. She also said that she had found much more evidence in those texts expressing proto-panspermia ideas. She and I will be producing a joint paper on this subject during 2019, which will considerably enlarge the discussion of the prehistory of Panspermia.

I would like also to mention that since my 2007 paper, I have come to know and appreciate the particular interest of Professor Otto Rössler in the same crucial passage by the ancient Greek philosopher Anaxagoras (510-428 BC) which I had discussed. He and I are in frequent contact and it is interesting that we both found the Anaxagoras passage astonishing, though from two separate, albeit probably compatible, perspectives. Rössler's interest relates to his seminal work in chaos theory (he is for example the discoverer of the Rössler Attractor), and he did not consider this passage from the point of view of Panspermia at all. But as his views on the same passage are so important, I feel that I should mention them and refer readers to the remarkable volume of scientific dialogue with him, 'Chaotic Harmony' (Sanayei and Rössler, 2014), which contains non-mathematical accounts of what he saw in that passage of Anaxagoras. In the meantime Rossler and I have published a joint paper in 2019 entitled 'Early Einstein Completed', concerning the equivalence principle and global-c.

I return now to our present time. There are several aspects of the Panspermia field which in my opinion have scarcely been touched. I shall address these in a succession of headings.

Transport through space of the microbiota

The part of this subject which we understand very well is the dispersal of dust and microbiota into the Earth's atmosphere and its slow drifting down to the surface, namely the 50–100 tonnes per day of cosmic dust and debris which reaches the surface of our planet daily, which is referred to in the main text above. We can also understand the transport of much of this material by comets and its dispersal from the comet tails. There is nothing about either of these processes which is really unusual or indeed unexpected, once they have been suggested and brought to our attention, as they first were by Fred Hoyle and Chandra Wickramasinghe in numerous publications (which has founded the Science of Panspermia as we now understand it).

The long life of the microbiota, or should we say cosmic spermata (to use the ancient Greek word), is a more than plausible concept, as witness the main text above. Thus we know from available evidence that it is possible for cryopreserved cosmic spermata to survive interplanetary, interstellar, and even inter-Galactic distances of travel and still be viable entities.

But what is lacking is a full understanding of all the available means of transport of spermata in those regions where there are no comets, or where radiation pressure is somehow ineffective. What then? How do they get around? So far the thinking seems to be of a slow drifting through space and a tediously ponderous passive dispersal, mostly by pressure from light rays from stars (radiation pressure).

My idea is 'a better design', and provides for rapid transport through space of vast quantities of cosmic spermata, so that the slow part of the transport process would not be across the vast interstellar and inter-Galactic distances, but would be when the particles of dust and biota reach a more cluttered region such as our solar system, where the entire transportation process would significantly *slow down*, like a plane coming in for a landing. Charged dust entering a protoplanetary or planetary environment with denser plasmas and higher values of magnetic field might be magnetically braked with charge repulsion rather than collisions playing a dominant role.

The hypothesis here is that the means of transporting the cosmic spermata could be through the moving of sheathed and internally structured plasmoids within gigantic Birkeland Currents on a cosmic scale (Peratt, 1992). They would be hurtled through vast distances at nearly relativistic speeds between star systems and even between galaxies. These Birkeland Currents would be super-highways full not only of the charged particles which we know them to contain but of opportunistic cosmic spermata hitching a ride. And lest we think this unlikely, we only need to understand enough about plasma in space to realise that it is always full of dust particles, not only grains, and frankly plasma is not particularly bothered about what kind of dust, since essentially 'any old dust will do, and if some of it is "alive", well what the hell, jump in for the ride'. And the other thing is that all dust particles are *charged*, which thus most likely helps lock them in the cosmic streams of the Currents.

Chandra Wickramasinghe and I are currently exploring the details of how this process works, and the evidence of the Birkeland Currents in space. It provides an additional mechanism for meaningful and effective cosmic transport of the cosmic spermata anywhere and everywhere in the Universe.

Dust clouds

We all know that the Universe is full of gigantic dust clouds, some 100 light years or more across - so full of them in fact that it might be asked 'Does God smoke?' and is the Universe really a smoke-filled room? There is much more to be said about cosmic dust clouds and their relationship to Panspermia. Chandra Wickramasinghe and I will also be revisiting this question in a future more detailed investigation (Temple and Wickramasinghe, 2019). A key factor in what we have to relate is that *all cosmic dust clouds are charged.* The charges can be positive or negative, and even if an entire cloud appears to have zero net charge in total, the internal structures within the cloud can be so complicated that isolated and ensheathed regions within the cloud can have opposite charges which are isolated, and a vast variety of different regions containing different things. Within the clouds, as within the Birkeland Currents, pockets of living things can be isolated from barren regions. The key to understanding this is to understand complex dusty

plasmas. We should try now to think of cosmic dust clouds not as just a lot of stuff floating around at random and see them for what they possibly are, highly structured and immensely complex genuine entities having a biological provenance. This will all be further explained in a forthcoming paper.

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