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# Cause of Cambrian Explosion - Terrestrial or Cosmic?

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## ABSTRACT

We review the salient evidence consistent with or predicted by the Hoyle-Wickramasinghe (H-W) thesis of Cometary (Cosmic) Biology. Much of this physical and biological evidence is multifactorial. One particular focus are the recent studies which date the emergence of the complex retroviruses of vertebrate lines at or just before the Cambrian Explosion of ~500 Ma. Such viruses are known to be plausibly associated with major evolutionary genomic processes. We believe this coincidence is not fortuitous but is consistent with a key prediction of H-W theory whereby major extinction-diversification evolutionary boundaries coincide with virus-bearing cometary-bolide bombardment events. A second focus is the remarkable evolution of intelligent complexity (Cephalopods) culminating in the emergence of the Octopus. A third focus concerns the micro-organism fossil evidence contained within meteorites as well as the detection in the upper atmosphere of apparent incoming life-bearing particles from space. In our view the totality of the multifactorial data and critical analyses assembled by Fred Hoyle, Chandra Wickramasinghe and their many colleagues since the 1960s leads to a very plausible conclusion – life

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may have been seeded here on Earth by life-bearing comets as soon as conditions on Earth allowed it to flourish (about or just before 4.1 Billion years ago); and living organisms such as space-resistant and space-hardy bacteria, viruses, more complex eukaryotic cells, fertilised ova and seeds have been continuously delivered ever since 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. © 2018 Published by Elsevier Ltd.

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" The historian of science may be tempted to claim that when paradigms change, the world itself changes with them." *The Structure of Scientific Revolutions* (Thomas S Kuhn, 1962, 2nd ed. 1970)

When presented with the uncanny survival attributes of Tardigrades, a friend exclaimed: "**How on earth did they evolve?**" (*Anon.* 2017)

" The idea that in the whole universe life is unique to the Earth is essentially pre-Copernican. Experience has now repeatedly taught us that this type of thinking is very likely wrong. Why should our own infinitesimal niche in the universe be unique? Just as no one country has been the centre of the Earth, so the Earth is not the centre of the universe." *Life Cloud* (Fred Hoyle and N Chandra Wickramasinghe, 1978 J.M. Dent & Sons, London, p.132).

### 1. Purpose of article

This review article is intended to represent, in the main, the collective knowledge and wisdom of over 30 scientists and scholars across many disciplines of the Physical and Biological sciences. We review much of the key experimental and observational data gathered over the past 60 years consistent with or predicted by the Hoyle-Wickramasinghe (H-W) thesis of Cometary (Cosmic) Biology.

We are acutely aware that mainstream thinking on the origin and further evolution of life on Earth is anchored firmly in the "Terrestrial" paradigm. Our aim here is to facilitate further discussion in the biophysical, biomedical and evolutionary science communities to the quite different H-W "Cosmic" origins viewpoint which better handles, in our opinion, a wider range of physical, astrophysical, biological and biophysical facts often quite inexplicable, if not contradictory, under the dominant Terrestrial neo-Darwinian paradigm. Further, if some readers are hoping to read a disquisition based on Population Genetics-type analyses, as one reviewer has put it, " ... analyses of evolutionary rates, examples of appearance of new genes with no homology to old ones, etc" they will mostly be disappointed; although some genetic features from recent data in the Octopus and other Cephalopods provide challenging examples to conventional evolutionary thinking. But that is not the main thrust of this review.

The general, and admittedly unusual, scientific writing style is to ensure clear plain-English communications across many scientific disciplines. However of iconic specific interest, we discuss the recent phylogenetic data which date the emergence of the complex retroviruses of vertebrate lines at or just before the Cambrian Explosion of ~500 Ma (the widely agreed epochal event in the evolutionary history of multicellular life on Earth). These types of reverse transcribing and genome integrating viruses are speculated to be plausibly associated with major evolutionary genomic processes. We believe this coincidence with the Cambrian Explosion

may not be fortuitous but consistent with a key prediction of H-W theory whereby major extinction-diversification evolutionary boundaries coincide with cometary-bolide bombardment events delivering hypothesized viruses, microorganism, and more complex eukaryotic systems to Earth during the past 4.5 Billion years of Earth history. Not all of such incoming living systems would necessarily take hold, and substantial terrestrial based evolutionary processes (whatever the actual molecular genetic mechanisms) are also expected to be on going.

In our considered view the totality of the multifactorial data and critical analyses assembled by Fred Hoyle, Chandra Wickramasinghe and their many colleagues leads to the bare minimum yet plausible scientific conclusion – that life was seeded here on Earth by life-bearing comets as soon as conditions on Earth allowed it to flourish (at or just before 4.1 Billion years ago); and living organisms such as space-resistant and space-hardy bacteria, viruses, more complex eukaryotic cells and organisms (e.g. Tardigrades), perhaps even fertilised ova and plant seeds, may have been continuously delivered ever since to Earth helping to drive further the progress of terrestrial biological evolution. This process, since the time of Lord Kelvin (1871) and Svante Arrhenius (1908) has the scientific name "Panspermia".

Perhaps the most important astronomical data relevant to the theory of cosmic life to emerge in the past decade are the detections of habitable exoplanets – planets outside of our solar system. The total estimated tally of such Earth-like planets in our Milky Way galaxy alone now stands at 100 billion, and with 100 billion or so galaxies in the observable universe the grand total stands at  $10^{22}$ . Because exchanges of possibly fecund material between neighbouring habitats is more than likely, panspermia and the theory of cosmic life could be argued to become inevitable facts.

The paradigm shift to this critical viewpoint, whilst underway, is by no means complete - yet we believe the historical moment has now arrived for a comprehensive and considered cross-disciplinary review of much of the relevant evidence, which this paper endeavours to represent. There are many and far reaching consequences of this new scientific awareness which we believe would be the privilege of future generations to explore.

#### 2. Introductory remarks

The Aristotlean paradigm of the spontaneous generation of life the idea that the simplest life-forms emerged spontaneously on Earth (fireflies from mixtures of warm earth and morning dew) has survived in one form or other for over 2000 years. It has withstood contradictory evidence on several occasions during this time. Pasteur's 1862 experiments on the fermentation of wine and the souring of milk led him to enunciate the dictum "Omne vivum ex vivo" or "All life comes from life". The implication of the Pasteur experiment was that every generation of every microbe, plant or animal was preceded by a generation of the same organism. This view was endorsed enthusiastically by others particularly by physicists, prominent amongst whom John Tyndall, who on 21 January 1870 lectured at the Royal Institution in London on the implications for panspermia. It is interesting and noteworthy that the newly established magazine Nature objected to this lecture in its Editorial columns with some passion. Behind the objection was the realisation that were Pasteur's dictum to be strictly true then the origin of life would need to be external to the Earth. The continuing antagonism to the panspermic implications of Pasteur's dictum led the way to the emergence of the dominant biological paradigm - abiogenesis in a primordial soup. The latter idea was developed at a time when the earliest living cells were considered to be exceedingly simple structures that could subsequently evolve in a Darwinian way. These ideas should of course have been critically examined and rejected after the discovery of the exceedingly complex molecular structures involved in proteins and in DNA. But this did not happen. Modern ideas of abiogenesis in hydrothermal vents or elsewhere on the primitive Earth have developed into sophisticated conjectures with little or no evidential support.

Even if we concede that the dominant neo-Darwinian paradigm of natural selection can explain aspects of the evolutionary history of life once life gets started, independent abiogenesis on the cosmologically diminutive scale of oceans, lakes or hydrothermal vents remains a hypothesis with no empirical support and is moreover unnecessary and redundant. With astronomical data now pointing to the existence of hundreds of billions of habitable planets in our galaxy alone (Abe et al., 2013; Kopparapu, 2013) such an hypothesis seeking an independent origin of life on any single planet seems to be no longer hardly necessary.

The recent report indicating evidence of microbial life in Canadian rocks that formed 4.1–4.23 billion years ago (Dodd et al., 2017), if accepted, makes it more difficult in our view to envisage the option of abiogenesis taking place anywhere on the Earth. The claim that these rocks may have been associated with hydrothermal vents still raises the question of how life could have originated *in situ* during the early Hadean epoch that was riddled with frequent and violent collisions by asteroids and comets. Rather we think it more reasonable to suggest that the particular evidence of microbial life in the Canadian rocks was delivered by cometary bolides, only to be instantly destroyed or carbonised on impact.

The conditions that would most likely to have prevailed near the impact-riddled Earth's surface 4.1–4.23 billion years ago were too hot even for simple organic molecules to survive let alone evolve into living complexity. This leaves panspermia as the most plausible valid option for the origin of terrestrial life; the first microbes were most likely delivered to the planet along with impacting comets and meteorites. This study, together with that of Bell and associates (2015) dating zircons in the Jack Hills of Western Australia to a similar time point, constitute the most recent discoveries that lead naturally into the data-based ideas that we discuss at length in this review.

From the turn of the 20th century the resistance to panspermia had become ever more deeply entrenched in our scientific culture. Attempts by Hoyle and Wickramasinghe (Hoyle and Wickramasinghe, 1979, 1981, 1986, 1993; Wickramasinghe, 2015a,b) to re-examine and re-instate panspermia in the light of new evidence from astronomy and biology were often met with hostility (Hoyle and Wickramasinghe, 1986; Wickramasinghe, 2015a).

A similar fate often befell attempts to re-instate certain crucial aspects of Lamarckism - the pre-Darwinian notion that the genes in our genome can be enriched in a 'directional' fashion through the inheritance of adaptive, environmentally-driven, acquired characteristics (Steele, 1979; Steele et al., 1998; Jablonka and Lamb, 1995, 2005; Lindley, 2010). This latter inheritance mechanism can be more precisely described as soma-to-germline feedback penetration of a semi-permeable (not absolute) Weisman's Barrier, a concept fashioned in the 19th Century at about the time of Darwin's death. There is now considerable evidence (Steele et al., 1998; Lindley, 2010; Steele and Lloyd, 2015; Steele, 2016a) consistent with the original 'somatic selection hypothesis' (proposed by one of us (EJS) in the late 1970s) which is hypothesized to operate via the agency of endogenous retroviral gene vectors and reverse transcriptase (Steele, 1979). Indeed there is much contemporary discussion, observations and critical analysis consistent with this position led by Corrado Spadafora, Yongsheng Liu, Denis Noble, John Mattick and others, that developments such as Lamarckian Inheritance processes (both direct DNA modifications and indirect,

viz. epigenetic, transmissions) in evolutionary biology and adjacent fields now necessitate a complete revision of the standard neo-Darwinian theory of evolution or "New Synthesis " that emerged from the 1930s and 1940s (https://royalsociety.org/science-eventsand-lectures/2016/11/evolutionary-biology/, Spadafora, 2008; Liu, 2007; Noble, 2011,2013; Noble et al., 2016; https://royalsociety. org/science-events-and-lectures/2016/11/evolutionary-biology/;

Mattick, 2012; Liu and Li, 2016a,2016b). This call was indeed also made by two of the present co-authors (EJS, NCW) many years ago based on the then available data and the plethora of inherent contradictions in the extant data (Hoyle and Wickramasinghe, 1979,1981, 1982; Steele, 1979).

We certainly do not want this paper to read, as one reviewer has put it ...

" somewhat like a last-ditch and exasperated attempt to convince the main stream of the scientific community that in following neo-Darwinism they have gone seriously astray, because life has been carried to this planet from elsewhere in the universe on comets/meteorites and does not result from abiogenesis on Earth." We actually consider that certain mechanistic aspects of neo-Darwinian and Population Genetic thinking is invaluable in biomedical research and clinical medicine (development of the "big data" algorithms that allow "personalised" navigation around the genetic features of thousands of human genomes by, for example, the Broad Institute in Boston and the Welcome Trust Sanger Institute in Cambridge). However these basic Darwinian basedconcepts need to be circumscribed, in our opinion, and be placed in a Cosmic rather than a solely Terrestrial setting. In our view then both Panspermia and Lamarckian issues therefore contribute to our wider understanding as they go to the very heart of how life originated on Earth and how it subsequently evolved and diversified to the higher levels of sophisticated complexity that we witness today. In our view "Natural Selection" in its essence (survival of fittest) still plays a crucial role in a changing environment but it is now in a Cosmic, rather than a pure Terrestrial, setting; and it occurs in concert with both non-Darwinian and non-Mendelian inheritance mechanisms. Yet we recognize that the whole topic of 'evolutionary mechanisms' is, like political beliefs, both fraught and is a heated area of social and cultural discourse - certainly in all those areas lying outside of normal scientific investigation. Yet the simple fact that cannot be denied is that the terrestrial biosphere is an infinitesimal part of the far, far bigger system which is the astronomer's cosmos and the two systems are inextricably connected.

This then is a trigger warning: Accurate scientific terminology can be unsettling because of their history, yet sometimes unavoidable - the terms *Panspermia* and *Lamarckian Inheritance* despite their emotive implications and prejudicial overtones will be used where deemed appropriate in this paper.

Our additional epistemological argument for reviving these admittedly controversial issues here is this: Wrong theories are simply *not fecund*. Correct theories however *always lead* in logical ways to successive confirmatory instances and predict the discovery of novel phenomena in the real world - that is, they do not selfrefute themselves by severe experimental and observational tests beyond their immediate explanatory domain. It is therefore in this spirit that we also discuss in the present paper, the exciting new virological evidence recently published in *Nature Communications* by Aiewsakun and Katzourakis (2017) which confirms an important prediction of the Hoyle-Wickramasinghe (H-W) theory of Cosmic Biology for the causes of the greatest epochal evolutionary event on Earth - the Cambrian Explosion of multicellular life a half billion years ago.

However, before we move into that detail, we set the scene for a better understanding of the Aiewsakun-Katzourakis discovery by discussing the salient experimental and observational data behind the H-W concept of an all pervasive Cosmic Biology impacting continuously on Earth and other general evolutionary issues and about virus particles and their general properties.

#### 3. Cosmic theory of life

In the mid-1970's the idea of prebiotic molecules existing in interstellar space or in comets was initially not part of mainstream of scientific opinion. The original proposal by one of us (NCW) for organic polymers in interstellar space in 1974 (Wickramasinghe, 1974) was followed by a long series of articles in collaboration with Fred Hoyle confronting head-on the reigning scientific paradigm of an origin of life on the Earth - the so-called Haldane-Oparin primordial soup theory (Hoyle and Wickramasinghe, 1976, 1977a, 1977b, 1978a, 1978b). After discussing a variety of possible interstellar and circumstellar settings for the beginnings of biochemistry (prebiotic evolution), Hoyle and Wickramasinghe (1978b) turned to the ensemble of the estimated 10<sup>11</sup> comets in our solar system alone as the favoured setting for the origin of life on Earth (Hoyle and Wickramasinghe, 1985, 1986). The anticipated radioactively heated interiors of these icy bodies containing liquid water domains (see below) replete with interstellar organics were argued to be enormously more favorable for an origin of life than anything that can be accomplished on the Earth.

### 4. Condition of liquid water

The existence of liquid water is a prerequisite not only for the origin of life but for active microbiology as well. This requirement has come to the fore and been much publicised with the recent conclusion of NASA's Cassini mission. When Fred Hoyle and one of us (NCW) first proposed and developed the theory of cometary panspermia (Hoyle and Wickramasinghe, 1979, 1981,1985) there was no direct evidence for liquid water anywhere outside the Earth. The inference of the presence of liquid water in comets and giant icy bodies of the solar system came from theoretical studies alone. Hoyle and Wickramasinghe (1985) argued that a largely icy body comprised of a normal solar system fraction of uranium and thorium would, through radioactive heating, maintain warm interior oceans of liquid water thus providing microbial habitats for billions of years. Hoyle and Wickramasinghe (1985) wrote: "There would evidently be no difficulty for a body of lunar size R > 1000km, maintaining a liquid condition in its interior, and some comets may have been able to do so over at least the first 500 million years history of the Solar System. Excess energy output would simply lead to a thinner surface shell, while a reduction of output would thicken the shell, in effect with the shell thickness adjusting itself to the reactor output. This solves the problem for the existence of chemoautotrophic biological systems under anaerobic conditions." More detailed studies of the same processes were carried out later by Wickramasinghe et al. (1996) and J.T. Wickramasinghe et al. (2009).

It was long afterwards that direct evidence of liquid water in comets as well as other icy solar system bodies came to be firmly established through space exploration. The Jovian moon Europa, the Saturnian moon Enceladus and the dwarf planet Ceres all have evidence of liquid water, maintained either through tidal energy dissipation or radioactive heating.

#### 5. Earliest terrestrial life

Three decades ago the earliest evidence for microbial life in the geological record was thought to be in the form of cyanobacterialike fossils dating back to 3.5 Billion Years (Ga) ago. From the time of formation of a stable crust on the Earth at 4.3 Ga following an episode of violent impacts with comets (the Hadean Epoch to which we have already referred) there seemed to be available a 800 million years timespan during which the canonical Haldane-Oparin primordial soup may have developed. Very recent discoveries, however, have shown that this time interval has been effectively closed (Dodd et al., 2017). Further, detrital zircons >4.1 Ga, discovered in rocks belonging to a geological outcrop in the Jack Hills region of Western Australia, have been found to contain micron-sized graphite spheres with an isotopic signature of biogenic carbon (Bell et al., 2015). The <sup>12</sup>C-enrichment found within these inclusions may thus be taken as plausible unequivocal evidence for the existence of microbial life on Earth before 4.1 Ga, during the epoch of comet and asteroid impacts. These data are consistent with the dating of first life on Earth for the just discussed data for early signs of cell-based life (>4.1Ga) in Canada's oldest hydrothermal vent precipitates (Dodd et al., 2017). The requirement now, on the basis of orthodox abiogenic thinking, is that an essentially instantaneous transformation of non-living organic matter to bacterial life occurs, an assumption we consider strains credibility of Earth-bound abiogenesis beyond the limit. A far more plausible possibility is that fully-developed microorganisms and maybe other eukaryotic organisms arrived at the Earth via impacting comets, and these later became carbonized and trapped within condensing mineral grain conglomerates. It is now becoming amply clear that Earth-like planets and other life-friendly planetary bodies exist in their hundreds of billions and exchanges of material between them (meteorites, cometary bolides) must routinely occur (Wickramasinghe et al., 2012; Kopparapu, 2013; Appendix A). One is thus forced in our view to conclude that the entire galaxy (and perhaps our local group of galaxies) constitutes a single connected biosphere.

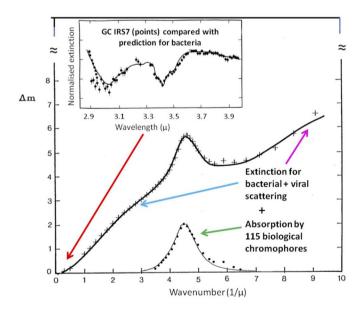
### 6. Origin of life

A facile criticism that is often leveled against the cosmic life theory is that it does not solve the problem of life's origin, but merely transfers it elsewhere (Appendix A). Whilst this may be true in the strictest sense, the importance of knowing whether or not life originated, or could have done so *de novo*, in the most minuscule of cosmic environments (here on Earth) as against the cosmos as a whole is a scientific question of paramount importance and one that needs to be addressed. The cosmic theory of life that extends the interactive biosphere of all life to encompass a cosmological volume connecting all habitable niches in the Universe has profound ramifications within evolutionary biology itself. Some of these ramifications will emerge in other sections of this article, and see the further extended discussion of view-points on the origin of life *per se* in the Universe in the supplementary information, Appendix A.

The transformation of an ensemble of appropriately chosen biological monomers (e.g. amino acids, nucleotides) into a primitive living cell capable of further evolution appears to require overcoming an information hurdle of superastronomical proportions (Appendix A), an event that could not have happened within the time frame of the Earth except, we believe, as a miracle (Hoyle and Wickramasinghe, 1981, 1982, 2000). All laboratory experiments attempting to simulate such an event have so far led to dismal failure (Deamer, 2011; Walker and Wickramasinghe, 2015). It would thus seem reasonable to go to the biggest available "venue" in relation to space and time. A cosmological origin of life thus appears plausible and overwhelmingly likely to us, and various ideas that have a bearing on this question have been explored in great depth by Hoyle and Wickramasinghe (1979, 1981,1982, 2000) and Gibson et al. (2011).

# 7. Organic molecules and biological dust in space and in comets

Detections of interstellar organic molecules of ever-increasing complexity have continued with the deployment of newer and better instruments and telescopes. Infrared, microwave, and radio observations are used to detect the presence of such molecules, and the current list of positive detections is likely to be circumscribed only by limitations of available techniques. Historically, the first mid-infrared spectrum of the Galactic Centre infrared source GC-IRS7 was shown to be very similar to the spectrum that was predicted earlier for a partially degraded (freeze dried) bacterium (Fig. 1) and this striking exact correlation between laboratory data and astrophysical observation was reasonably interpreted by Hoyle and Wickramasinghe as tenable evidence for life being a cosmic phenomenon (Hoyle et al., 1982, 1984). Evidence accumulated in the subsequent 3 decades has only served to strengthen this claim; a mixture of semi-bituminous coals and desiccated E-coli bacteria gave a similar match to the IR spectral features of GC-IRS7 over 3.2-3.8 µm as in Fig. 2 (Coulson and Wickramasinghe, 2000), suggesting that the process of bacterial degradation leads to the formation of interstellar coal. The standard rebuttal of this biological interpretation of spectroscopic data was to assert that an appropriately weighted ensemble of organic functional groups (produced abiotically) could be conceived in the biochemistry/ biophysical laboratory that exactly matched such a biological spectrum. But the conditions needed to produce such a finely tuned mixture infallibly and ubiquitously were never actually explored or published by those motivated by such a viewpoint. (While a skeptical scientific attitude in such matters is essential we nevertheless re-emphasize that deducing chemical and physical properties of extraterrestrial objects and entities in the wider Solar System and Universe from correlative spectroscopic data in Earth-



**Fig. 1. A composite of absorption and scattering properties of interstellar dust from the infrared to the far ultraviolet.** Lowest curve is the predicted behaviour around 2175A of an ensemble of biological aromatic molecules compared with average properties of interstellar dust; the middle curve is the total extinction (absorption + scattering) behaviour of an ensemble of bacterial and viral dust compared with astronomical data points for interstellar dust; the upper curve is the measured extinction of desiccated bacteria. The points are astronomical observations of D.T. Wickramasinghe and D.A. Allen for the Galactic Centre source GC-IRS7 (1986). Drawn from published data by NCW. For more details see refs. (Wickramasinghe, 2015a, 2015b; Hoyle et al., 1982, 1984).

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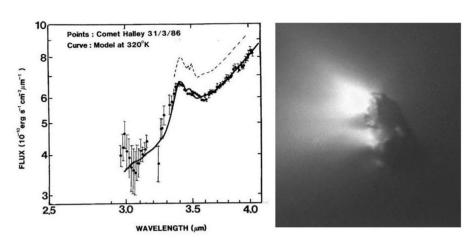
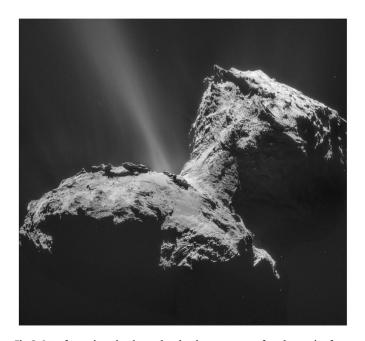


Fig. 2. Emission by dust coma of Comet Halley on March 31, 1986 (points) compared with normalized fluxes for desiccated *E-coli* at an emission temperature of 320K. The solid curve is for unirradiated bacteria; the dashed curve is for X-ray irradiated bacteria (Allen and Wickramasinghe, 1981; Wickramasinghe and Allen, 1986). Left hand graph drawn from published data by NCW. Right hand image Giotto image of the cometary nucleus is on the right frame (Courtesy of the European Space Agency).

based laboratories and telescopes, has been the bread and butter of Astrophysical deductive science at least since Galileo and the Renaissance, e.g. as illustrated in the extant data in Figs. 1-3).

The evidence based arguments in favour of complex organics in comets were first put forward by Vanýsek and Wickramasinghe (1975). In 1986 the presence of organic dust in comets was confirmed by D.T. Wickramasinghe and Allen (1986), Fig. 2. Hoyle and N.C. Wickramasinghe thereafter (1986) pointed out that the infrared spectrum of Comet Halley suggestively indicated bacteria-like material in comets (Fig. 1), and also that comets appear to have a tar-like surface layer resulting from the degradation of biological material near its closest orbital point near the Sun, or perihelion.

These data posed a serious challenge to Whipple's 'dirty snowball' comet model that was the reigning paradigm at the time. Space probes to Halley's comet in 1986 established its dust as high



**Fig. 3. Jets of organic molecules, and molecular oxygen were found emerging from comet 67P/C-G** (Courtesy of the European Space Agency). P/C ratio of gas analysed by the Rosetta orbiter revealed values of 1% that are consistent with degradation of bacteria (Capaccionne et al., 2015; Bieler et al., 2015; Altwegg et al., 2016).

in carbonaceous compounds and its surface as very dark, quite unlike ice or snow. Later exploration of several comets, using a variety of space technologies, has strengthened the case for microbial life in comets (and in carbonaceous chondrite residues) but this is not readily admitted in conservative astronomical and meteoritic circles. Solar system short-period comets as well as long period comets whose source is the Oort Cloud and adjacent star systems are hypothesized to be the carriers and amplifiers of microbial life on a galactic or even cosmological scale (Hoyle and Wickramasinghe, 1981, 1993). On this model it follows that interstellar dust should include a fraction of material that represents the detritus of biology.

Since 1980 the existence in interstellar clouds of complex organic molecules such as polycyclic aromatic hydrocarbons, is beyond dispute (Hoyle and Wickramasinghe, 1991, 2000). In addition to infrared data the ubiquitous 2175A absorption band in interstellar dust, although still "unidentified", appears fully consistent with either biochemical chromophores (break-up of microbiology) or radiation-processed microbial entities. Another astronomical dataset pointing to ubiquitous microbiology are the diffuse interstellar absorption bands in the visual spectra of stars that have defied identification for over 8 decades, but which match the properties of porphyrins (Hoyle and Wickramasinghe, 1991). It should also be noted that during the past 15 years the correspondences shown in Fig. 1 have been greatly extended to include the most distant galaxies (Wickramasinghe, 2015a). This would mean that a fortuitous match of biochemical spectra with astronomy must (according to critics and skeptics) stretch out to the very edge of the observable universe (redshift z = 4).

The Rosetta Mission's Philae lander has recently provided us novel information about the comet 67P/C-G (Capaccionne et al., 2015; Wallis and Wickramasinghe, 2015; Wickramasinghe et al., 2015). Jets of H<sub>2</sub>O vapour and organics issuing from cracks and holes in the black crust (Fig. 3) are plausibly consistent with biological activity occurring within sub-surface pools (Wickramasinghe et al., 1996, 2009). The most recent report of O<sub>2</sub> along with evidence for the occurrence of water and organics provides, in our view, a further compelling argument for ongoing biological activity (Bieler et al., 2015). Such a mixture of gases cannot be produced under thermodynamic conditions, since organics are readily destroyed in an oxidizing environment. The freezing of an initial mixture of compounds, including O<sub>2</sub>, not in thermochemical equilibrium, has been proposed, but there is no evidence to support such a claim. On the other hand the  $O_2/H_2O/$ 

organics outflow from the comet can be elegantly explained on the basis of subsurface microbiology. Photosynthetic microorganisms operating at the low light levels near the surface at perihelion could produce  $O_2$  along with organics. Many species of fermenting bacteria can also produce ethanol from sugars, so the recent discovery that Comet Lovejoy emits ethyl alcohol amounting to 500 bottles of wine per second may well be an indication that such a microbial process is operating (Biver et al., 2015).

### 8. Evidence for extant life on mars

The scientific history of the issue of life on Mars is a story in itself, yet very significant in the cosmic biology context (Hoyle and Wickramasinghe, 1997; Wickramasinghe, 2015a). The early positive results of Gilbert Levin and Patricia Straat (1976) on extant microbial life detected on the surface of Mars by the 1976 Viking Labelled Release (LR) experiment have never been properly refuted (Levin and Straat, 2016), and Levin and colleagues have fully considered and dealt with all the various comments and criticisms (Levin, 2007, 2013, 2015; Bianciardi et al., 2012). Indeed the prospects for a better quality of scientific search for life missions on Mars with Gilbert Levin's involvement have improved considerably (University of Buckingham Press Release, July 23, 2016). The pioneering 1976 studies are supported by the new results of Ruff and Farmer (2016) from the Mars Spirit rover which show silica deposits on Mars containing features resembling hot spring biosignatures at El Taion in Chile. Ruff and Farmer conclude that "Although fully abiotic processes are not ruled out for the Martian silica structures, they satisfy an *a priori* definition of potential biosignatures." It is therefore appropriate that the extensive dataset relating to the possibility of extant Martian life is fully appraised, and Levin and Straat's discoveries of 4 decades ago placed in context and they be accorded full credit for their discoveries.

#### 9. Microbial material in the stratosphere and meteorites

Data from cometary studies continue to be backed up by recoveries of microbial material in the stratosphere (under conditions where upwelling terrestrial contamination can be plausibly ruled out). Biological entities ranging from viable but non-culturable microbes to unexplained aggregates of microscopic biological entities continue to be recovered from heights in the range 30-41km in the stratosphere (Wainwright et al., 2014, 2015a, 2015b). The entities are composed of carbon and nitrogen and exhibit bilateral symmetry and organism-like morphologies. The evidence has been interpreted to show it is consistent with the plausible conclusion that these micro-organism-like entities are incoming to Earth from space, possibly transported by small comets (Frank and Sigwarth, 2001). The likely survival of biological materials descending through the Earth's atmosphere has been demonstrated in micronsized meteoroids (Coulson and Wickramasinghe, 2003) and in icy comet meteors with radii of ~1 m (Coulson et al., 2014). Early evidence of fossilized micro-organisms internal to carbonaceous meteorites has become well-established, with skepticism over terrestrial contamination now firmly countered (Pflug and Heinz, 1997; Hoover, 2005, 2011; Miyake et al., 2010; Wickramasinghe, 2015a). The most recent discovery of microbial fossils in meteorites that fell in Sri Lanka in 2012, and the unequivocal determination (based on Oxygen isotope data) that the rocks are not of Earth origin provides further strong evidence of panspermia (Wallis et al., 2013). Another related phenomenon concerns the red rain events recorded throughout history (McCafferty, 2008) but most recently in Kerala, India (Louis and Kumar 2006) and Sri Lanka in 2012. All the available evidence point to red pigmented organisms that are unlikely to have a terrestrial origin.

In spite of rigorous precautions and controls that have been undertaken for the investigations we have discussed in this section, the general trend has been to dismiss such discoveries that contradict the reigning paradigm as contaminants.

# 10. Principles of virology - viruses as dense information-rich control systems

Before embarking on a discussion of the new evidence on retroviral evolution (Aiewsakun and Katzourakis, 2017) it is important we recap the basic processes of the biology of viruses and their *modus operandi* as genetic vectors within and between cells.

All DNA and RNA viruses infecting bacterial or eukaryotic cells are tightly ordered and dense information systems. All known cellular systems carry integrated virus genetic information, or fragments thereof, or are potentially targets of virus attack and infection. These axioms do not contradict any principle in any modern textbook. Indeed, since Felix d'Herrelle and Frederick Twort in 1915-17 discovered the "filterable" agents that could infect and kill bacterial cells, we now have an almost complete understanding of the essential principles of virology.

To continue a short list summary we know that:

- The experience over decades from experimental transformation and transfection systems leads to the conclusion that any given virus particle or nucleic acid agent (viroid) can in principle potentially enter any cell.
- Replication within the cell is another matter, as the incoming information-rich molecular system must both gel, mesh and integrate with the host cell's complex biochemical and genetic circuits (Fig. 4).
- But florid replication can lead to explosive production of virions and death of the host cell (cf. cytopathic viruses). Such events occur because both the cell's immediate Innate Immunity mechanism and then later the organism's more delayed Adaptive Immune Response fail to stop the virus infection. The explosive production of virions is rarer than a more measured replication and extracellular virion export, accommodating both viral and host cell growth (or even integration of the viral DNA/ RNA into the host cell genome, as latent virus). These then are the essential three main outcomes of the first stage of the hostparasite relationship (Fig. 4).
- Usually the explosive cytopathic growth type of infection (leading to the rapid death of the host) is rare because most terrestrially circulating (and evolving) viruses have established 'host-parasite' rules of engagement (in both their Innate and Adaptive defence arms).
- So the explosive cytopathic infections, typical of unexpected fast emerging epidemics and pandemics are likely, on a first pass, to have causes unrelated to the normal constraints of the hostparasite relationship (below).
- Thus, the host-range of all plant, animal and bacterial viruses is defined not by entry of the virion into the cellular microenvironment, but by whether it can productively replicate or integrate and then express itself (such as a retrovirus). In practice this is usually manifest as an observable viral disease with characteristic non-life threatening first symptoms.
- Viruses then are dense information-rich polynucleotide macromolecules of ≥ 3000 bp (SanJuan, 2010, 2012; Sanjuan and Domingo-Calap, 2016). They are in a sense, in susceptible host cells, condensed regulatory blueprints in tune with the essential transcriptional regulator genes and nodal biochemical pathways critical to the growth and viability of the cell.

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• We should then plausibly view viruses as among the most information-rich natural systems in the known Universe (Fig. 4). Their size dictates they are very small targets minimizing the probability of destruction by flash heating or ionizing radiation, Hoyle and Wickramasinghe (1979) e.g. Chapter 1. Their nanometer dimensions plausibly allow easy transport and dispersal by micrometer sized dust grains and other protective physical matrices of similar size. They are then nanoparticle-sized genetic vectors which contain all the essential information to take over and drive the physiology of any given target cell within which they mesh. Their replicative growth means they are produced, and exist, in huge numbers on cosmic scales; so that they (and to a lesser quantitative extent their cellular reservoirs) can suffer huge losses by inactivation while still leaving a residue of millions of surviving particles potentially still infective. A virus then is a type of compressed module in touch with the whole of the cell's very ability to grow and divide to produce progeny cells and thus to evolve.

This check list is underpinned by the important experiments on RNA viruses by Sanjuan and his associates (Sanjuan, 2010, 2012; SanJuan et al., 2004, 2010; Combe et al., 2015). It will be expected that finely tuned information-dense viral genomes are susceptible to random mutations which cripple their speed of replication and infectivity. Using site-directed mutagenesis to produce randomized mutations in viral genomes (SanJuan et al., 2004; Sanjuan, 2010) up to 40% of such mutated nucleotides result in clear lethals. This is only an estimate as substitutions leading to amino acid replacements (non-synonymous mutations) is not the only mutation hazard a virus can encounter. Silent substitutional changes in the 3rd position 'Wobble Site' in a codon can have functional consequence affecting replication and infective efficacy caused by cotranslational pausing/delays as the polypeptide exits the Ribosome. These effects lead to anomalies in folding kinetics due to variations in the composition of the nucleotide triphosphate precursor pool (Buhr et al., 2016). Well-conserved RNA structures in the HCV RNA genome when manipulated at 3rd position synonymous sites can alter the ability of the virus to replicate, and hence infect (Pirakitikulr et al., 2016).

The sophistication of viral infectivity and their *modus operandi* of cell-cell spreading does not end here. To ensure maximal gene complementation defective viral genomes carrying stop codons (Aaskov et al., 2006) can be propagated almost indefinitely (Combe et al., 2015) as "virion clusters" of mixtures of infective and crippled genomes with significant numbers of newly minted virus particles enwrapped in protective membrane vesicles – a type of multiunit nanoparticle. This then constitutes the actual infective dose rather than just a single exported virion entering a nearby target cell to cause a productive infection as is commonly believed (Combe et al., 2015; Chen et al., 2015).

However it needs pointing out again that most terrestrial viruses have already evolved established molecular-interactive hostparasite relationships. Many, by themselves are benign and noncytolytic, such that many initial infections are usually silent and asymptomatic. Physicians and Clinicians now understand that the main health problem is often the unintended tissue damage caused by inflammatory responses by the host's adaptive immune response launched prior to the establishment of chronic infection states e.g. HCV induced hepatitis (in those patients who fail to naturally and quickly clear the initial infection).

There seems no end to the inventive strategies that viruses employ to infect and take over their target cells, whether they are bacterial (normal prokaryotes, extremophile archaebacteria) or eukaryotic metazoan cells. If we just consider a recent RNA virome sample for invertebrate hosts, the complex magnitude of which, with the swapping and sharing of viral gene sequences, is staggering in its scope (Shi et al., 2016). In the more extensively studied vertebrates, where similar sharing and gene swapping has occurred, the evasion of both the innate and adaptive immune responses are key facets of the viral life cycle. Recently it has been pointed out that one possible reason why the HIV retrovirus cannot be controlled by conventional immunological vaccines (producing neutralizing antibodies in advance of the infection by a HIV-1 variant) is because the main cellular focus of proviral integration may not be the T lymphocyte or the macrophage/dendritic cell as commonly supposed, but more likely the B lymphocyte (Steele and Dawkins, 2016), the cellular home of the somatic hypermutation mechanism (Franklin et al., 2004; Steele, 2016b; Steele and Lindley, 2017). Thus it was reasonably postulated that HIV by co-opting the adaptive somatic hypermutation mechanism of the antibody system will always be a mutational step ahead of the patient's own adaptive immune response (Steele and Dawkins, 2016). This proposal has not been publicly challenged by mainstream critics in immunology and virology since it was circulated and remains a conceptual option in better understanding the modus operandi of HIV and retroviruses related to it.

# 11. Criticism of host specificity and survival under space conditions

A criticism that has been levelled against the concept of viruses causing disease and contributing to the evolution of life is encapsulated in a single rhetorical question: how can a virus from space know ahead of its coming here the range of organisms that are available with which it can interact? In the previous section we have elaborated on the correct answer to this question: viruses originating in a cosmic context and evolution on the Earth are inextricably intertwined. The host specificity of viruses is maintained only over fairly narrow ranges of species that are defined by their evolutionary history. Thus the influenza A virus can be cultured in hen's eggs so attesting to host specificity to within 50 million years of evolutionary history (and is known to infect many vertebrate and mammalian species). Again the Ebola virus affects the class of primates.

The criticism that bacteria and/or viruses are incapable of surviving under the harsh conditions of space is certainly not borne out by all the data that has accumulated over the past 3 decades. Bacteria and viruses embedded in grains of rock, carbonaceous material or ice, are protected effectively from radiation damage and can remain fully viable for millions of years under space conditions. Microorganisms including virions deep frozen within cometary bodies could remain viable indefinitely, and certainly for cosmological timescales. Recent space experiments including those conducted aboard the International Space Station have shown remarkable survival properties of bacteria and viruses.

Thus Hiel et al. (2014) have recently conducted an experiment in which plasmid DNA was placed on the outer surface of a TEXUS-49 sounding rocket that was blasted through the atmosphere into space and which subsequently re-entered the atmosphere. The conditions endured by the DNA would closely mimic what actually happens in the high-speed entry of viruses attached to meteor/ comet dust. The data of Hiel et al. (2014) show that a significant fraction of DNA remained viable and infective - a clear indication that extraterrestrial viruses can indeed arrive at the Earth in viable form.

The microorganism (*D. audaxviator*) discovered at a depth of 2.8km in a South African gold mine has been found to derive its energy from radiolysis induced by particles emitted from the decay of U, Th and K (Chivian et al., 2008). A bacterium such as *D. audaxviator* would survive not only in interstellar transits but

they would thrive on the energy derived from galactic cosmic rays that reach the interstellar or interplanetary frozen bodies.

### 12. Retroviral induction model

We now also have a far better understanding of clear non-Darwinian and non-Mendelian evolutionary inheritance mechanisms shaping both the immune and central nervous systems in particular (e.g. retroviral and RNA/RT-based Lamarckian Inheritance (Steele, 1979; Gorczynski and Steele, 1980, 1981; Steele et al., 1984; Steele et al., 1998; Steele, 2016a) as well as retroviral/retro-element drivers of segmental duplications and genomic block structure of Ancestral Haplotypes and related non-Darwinian inheritance phenomena of medical significance (Dawkins et al., 1999; Dawkins, 2015; Steele, 2014, 2015; Steele and Lloyd, 2015). The plethora of adaptive Lamarckian-like inheritance mechanisms in general are discussed elsewhere (Campbell and Perkins, 1988; Jablonka and Lamb, 1995; Lindley, 2010; Liu, 2007; Noble, 2013; Mattick, 2012; Liu and Li, 2016a, 2016b) some involving mobile lymphocytes delivering endogenous retroviruses and somatic genes to the germline (Rothenfluh, 1995) or other types of soma-to-germline transfer mechanisms involving vesicles or exosomes have been considered (Spadafora, 2008; Cossetti et al., 2014; Devanapally et al., 2015; Sharma et al., 2015). A clear causal chain of new viruses arriving from space potentially driving evolution on Earth can thus be discerned and rationally understood (Wickramasinghe and Steele, 2016). Indeed LINE retro-element transposition (and Alu repeat element co-mobility, Appendix B) is a normal part of genomic rearrangement during specific neuron commitment, much like the V-> DJ rearrangement in specific B and T lymphocyte commitment in the Immune System (Erwin et al., 2016).

With respect to HIV and retroviral evolution in general viz. the genomic duplicative processes generating the polymorphic block (Ancestral) haplotype structure of the human genome, the key concepts can be traced to what is now known as the "Retroviral-Induction Model " (Dawkins et al., 1999; Steele, 2014) and Steele (2015, p.95). Thus when a retrovirus infects a human cell all measure of mutagenic processes are unleashed, including: AID/ APOBEC-deaminase induced C-to-U events leading to C-to-T mutations, Abasic sites, and ssDNA nicks, as well as ADAR-deaminase induced A-to-I RNA editing events. Both of these DNA and RNA deaminations are now identified as strand-biased and codoncontext Targeted Somatic Mutations (TSM) in the human cancer genome (Lindley, 2013; Lindley and Steele, 2013; Lindley et al., 2016; Steele and Lindley, 2017). As well as these we have LINE/ Alu-retro-element mutagenic mobility (Harris and Liddament, 2004; Chiu et al., 2006; Muotri et al., 2007; Doria et al., 2009; Refsland and Harris, 2013; Jones et al., 2013). So as discussed already LINE/Alu retro-mobility now appears as a normal part of specific synaptic neuronal Brain development (Erwin et al., 2016). RNA editing (A-to-I) targeting neural Alu inverted elements (in the introns, creating alternative spliced isoforms) is an established synaptic neural diversification process in the Brain (Paz-Yaacov et al., 2010). Thus retroviruses and other viruses hypothezed to be liberated in cometary debris trails both can potentially add new DNA sequences to terrestrial genomes and drive further mutagenic change within somatic and germline genomes (Appendix B). Indeed Frank Ryan has termed virus-driven terrestrial evolution with the appropriate catch-phrase, 'virolution' and this concept has been supported and expanded by Oliver and Greene (2012) in the Transposable-Element Thrust Hypothesis (Appendix B).

Yohn et al. (2005) have stated that their data are consistent with a retroviral infection that bombarded the genomes of chimpanzees and gorillas independently and concurrently, 3–4 million years ago, with no horizontal transmission being implied. Recently Diehl et al. (2016) have shown that a specific endogenous retrovirus group (ERV-Fc) has somehow come to be spread globally across many mammalian species about 33-15 million years ago. There have also been suggestions that the later evolutionary development of hominids, including enhanced cognitive capacity, may also have viral origins (Villareal, 2004). A plausible externally driven viral involvement appears to have been identified in the development of mammalian placenta in ancestors of all mammals including humans about 150 million years ago (Katzourakis (2013)).

### 13. Evolution of intelligent complexity

Evidence of the role of extraterrestrial viruses in affecting terrestrial evolution has recently been plausibly implied in the gene and transcriptome sequencing of Cephalopods. The genome of the Octopus shows a staggering level of complexity with 33,000 protein-coding genes more than is present in Homo sapiens (Albertin et al., 2015). Octopus belongs to the coleoid sub-class of molluscs (Cephalopods) that have an evolutionary history that stretches back over 500 million years, although Cephalopod phylogenetics is highly inconsistent and confusing (see Carlini et al., 2000; Strugnell et al., 2005, 2006, 2007; Bergmann et al., 2006). Cephalopods are also very diverse, with the behaviourally complex coleoids, (Squid, Cuttlefish and Octopus) presumably arising under a pure terrestrial evolutionary model from the more primitive nautiloids. However the genetic divergence of Octopus from its ancestral coleoid sub-class is very great, akin to the extreme features seen across many genera and species noted in Eldridge-Gould punctuated equilibria patterns (below). Its large brain and sophisticated nervous system, camera-like eyes, flexible bodies, instantaneous camouflage via the ability to switch colour and shape are just a few of the striking features that appear suddenly on the evolutionary scene. The transformative genes leading from the consensus ancestral Nautilus (e.g. Nautilus pompilius) to the common Cuttlefish (Sepia officinalis) to Squid (Loligo vulgaris) to the common Octopus (Octopus vulgaris, Fig. 5) are not easily to be found in any pre-existing life form - it is plausible then to suggest they seem to be borrowed from a far distant "future" in terms of terrestrial evolution, or more realistically from the cosmos at large. Such an extraterrestrial origin as an explanation of emergence of course runs counter to the prevailing dominant paradigm.

However consistent with this conclusion are the recent RNA editing transcriptome-wide data on the somatic RNA diversification mechanisms in the behaviourally sophisticated Cephalopods such as Octopus. These data demonstrate extensive evolutionary conserved adenosine to inosine (A-to-I) mRNA editing sites in almost every single protein-coding gene in the behaviorally complex coleoid Cephalopods (Octopus in particular), but not in nautilus (Liscovitch-Brauer et al., 2017). This enormous qualitative difference in Cephalopod protein recoding A-to-I mRNA editing compared to nautilus and other invertebrate and vertebrate animals is striking. Thus in transcriptome-wide screens only 1-3% of Drosophila and human protein coding mRNAs harbour an A-to-I recoding site; and there only about 25 human mRNA messages which contain a conserved A-to-I recoding site across mammals. In Drosophila lineages there are about 65 conserved A-sites in protein coding genes and only a few identified in C. elegans which support the hypothesis that A-to-I RNA editing recoding is mostly either neutral, detrimental, or rarely adaptive (reviewed in Liscovitch-Brauer et al., 2017). Yet in Squid and particularly Octopus it is the norm, with almost every protein coding gene having an evolutionary conserved A-to-I mRNA editing site isoform, resulting in a nonsynonymous amino acid change (Liscovitch-Brauer et al., 2017). This is a virtual qualitative jump in molecular genetic strategy in a supposed smooth and incremental evolutionary lineage - a type of

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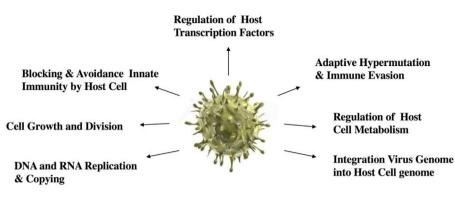


Fig. 4. Typical main functions of viruses. They are in tune with all the essential growth aspects of their own production and the wider cellular machinery. Virus image from: https://www.dreamstime.com/royalty-free-stock-photo-h1n1-viruses-image11898035.

sudden "great leap forward". Unless all the new genes expressed in the squid/octopus lineages arose from simple mutations of existing genes in either the squid or in other organisms sharing the same habitat, there is surely no way by which this large qualitative transition in A-to-I mRNA editing can be explained by conventional neo-Darwinian processes, even if horizontal gene transfer is allowed. One plausible explanation, in our view, is that the new genes are likely new extraterrestrial imports to Earth - most plausibly as an already coherent group of functioning genes within (say) cryopreserved and matrix protected fertilized Octopus eggs.

Thus the possibility that cryopreserved Squid and/or Octopus eggs, arrived in icv bolides several hundred million years ago should not be discounted (below) as that would be a parsimonious cosmic explanation for the Octopus' sudden emergence on Earth ca. 270 million years ago. Indeed this principle applies to the sudden appearance in the fossil record of pretty well all major life forms, covered in the prescient concept of "punctuated equilibrium" by Eldridge and Gould advanced in the early 1970s (1972, 1977); and see the conceptual cartoon of Fig. 6. Therefore, similar living features like this "as if the genes were derived from some type of preexistence" (Hoyle and Wickramasinghe, 1981) apply to many other biological ensembles when closely examined. One little known yet cogent example is the response and resistance of the eye structures of the Drosophila fruit fly to normally lethally damaging UV radiation at 2537 Å, given that this wavelength does not penetrate the ozone layer and is thus not evident as a Darwinian selective factor at the surface of the Earth (Lutz and Grisewood, 1934) and see Hoyle and Wickramasinghe (1981, p.12–13). Many of these "unearthly" properties of organisms can be plausibly explained if we admit the enlarged cosmic biosphere that is indicated by modern astronomical research – discoveries of exoplanets already discussed. The average distance between habitable planets in our galaxy now to be reckoned in light years – typically 5 light years (Wickramasinghe et al., 2012). Virion/gene exchanges thus appear to be inevitable over such short cosmic distances. The many features of biology that are not optimised to local conditions on the Earth may be readily understood in this wider perspective.

Given that the complex sets of new genes in the Octopus may have not come solely from horizontal gene transfers or simple random mutations of existing genes or by simple duplicative expansions, it is then logical to surmise, given our current knowledge of the biology of comets and their debris, the new genes and their viral drivers most likely came from space. However, it is also clear that to accept such a proposition also requires that we diminish the role for highly localised Darwinian evolution on Earth which is likely to be strongly resisted by traditional biologists. That should not, of course, be of concern as the focus of our attention, for general evolutionary molecular processes, now shifts to the Cosmos and beyond our immediate solar system. This evidence provides for, and allows the study of, *Cosmic Gene Pools* – and these are capable of driving, and, dare we say, controlling and thus steering biological evolution here on Earth (via Darwinian and non-

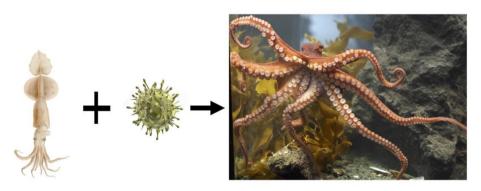
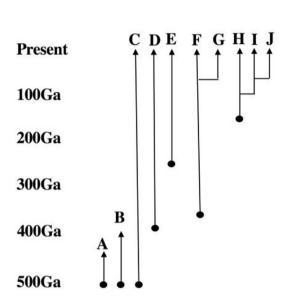


Fig. 5. The evolution from squid to octopus is compatible with a suite of genes inserted by extraterrestrial viruses. An alternative extraterrestrial scenario discussed is that a population of cryopreserved octopus embryos soft-landed *en mass* from space 275 million years ago. Squid image - Grimalditeuthis bonplandi. jpg.From Wikimedia Commons -Author: Jeanne Le Roux & L. Joubin URL (http://www.archive.org/stream/rsultatsdescam17albe#page/ n165/mode/2up)

Octopus Image - File:Octopus at Kelly Tarlton's.jpg From Wikimedia Commons Author: Pseudopanax at English Wikipedia https://upload.wikimedia.org/wikipedia/commons/f/ff/Octopus\_at\_Kelly\_Tarlton%27s.jpg Virus image from: https://www.dreamstime.com/royalty-free-stock-photo-h1n1-viruses-image11898035.

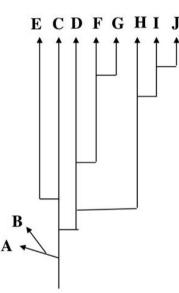
## **Consequences of the Paradigm Shift for Phylogenetic Sequence Relationships**



Separate In-fall Cosmic-Derived Lines

with Some Branch Terrestrial Evolution

A Phylogenetic Tree is Forced by Assuming Evolutionary Precursor Relationships



**Fig. 6. Conceptual Cartoon - Cosmic Evolution after an in-fall versus Terrestrial Evolutionary Relationships.** Evolutionary patterns for an essential conserved protein such as, for example, Haemoglobin (O<sub>2</sub> transfer) or Cytochrome C (electron transfer). The 10 different variant proteins are A through to J. This cartoon illustrates the conceptual differences for evolutionary schemes caused by the in-fall of a species of organism from space followed by subsequent terrestrial evolution (on the left) versus the evolutionary relationships between the same groups of conserved proteins after a phylogenetic tree is forced on the data by quantitative assessment of the homology relationships based on, for example, Kimura's Neutral Theory (of third position synonymous variation). On the left independent lines are initiated at different times on in-fall from space (from the •). On the right a "Tree" is formed by the algorithm which assumes direct precursor evolutionary relationships for all the homologus variants of the conserved protein. The branched groups F, G and HJJ are genuine terrestrial evolutionary diversifications. A, and B go extinct shortly after in-fall. Adapted from the concepts outlined in Hoyle and Wickramasinghe (1981). Fig. 6.3 and 6.4 pages 83–85. The essential concept on the left fits the punctuated equilibria scheme of Eldredge and Gould (1972), Gould and Eldredge (1977). Conventional phylogenetics of any type thus operates on the tacit assumption that all homologies are related by arising *only on Earth* ignoring the contribution of a Cosmic evolutionary dimension to the data.

Darwinian adaptation mechanisms). The main effect of terrestrial Darwinian evolution is to act on these new cosmic-derived genes and fine-tune them by further somatic and germline Lamarckian gene feedback and haplotype-block shuffling mechanisms to fit the environment and also the recipient organism (Wickramasinghe and Steele, 2016). Indeed it has been shown that viral footprints are evident in human brain tissue which seem to mark important steps that led up to the present human condition (Villarreal, 2004; Ryan, 2009).

## 14. Evolutionary origin of vertebrate retroviruses

This now leads us to the crux and an important take home lesson of this review. While all viruses, when looked at closely, are exceedingly clever, the Retroviruses (family *Retroviridiae*) are up there with the most sophisticated and compact of all known viruses. These viruses and their elements (reverse transcriptase enzymes, associated with induced mobile retro-elements) now appear to be important viral-drivers of major evolutionary genetic change on Earth over the past few hundred million years (Wickramasinghe, 2012), and see (Hoyle and Wickramasinghe, 1979, 1981). Cell-derived reverse transcriptase (RT) activity is also a principal molecular player in adaptive somatic hypermutation of antibody genes (Franklin et al., 2004; Steele, 2016b; Steele and Lindley, 2017). As just discussed endogenous retroviral vectors as well as RT activities are likely to be involved in soma-to-germline Lamarckian transmissions in the immune system (Steele, 1979; Steele et al., 1984; Steele et al., 1998; Steele and Lloyd, 2015; Steele, 2016a) including the shaping, duplicative expansions and the adaptive shuffling of the block-ancestral haplotype structures of the human and higher mammalian genome (Dawkins et al., 1999; McLure et al., 2013; Steele, 2014, 2015; Dawkins, 2015).

The main genetic and evolutionary feature of an RNA retrovirus is that on productive infection the virus ensures that a double stranded (ds) DNA copy of the viral single stranded (ss) RNA genome is made and that this is integrated as a provirus into the host cell genome (Temin, 1974). When active this potentially latent provirus is transcribed and produces viral progeny in the infected cell for export to other cells. If the host cell is a germline cell then the integrated provirus can be transmitted vertically to progeny organisms.

Retroviruses can infect a wide range of animal cells and the integrated proviruses produced can leave their trace as "genomic fossils" termed endogenous retroviruses (ERVs). These DNA sequences are therefore relics of past, and probably, virulent HIV-like epidemics whereby the survivors, and now partially immune to the immediate HIV-like variant, have genomic integrations in their germ-line cells (leading, as discussed, to the duplicative expansion and diversification of functional ancestral haplotype blocks

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#### (Dawkins et al., 1999; Dawkins, 2015).

These fields of retroviral research are now blossoming with much data in public databases. Many ancient ERVs have now been discovered, allowing the examination of the early evolutionary history of retroviruses by bioinformatic techniques. Until just recently the oldest age estimates from analyses of mammalian retroviruses and ERVs were directly inferred to be dated back about 100 million years, to the beginning of the mammalian radiation. It is now clear in a comprehensive co-evolutionary phylogenetic analysis (Aiewsakun and Katzourakis, 2017) that bony fish endogenous retroviruses display a co-speciation pattern with their hosts (yet not so clear for amphibian endogenous retroviruses). However the overall co-speciation pattern of an ERV with the known times of emergence of their vertebrate host species is very convincing. Other possible ancient viral cross-species and class transmissions have taken place at a low rate (involving lobe-finned fish, shark and frog) yet the analyses reveal two major lineages of ray-finned fish ERVs: one line of which gained two novel accessory genes within their much larger genomes (~20 Kb, or twice the size of extant mammalian retroviruses). This major retroviral lineage (and retroviruses as a whole) appears therefore to have an ancient marine origin which " ... originated together with, if not before, their jawed vertebrate hosts >450 million years ago in the Ordovician period, early Palaeozoic Era " (Aiewsakun and Katzourakis, 2017). This is a very important result, and the authors conclude " ....our analyses provide evidence, both phylogenetically and temporally, that retroviruses emerged together with their vertebrate hosts in the ocean, ~460 - 550Ma, in the early Palaeozoic Era, if not earlier".

This of course dates these sophisticated viral gene vectors and their associated gene-manipulative evolutionary driver effects - to just at or before the Cambrian Explosion. Certainly they are emerging before the later evolutionary appearance of the far more complex animal and plant species now extant on Earth. In other words, we can now make the plausible scientific argument that a key feature of information-dense genetic systems to make more complex organisms was already here on Earth before the actual emergence of subsequent greater terrestrial complexity. This is a contradiction if we consider our just discussed viewpoint that all viruses, and particularly the retroviruses, are a "reflection in microcosm of the host's genetic regulatory make-

#### 15. Cambrian Explosion

It is well known that a mass extinction event, or events, occurred at the end of the Ediacaran period about 542 million years ago. This was the immediate forerunner of the Cambrian explosion and the mass extinction scale suggests the passage of our Solar System through a Giant Molecular Cloud dislodging multiple long period Oort Cloud comets into the inner Solar System setting up impacts with the Earth (Hoyle and Wickramasinghe, 1981, 1993). It takes little imagination to consider that the pre-Cambrian mass extinction event(s) was correlated with the impact of a giant lifebearing comet (or comets), and the subsequent seeding of Earth with new cosmic-derived cellular organisms and viral genes (Hoyle and Wickramasinghe, 1979, 1981). There may indeed have been a complex comet debris stream implying multiple impacts over the estimated 25 million years at the start of the Cambrian explosion.

The pre-Cambrian impact event is not unique. There is other evidence for the coincidence of cosmic bolide impacts at mass extinction event-diversification boundaries (e.g. K-T Boundary 65 Million years ago extinction of the Dinosaurs and rise of small mammals) and the now well established 26 Million yr periodicity (Galactic Tide-Holmes cycle) with cometary impacts coinciding with mass extinction events (Clube et al., 1996) and evolutionary diversifications (Napier et al., 2007). The exotic amino acids in the K-T boundary rocks and the rise of microfungi are also indicative of novel genetic material arriving in the impact (Wallis, 2007).

In this regard the work of Martin Brasier showing a 20–30 million year periodicity in foraminifera-alga coevolution could be interpreted from a Cosmic perspective rather than the Terrestrial perspective favoured by Brasier (2012, p156 -157) viz. that the 20–30 million year periodicity is an uproven systems property of large organisms to be vulnerable to small changes. Although H-W theory and analyses predicts such a large Cosmic-driven environmental change, our conclusion is consistent with Noble's recent view that "Causality is multiple in biology" (Noble, 2011). It should also be stressed in this context that Eldridge-Gould "punctuated equilibrium" (Fig. 6) is often presented as an explanation of the observed facts of evolution, but it is not. It is the use of words to describe a striking phenomenon which itself lacks a plausible explanation within the framework of Earth-centred biology.



Hypsibius dujardini

" Tardigrades (0.5 mm long fully grown) form the phylum Tardigrada, part of the superphylum Ecdysozo.. an ancient group, with fossils dating from 530 million years ago, in the Cambrian period. About 1,150 species of tardigrades have been described .. [and they] can be found throughout the world, from the Himalayas (above 6,000 m (20,000 ft)), to the deep sea (below 4,000 m (13,000 ft)) and from the polar regions to the equator. [They] are water-dwelling, eight-legged, segmented micro-animals. and have been found everywhere from mountaintops to the deep sea, from tropical rain forests to the Antarctic....the most resilient animal known.(able to). survive extreme conditions that would be rapidly fatal to nearly all other known life forms, withstand[ing] temperature ranges from 1 K (-458 °F; -272 °C) (close to absolute zero) to about 420 K (300 °F; 150 °C)...pressures about six times greater than those found in the deepest ocean trenches, ionizing radiation at doses hundreds of times higher than the lethal dose for a human, and the vacuum of outer

space.. They can go without food or water for more than 30 years, drying out to the point where they are 3% or less water, only to rehydrate, forage, and reproduce." *Wikipedia* 

up". That is, " a type of compressed module of genetic information in touch with the whole of the cell's very ability to grow and divide to produce progeny cells and to evolve."(Fig. 4). It goes without saying that Tardigrades, micro-segmented tiny eukaryotic animals, which emerged in the Cambrian period pose a serious challenge to traditional neo-Darwinian thinking (see

Wikipedia summary Box above and the further detailed references at the Wikipedia site https://en.wikipedia.org/wiki/Tardigrade, and the data discussed in Jönsson et al., 2008). The catalogue of 'living' space-hardy properties is entirely consistent with 'evolutionary natural selective events' acting on Tardigrades evolving in extraterrestrial space environments. These properties are incompatible with known purely terrestrial 'natural selection' conditions, either now or 500 million years ago. A plausible evidentiary case for proof of Cosmic Panspermia could rest entirely on this one example. However as has been discussed at some length there are many other living examples like this (space-hardy bacterial species and their spores), the Tardigrades being an extreme case which appears to prove the rule (Hoyle and Wickramasinghe, 1981, 1993).

The results reported recently (Leya et al., 2017) of an experiment conducted by Dr. Thomas Leya at the Fraunhofer Institute for Cell Therapy and Immunology IZI in Potsdam, Germany, in cooperation with German and international partners are consistent with this picture.

The group reports evidence that two algae species survived 16 months on the exterior of the International Space Station (ISS) despite extreme temperature fluctuations and the vacuum of space – as well as considerable UV and cosmic radiation (http://www.algaeindustrymagazine.com/algae-survive-outside-space-station/). The logical implications of these data for a Cosmic Biology are obvious - indeed we argue such findings make far better sense under the cosmic evolutionary paradigm of H-W Cosmic Biology-Panspermia (Appendix A).

#### 16. Implications of Cambrian Explosion and retroviral data

Before the extensive sequencing of DNA became available it would have been reasonable to speculate that random copying errors in a gene sequence could, over time, lead to the emergence of new traits, body plans and new physiologies that could explain the whole of evolution. However the data we have reviewed here challenge this point of view. It suggests that the Cambrian Explosion of multicellular life that occurred 0.54 billion years ago led to a sudden emergence of essentially all the genes that subsequently came to be rearranged into an exceedingly wide range of multicelled life forms - Tardigrades, the Squid, Octopus, fruit flies, humans – to name but a few.

The expression of an entire new suite of retroviral genes (of presumed external origin) appears to have taken place mainly via genomic rearrangements that followed ERV integrations. This was precisely the logic of evolution proposed by the late Sir Fred Hoyle and one of us (NCW) as far back as 1981. It was argued that copying errors of existing genes could not, on the average, produce new genes with functional utility. By analogy with computer programing, it was pointed out that errors generated in copying a computer code would not lead to enhanced or new capabilities but overwhelmingly to degradation of the original program. It was argued therefore that new genes for evolution must logically be supplied by the ingress of extraterrestrial virions and other microorganisms.

#### 17. Cosmic biology and the rise of mankind

Hoyle and Wickramasinghe (1979, 1981,1986) thus argued and predicted on the basis of the then available evidence (Figs. 1 and 2) – as well as the species mass extinction record and astronomical infra-red spectra on interstellar and cometary bodies and, more recently on the known periodic cratering and comet impact records (Clube et al., 1996) – that microorganisms and virus populations in the comets and related cosmic bolides appear to have regularly delivered living systems (organisms, viruses and seeds) to the Earth since its formation, and continue to do so. Of course the Earth needed to be a 'hospitable' place and thus receptive to these cometderived living systems. This then provides one plausible explanation as to why Cambrian-like explosions did not occur in the previous 3500 million years prior to 500 Ma despite the likely passage of our Solar System through many other Galactic Molecular Clouds in that time interval, given our Sun's approximately 240 Million Year galactic periodicity in its orbit around the Galactic Centre (Hoyle and Wickramasinghe, 1993; JT Wickramasinghe et al., 2010). The alternative is that a large dump stream of cosmically-derived complex eukaryotic organisms (plants, animals, fungi) arrived during the 25 million years at the start of the Cambrian, a rare and large cosmic seeding-event that happened ca. 500-550Ma but not in the previous 2000–3000 million years. The discussion here therefore, is by necessity, on Cosmic space-time scales.

So the evidence consistent with the H-W Cosmic Biology viewpoint has grown both in quantity and strength over the past decade (Napier et al., 2007; Rauf and Wickramasinghe, 2010; Wickramasinghe, 2010, 2011, 2012, 2015a, 2015b; Smith, 2013; Wickramasinghe and Smith, 2014). We are of the conviction that an extensive Cosmic Biology is the most plausible driver of the evolutionary complexity of life on Earth, and the recent report by Aiewsakun and Katzourakis (2017) provides a major jig-saw piece of evidence fitting in and consistent with this picture.

Darwinian evolution and its various non-Darwinian terrestrial drivers (Wickramasinghe and Steele, 2016) are therefore most likely caused by the continuing supply of new virions and microorganisms from space with their genetic impact events written all over our genomes (Wickramasinghe, 2012). Indeed a strong case can be made for hominid evolution involving a long sequence of viral pandemics, each one of which was a close call to total extinction of an evolving line. The most crucial genes relevant to evolution of hominids, as indeed all species of plants and animals, seems likely in many instances to be of external origin, being transferred across the galaxy largely as information rich virions. In some cases it is possible to imagine - fanciful as it might seem multicellular life-forms that were established on an icy cometary or planetary body to be transferred as frozen eggs, embryos or seeds (Tepfer and Leach, 2017) in large icy bolides that have been transported to the Earth in soft landings (Frank and Sigwarth, 2001; Snyder, 2015); certainly the terrestrial evidence for Earth's own pervasive Icy Biosphere is compelling and consistent with such a picture (Priscu and Christner, 2004; Fox, 2014; Christner et al., 2014). It is plausible that in the warmed and liquid subsurface interiors of the comets, or planetary moons such as Jupiter's Europa and Saturn's Enceladus (Hoover, 2011; Snyder, 2015) cellular reservoirs for viral replication would, by necessity, need to exist.

# 18. The causes of epidemics and pandemics: a new virology principle

That many disease epidemics and pandemics have afflicted mankind is beyond dispute. HIV/AIDS is one of the biggest and most recent. A sexually transmitted retroviral disease apparently targeting the immune system and causing its eventual collapse came out of the blue - and it was not science fiction! Major monitoring centres such CDC in Atlanta, and Pirbright in the UK were caught completely unawares and unprepared. However the 1918 Spanish Flu Pandemic was probably just as devastating and equally unexpected. The highly unusual epidemiology of the 1918 Spanish Flu Influenza virus pandemic - in the pre-air travel era - has been analysed in great detail, as have the epidemiological minutiae of more recent Influenza epidemics (Hoyle and Wickramasinghe, 1979). These analyses completely refute the popular and traditional biomedical view that the Influenza virus spreads in such

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epidemics largely by person-to-person transmission. This extremely strong evidence is analyzed and documented in detail in Hoyle and Wickramasnghe (1979). The many colleagues of coauthor NCW in this review article would argue that this cogent evidence should be confronted in its totality by all biologists and biomedical scientists wanting to understand the most likely drivers of many apparently unexpected (and fully unexplained) infectious epidemics that occur all the time, many with annual periodicities or periodicities that coincide with the 11 year sun-spot cycle (Wickramasinghe et al., 2017). In the case of Influenza the sudden appearance of multiple yet patchy location strikes (many, as indicated, before the advent of air travel) cannot be explained by simple infectious person-to-person disease models. However they are more completely understandable by multiple strikes or in-falls from space at widely disparate global locations dependent on vagaries like weather, topography and geography, and in particular the periodicity of the significant correlation with the 11 year Sun Spot flare cycle (Hope-Simpson, 1978; Hoyle and Wickramasinghe, 1979; reviewed in Qu, 2016; Wickramasinghe et al., 2017). With respect to the latter correlation "..the peaks of solar activity will be expected to assist in the descent of charged molecular aggregates (including viruses) from the stratosphere to ground level..along magnetic field lines that connect the Sun and the Earth" (Wickramasinghe, 2015a, p.81; Wickramasinghe et al., 2017).

It could be argued that both H-W theory and person-to-person (P-P) contact are responsible for epidemics, some epidemics being more of the H-W kind and some more of the P-P kind. In apparent support of this we all have had experiences of catching a cold from someone else, and can remember exactly who and when we encountered the person who gave it to us. This experience of course gives us all a bias in thinking that "this is the only way to catch a virus, directly or indirectly from someone else." Yet it is precisely this widely held belief which is directly refuted in the detailed analyses of suddenly appearing Influenza epidemics (Hoyle and Wickramasinghe, 1979, see in particular Chapter 6 " Anatomy of an epidemic" and Chapter 5, the critical analysis of the 1968 Influenza pandemic): where such potential intimate P-P physical transfers cannot explain the patterns in Influenza spread (i.e. spread by body fluid vehicles such as saliva, blood, semen or in your face explosive P-P aerosols). In other cases such as Vibrio cholerae, a water borne bacterium, contaminated water can be identified as the direct physical vector causing Cholera diarrohea - consumed straight into the mouth and digestive tracts of susceptible victims. Salmonella food poisoning outbreaks are another familiar example of this type. So while there is clearly a mix of H-W and P-P transmission modes it does depend on the disease being studied. But if it is unexpected and explosive and on a large epidemic or pandemic scale then "in-fall from space" should be one possible default first cause to fall under suspicion. This is all discussed in detail elsewhere (Hoyle and Wickramasinghe, 1979). And it is still the case now, despite many years of flu vaccine research and improved understanding of avian flu viral reservoirs that seasonal Influenza and epidemics/pandemics are poorly understood. This ignorance is both with respect to the emergence of new antigenically unpredictable strains as well as the actual mode of transmission of the disease during outbreaks and epidemics (Paules et al., 2017).

An all pervasive Cosmic Biology means that many novel emergent disease-causing micro-organisms and viruses will show phylogenetic relationships with existing viral species and genera, as we are now considering a "Cosmic Gene Pool" under this viewpoint (Fig. 6). We should then assume, as one first reactive response, they have come from space - even if there are also plausible alternative terrestrial explanations of first cause i.e. the cosmic cause should be part of the possible mix of causative explanations to be ruled either in or out. But what to do about the Cosmic possibility? At this juncture our response can only be a long-term surveillance strategy building up knowledge of the warning signs of impending pathogenic cometary debris strikes. This means organised deployment of spacecraft monitoring and recording stations, as well as more wide-spread and systematic higher atmosphere balloon-lifted sampling techniques (Wainwright et al., 2014, 2015a, 2015b) and a sophisticated monitoring system for which a prototype known as the "Hoyle Shield" has been proposed and is in very early design (Smith, 2013).

### 19. Paradigm shift

In our considered view Mankind is now entering a historic paradigm shifting moment in both our understanding of the evolution of life on Earth and the origins of the many pandemics that have exacted huge tolls on mankind in the recent past. Indeed all of us have contributed directly as co-authors of this paper because, in our considered opinion in confronting the wide range of scientific data, all the scientific and societal evidence seemingly points in one direction, an all-pervasive Cosmic Biology, mediated mainly by cometary transfers, being a driver for life on Earth. We believe the signs of this change are now so apparent that one of the biggest back-flips in the history of science is now on our door step (Appendix C).

If you think that our position here is farfetched, or even alarmist, we quote the late great Cornell Professor, Thomas Gold, a farsighted and creative astronomer and geophysicist (Gold, 1992, 1999) who observed closely many scientific back-flips in his long career, the most notable being in the Geosciences in the mid to late 1960s with the gigantic about-face over Alfred Wegner's 1912 theory of Continental Drift. In 1989 Tom Gold wrote:

"What does the refereeing procedure really look like? How does it really go on? If, for example, an application was made in the early 60's or late 50's suggesting that the person wanted to investigate the possibility that continents are moving around a little, it would have been ruled out absolutely instantly without questions. That was crack-pot stuff, and had long been thought dead. Wegener, of course, was an absolute crack-pot, and everybody knew that and you wouldn't have any chance.

Six years later you could not get a paper published that doubted continental drift. The herd had swung around - but it was still a firm and arrogant herd." Check it out at http://amasci.com/freenrg/ newidea1.html.

A related example was the wide-spread institutional denial of the reality of meteorites during Lavoisier's time (1768) who "rejected eye-witness accounts of the fall of meteorites for the sound common sense reason that 'stones cannot fall from the sky as there are no stones in the sky' (Haynes, 1980)."

The Hoyle-Wickramasinghe thesis on the influence of an all pervasive Cosmic Biology delivered to Earth mainly via Comets is wholly in keeping with the experimental and observational evidence that has been accumulated over the past 40–50 years since first proposal. While the acceptance of these multifactorial and specific data will be long overdue this will still be a great scientific advance and we hope and trust that the new devotees will be kind, considerate and respectful to those who pioneered the field and acknowledge the priority of their scientific discoveries.

So with an avalanche of data from diverse fields all pointing to an all pervasive Cosmic Biology implying an origin of life external to Earth, the continuing reluctance of the scientific community to recognise this fact might seem strange. Yet as Tom Gold clearly shows - and we are all aware of this force in our daily lives - "Group Think" and the safety of "Running with the Herd" are powerful driving motivating forces both in science and society (Gold, 1989). These forces are quite irrational (scientifically speaking) yet very

powerful socially and culturally. However, the long-overdue scientific paradigm shift from Earth-centred biology to Cosmic Life will have profound implications that would extend well outside the bounds of Science (Wickramasinghe and Tokoro, 2014a, 2014b). Certainly just within biomedical sciences the straightforward implication for phylogenetic analyses based on DNA or amino acid sequence data will require a fundamental reappraisal (compare Left and Right evolutionary conceptual trajectories in Fig. 6). However the resulting upheaval in the realms of politics, religion and human self-understanding is likely to be even more dramatic and more profound than any that has happened in the past 500 years.

In a final reckoning it would have to be admitted that ultimately all of evolution has been controlled and continues to be controlled by space-borne organisms, microbes and viruses. It is important that we not allow Science to be stifled by a reign of dogmatic authority that strives to restrict its progress along narrow conservative lines. The current situation is strikingly reminiscent of the Middle Ages in Europe — Ptolemaic epicycles that delayed the acceptance of a Sun-centred planetary system for over a century (Appendix C). The current evidence suggests we came from space, we are made of viral genes, and eventually our evolutionary legacy would in full measure return to space. This will then complete the second and final phase of the Copernican revolution that was started over half a millennium ago.

### **Conflicts of interest**

The authors declare no conflict of interest.

### **Author contributions**

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### Note added in proof

A crucial prediction of the Hoyle-Wickramasinghe cosmic theory of life is that new genetic material (DNA/RNA) in the form of bacteria and viruses arrives at the Earth from space both continuously as well as in sporadic bursts. Such a process is envisioned to extend the processes of biological evolution to involve horizontal gene transfer over galactic or cosmic dimensions. The search for such incoming bacteria and viruses using balloon-borne equipment lofted to the stratosphere has been carried out for nearly two decades (Harris et al. 2002: Wainwright et al. 2003: Shivaji et al. 2009). Stratospheric air samples recovered from heights ranging from 28 to 41 km have indeed yielded evidence of microorganisms, but these have been widely regarded as most likely to have been lofted from the Earth's surface. The situation has changed dramatically in recent months, however. T.V. Grebennikova et al (2018) have now confirmed the discovery of several microbial species associated with cosmic dust on the exterior windows of the International Space Station (ISS), and contamination at source and in the laboratory has been ruled out. The results of PCR amplification followed by DNA sequencing and phylogenetic analysis have established the presence of bacteria of the genus Mycobacteria and the extremophile genus Delftia, amongst others, associated with deposits of cosmic dust, which are now from a height of some 400km above the Earth's surface. A terrestrial origin seems most unlikely. Studies by Wickramasinghe and Rycroft (2018) have shown that all possible mechanisms for lofting these organisms against gravity to heights of 400km in the ionosphere fall short by many orders of magnitude.

# Appendix A. Origins of life and scientific alternatives to the H-W cosmic panspermia?

" "Let us seek to fathom those things that are fathomable and reserve those things that are unfathomable for reverence in solitude.." Johann Wolfgang von Goethe"

At this stage of our scientific understanding we need to place on hold the issue of life's actual biochemical origins - where, when and how may be too difficult to solve on the current evidence. The current paper is focused on the evidence for an all pervasive Cosmic Biology and its effects on the emergence of life on Earth and its further evolution. Certainly all attempts at abiogenesis in the laboratory on Earth have been unsuccessful. It is many orders of magnitude more likely that it emerged in one of the trillions of comet-like incubators or water-bearing planets (cosmic-wide versions of Darwin's 'warm little ponds') at a very early time in the growth of this Universe, perhaps 12 Billion years ago (Wickramasinghe, 2015a) which then went on to infect via knockon effects other life-favourable sites (planets, moons, comets) throughout that Galaxy and then in an interconnected and interactive way throughout the Cosmos as the Universe expanded. The spherical Oort Cloud, the source of long period Comets around our solar system provides a causal connection and explanation. Possibly the majority of these billions of comets did not originate from our Solar System accretion plane - they have most likely arisen by capture of Comets by our Sun's gravity from other passing Solar Systems (Levison et al., 2010).

One of us (BK) thinks " that the complexity and sophistication of life cannot *originate* (from non-biological) matter under any scenario, over any expanse of space and time, however vast. If this were to be so, then, supernatural intervention or intelligence would be required, following the standard big bang (see also Walker and Wickramasinghe, 2015). A strictly scientific way around this dilemma would be to amend or tweak the big bang theory to allow for life from the eternal past. After all, the big bang theory is relatively new and still occasionally amended. Therefore it seems unready to forever overrule the unviolated principle and consistent evidence that life comes from life."

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Another of us (EIS) might state this same scenario a little differently, based on the positions published in Hoyle and Wickramasinghe (1978b, 1979, 1981): "Is the Universe an Infinite Steady-State (a rolling series of big bangs and contractions) - as advanced in 1948 by Fred Hoyle, Tom Gold and Herman Bondi - or just the conventional "Big Bang"? The latter is what most Mathematical Physicists and Astronomers adhere to at the present time. but it cannot by any means be regarded as set in stone (Tegmark. 2014). Both alternatives make the rational scientific mind boggle. But if we are to choose, then on the basis of the existence of Cosmicwide, mutually interactive Biology, a Steady-State Universe (or a Quasi-Steady State Universe, Hoyle et al., 2000) with infinite time provides all the time needed for abiogenesis by trial-and-error elimination in trillions of warm-little ponds throughout the Cosmos (to put together the incredible phenomenon of the living cell with its thousands of interacting genes driving the processes of cellular life on a cosmic scale). Thus Hoyle and Wickramasinghe (1981) concluded that the improbabilities for the non-random assemblage of living proteins and nucleic acids are so huge (1 part in 10<sup>40,000</sup>) that maybe an 'Infinite Universe' or super intelligent God would be required to produce a living miracle, which then spread and evolved on a Cosmic scale." It is the confrontation with these profound empirical-based issues that may well explain the honest and very public back-flip of the late noted humanist philosopher, Antony Flew (2007).

However with respect to the immediate origin of life on Earth we think, based on the evidence, there is no serious alternative scientific theory to the Hoyle-Wickramasinghe model of Cosmic (Cometary) Panspermia as the major driver of life on Earth. About 1960 Tom Gold when asked in public, and then after surveying the evidence before him, apparently stated in half jest: " A space-ship landed on the Earth in the early days, scattering living cells, which have evolved and persisted ever since." Hoyle and Wickramasinghe, 1981, p.30]. And this was given some considerable gravitas in 1973 by Francis Crick and Leslie Orgel who published their own theory of "Directed Panspermia" ie. a super intelligent civilization seeded life by sending space ships three to four billions of years ago. Their scientific reason for advancing such a theory was to explain the extraordinary facts of the exquisite complexity yet 'generality' of the Genetic Code: which indeed allows us to clone and express human genes in bacteria and vice versa - and underpins all modern biotechnology, biomedical therapeutics and biomedical research. The H-W explanation is far more reasonable and scientific in our view (a parsimonious model).

It has been suggested by a critical co-author (KAA) that both H-W theory and life emerging from non-life on Earth are both possibly true. Thus for KAA " Life could have emerged from non-life in many different ways and places, *including* here on Earth." Thus Panspermia is perfectly consistent with life also having emerged here on Earth. In a recent book The Vital QuestIon Nick Lane (2015) provides a possible theory of life emerging from non-life on Earth and suggests that life could have emerged in a similar fashion independently at many locations in the Universe. Hoyle and Wickramasinghe have already considered this possibility for terrestrial origins in depth. To Hoyle and Wickramasinghe it is a sophisticated variant of the spontaneous generation view refuted by Louis Pasteur in the 19th Century. Moreover, it merely compounds indefinitely the gross difficulties envisaged with an origin of life at one site only. It also takes no account of the recognised modern fact that hundreds of billions of habitable planets exist in the galaxy alone, with average separations of the order of a few light years. Exchanges of biotic material between adjacent planets and therefore a single connected biosphere appears inevitable. We suggest an extraterrestrial emergence of life in the early Cosmos as the most likely based on all the current evidence (again H-W is the more parsimonious model).

However what is very strange about the book The Vital Question by Nick Lane (2015) is that he dismisses panspermia as irrelevant: " Panspermia fails utterly to address those principles (the steps he outlines as important in life's abiogenic origin), and so is irrelevant." (p.94n). This completely misses the point of an extant all pervasive extraterrestrial Biology, throughout the Solar System, and almost certainly from the interstellar infra red extinction data. throughout the wider Cosmos. Of this Nick Lane seems oblivious. Yet in a striking contradiction in the same book (p.55–56) Lane discusses the Tardigrades (Wiki Box) and accurately describes in detail their space-hardy characteristics! The key issue then is the extensive evidence, briefly reviewed here in our paper, for an all pervasive Cosmic Biology that mankind now needs to confront. This knowledge will allow us to better understand the ongoing evolutionary process and also the emergence of new explosive disease epidemics in our domestic animals and plants, as well as in human beings.

Writers of popular science books such as Nick Lane of University College London, have considered it fashionable to dismiss the Hoyle-Wickramasinghe thesis in one-line disproofs. This is disappointing because his book displays much innovative and imaginative thinking on likely scenarios for the emergence of life, not only on Earth but also throughout the Cosmos. There is no need to be dismissive of the manifest data all around us for Cosmic Biology. While abiogenesis causation may be unlikely for Earth, his vivid and knowledgeable scenarios for porous alkaline hydrothermal (temperate) deep sea vents as sites of early likely bioenergenesis (early mitochondrial-like proton-gradient driven membrane bounded energy systems) are being tested in the laboratory. Indeed the plethora of experiments that Nick Lane's thinking inspires (with his collaborators such as Bill Martins and his PhD students) needs to be encouraged and funded. Sooner or later, after much Popperian trial and error elimination of the numerous steps to self-replicating energetic living systems, we have no doubt that mankind led by people like Nick Lane will eventually execute a successful abiogenesis experiment. This will be informed by the integrated insight of past failures to pull off an "origins of life" demonstration from simple cosmic-wide starting materials (H<sub>2</sub>, CO<sub>2</sub>, CO, silicates, phosphates, iron-sulphur aggregates, H<sub>2</sub>O, etc) in the test tube. That would truly be an epoch-changing experiment for mankind. But at the moment we have the mountain of parsimonious data of extraterrestrial life all around us to integrate and understand the full consequences.

Another co-author and theoretical physicist (AZ) takes the Tom Gold scenario further and considers the probabilities of a Cosmic origin thus: " Since the idea of a cosmic origin of life is not yet accepted in the field of evolutionary biology, it has not entered the mainstream of general scientists either - however, that might change. In his 2014 book "Superintelligence", Oxford philosopher Nick Bostrom argues that humanity sooner or later will develop forms intelligence that vastly exceed the human level. Whether this will occur on a short timescale (via artificial intelligence generated by new algorithms in existing hardware) or in the more distant future when nanotechnology will allow building copies of the human brain, is irrelevant for our discussion here - on astronomical timescales, it will be a blink of an eye in both cases. Such a superintelligence will easily be able (and likely willing) to build spacecraft (or smaller units) that can efficiently distribute primitive forms of life in other regions of the Milky Way far from the solar system - thus panspermia. The timescale for this would be thousands rather than millions of years, that is, negligible. So it is certainly a reasonable hypothesis that such a superintelligent planet could have 10-100 descending civilizations. That would imply however we have an a priori likelihood of 90-99 percent of

being of cosmic origin - that's what a simple Bayesian analysis suggests after just one 'generation'.

AZ goes further: " It is remarkable that Bostrom's thesis has passed unchallenged so far - it appears that no serious counterarguments exist (see, e.g. Wikipedia - Superintellligence). Yet it has profound consequences for our discussion here. Science is sometimes schizophrenic - a hypothesis can be interesting and convincing in one field (here: Neurobiology) whereas in another field it is considered not worth debating (Evolutionary Biology)."

But there is clearly one very fundamental process discovered and developed by Irena Cosic and her colleagues, the molecular resonance recognition between receptor-ligand macromolecules (proteins, nucleic acids), that needs to be integrated *into all thinking* of how life may have emerged in the first place and continues to evolve. This is electromagnetic-mediated intermolecular recognition and functional activation *prior to* actual binding which is essential in all living systems and should be factored into all models and experiments on abiogenesis (Cosic, 1994; Cosic et al., 2015, 2016; Cosic and Cosic, 2016).

With the rapidly increasing number of exoplanets that have been discovered in the habitable zones of long-lived red dwarf stars (Gillon et al., 2016), the prospects for genetic exchanges between life-bearing Earth-like planets cannot be ignored. In our view the idea of life emerging de novo in multiple locations through a process of in situ abiogenesis appears far-fetched and merely compounds the difficulty of a single origination on the Earth. The internal evidence from terrestrial biology that we have discussed in this paper suggests that the entire ensemble of habitable planets in the galaxy constitutes a single interconnected biosphere. Lifeforms elsewhere, on this viewpoint, will be expected to exhibit a converging pattern of genotypes and phenotypes, subject to natural selection (Darwinian and Lamarckian) within individual planetary habitats. The recent announcement of 7 "habitable" planets around the star Trappist 1 located 40 light years away is therefore timely (Gillon et al., 2016) and relevant to the thesis discussed in the present paper. Future investigations are planned to search for spectral signatures of molecular oxygen and methane in the planetary atmospheres as indicators of life; although such molecules (and much more) have indeed been detected in dwarf planets and comets within the solar system with no reference being made to biology.

Finally, the idea of 'Necropanspermia should be addressed (Wesson, 2011) - the idea that organisms are continually arriving on Earth but are so degraded by ionizing radiation and the desiccation rigours of space, they are dead on arrival. Yet they will add to the terrestrial gene pool (DNA/RNA) albeit dead. We had considered this in an earlier draft but decided not to include it in the main section. We thought then (Wickramasinghe, 2011), and still think, Wesson's ideas are contradictory and thus non-viable scientifically in the broad sweep of all the evidences for the continued arrival of living organisms to Earth (with their space–hardy and space-resistant properties over the past 4 Billion years).

# Appendix B. Retroviruses, Alu and LINE retroelements - structure, function, genome mobility and significance

The interspersed short (SINE) and long (LINE) repetitive retroelements elements (RLEs) in the human and mammalian genome are major features of genome structure and drivers of genomic evolutionary diversity (see reviews by Kapitonov and Jurka, 1996; Arcot et al., 1996; Cordaux and Batzer, 2009) and germline retrotranspositions of this type discussed much earlier as general evolutionary mechanisms in Steele et al. (1984). They exist in multiple copies dispersed by reverse transcriptase-mediated retrotransposition across the genome. The LINE RLEs are long interspersed nuclear elements (about >500,000 copies in the human genome) and different families of elements have been continuously active (in their genomic mobility) for the past 150 Mya, and the current activity of the main L1 elements are in the Brian, where each neurone has a unique mobilized L1 element indicative of a normal physiological role in the healthy human Brain and CNS development in specific neurone commitment (Erwin et al., 2016). They are about 6Kb and encode their own reverse transcriptase (RT) and supply this RT activity to co-mobilise the smaller Alu elements (approx. 300 bp, about 1.1 million copies in the human genome). LINE and Alu RLEs are located in the transcriptionally active gene rich regions of the genome, usually in introns (as their insertion in coding regions, while it happens, usually leads to such dramatic gene disruptions, that strong purifying selection purges the organism of such lethal mutations, only tolerating harmless and 'neutral' LINE and Alu insertions which usually lie outside protein-coding portions). However, LINE and Alu retroelements are of functional importance (Steele, 2015; Erwin et al., 2016) with Alu repeats located in the intronic regions of Brain and CNS neurones of major significance (Paz-Yaacov et al., 2010). The Alu elements have a dimeric structure originally derived from the RNA of the 7SL RNA of gene-signal recognition particle and in their central portions they are adenosine (A)-rich and thus ideal targets in dsRNA structures for Adenosine-to-Inosine (A-to-I) pre-mRNA editing mediated by ADAR deaminases, again a prominent activity of great significance in the human and higher primate Brain and CNS (Paz-Yaacov et al., 2010). Indeed "Alu-exonization", or new gene creation via RNA editing leading to new pre-mRNA splice sites (thus exon skipping during pre-mRNA splicing) both generates and destroys existing exons and thus make new gene isoforms (on which physiological somatic selection may act to enhance the synaptic functions of the Brain and CNS). Such somatic neuronal gene re-arrangements can of course, also lead to pathology and diseases such as Alzheimer's Diseases, Parkinson Disease, Autism Spectrum Disorder. Recognised Alu families are very good evolutionary markers. Based on consensus sequences they can be divided into at least three families (and their subfamilies). The oldest Alu J. expanded by transcription/reverse transcription 81 mya; the primate specific Alu S, subfamilies Sx, Sq, Sp, Sc all platyrrhine specific, expanded across the genome 35–44 mya; and Sg about 31 mya. The Primate specific Alu Y subfamily spread 19 mya to as recently as several hundred thousand years ago. Such markers linked to other emerging new genes allow molecular "dating" of emergence of new germline gene families in the Primate lines leading to Homo Sapiens. Along with the similar endogenous retroviruses (ERVs, about 10 Kb and >200,000 copies per haploid human genome) the multiple copies of the LINE and Alu retroelements elements are drivers of duplicative genomic expansions as their similar sequences, separated yet physically in tandem nearby, can drive large segmental duplications by unequal crossing over during meiosis thus increasing both genome size and functional diversity (Dawkins et al., 1999; McLure et al., 2013; Steele, 2014, 2015).

A feature of retroviruses is their ability to incorporate nonrandomly host cell enzymes and small RNAs of various types into virions. As well as reverse transcriptase (RTs) proteins (>50 per virion) and host-derived APOBEC3G enzymes which are DNA mutators (C-to-U deamination of ssDNA) and host specific pretRNAs that prime reverse transcription, selective packaging of multiple host cell noncoding RNAs also includes signal recognition particle 7SL RNA, (the 300 nt RNA precursors of Alu RNA retroelements) as well as host Alu RNAs themselves, specific regulatory microRNAs and spliceosomal U6 small nuclear RNA (snRNA), normally thought of as residing only in mammalian nuclei, suggesting new mechanisms involving these RNAs in retroviral assembly and infectivity. Thus whilst the two 10 kb viral genomes are

the main occupants of mature retroviral virions it is now recognised that the infecting virus delivers many more additional specific proteins and nucleic acid species to the intended target cell than previously thought (Tian et al., 2007; Bach, 2008; Hu et al., 2012; Lin et al., 2012; Eckwahl et al., 2016; Telesnitsky et al., 2016) – no doubt assisting the very mutagenic cellular environment triggered by the infection of HIV and other viruses.

In the text the "The Transposable -Element (TE) -Thrust Hypothesis " of Oliver and Greene was mentioned (2012). This is envisaged as an intrinsic force, intermittently thrusting adaptation, speciation, and the evolution of novelties forward, often, but not always, in a punctuated equilibrium manner. When most of the TEs become deactivated by accumulated mutations, and if they are not replaced by horizontal transposon transfer, or by endogenised retroviruses, etc. lineages can become "Living Fossils", and further, if this lack of TE-Thrust continues then lineages can become extinct, as a part of the background extinction, which appears to accounts for the overwhelming majority of the extinctions on Earth.

# Appendix C. Visualizing the causes and drivers of the history of life on earth implied by this paper

(By co-author John A Schuster, Historian and Philosopher of Science, an authority on Descartes and the Copernican Revolution who did his PhD under Thomas S Kuhn). "The foregoing paper implies a radical challenge to the present scientific consensus about the causes that are taken to explain the history of life on Earth. The presently accepted Darwinian mechanisms, related to best practice geological history of the Earth, are not questioned. They are, however, placed in a new set of relations to a wider theoretical nexus, grounded, on the one hand, in developments in astrophysics, then astrobiology since the original and ongoing contributions of Fred Hoyle and N. Chandra Wickramasinghe and their colleagues, and on the other hand, in the developments in virology and molecular biology, including, most importantly, the ongoing improvements in neo-Lamarckian models in molecular immunology developed by Edward J. Steele and various colleagues over the past forty years.

One may initially envision the nature and scope of the new synthesis on analogy to how differential equations describing known laws interact with the boundary conditions that need to be fed into them to produce concrete solutions. We may say that the normally agreed Darwinian processes, along with Steele's neo-Lamarckian ones, always operate on Earth. They are analogous to the routine equations or algorithms employed to describe a system. As to the boundary conditions applied to the equations in order to produce concrete solutions, we now have a radical new vision. There are shifting, unpredictable and, in geological terms, sudden astrobiological inputs. It is as though someone were insisting on changing the boundary conditions randomly from time to time. The history of life on Earth becomes the temporal record of the outputs of the underlying Darwinian/neo Lamarckian mechanisms or equations as they have worked over time upon a concatenation of randomly timed, quickly and radically altered boundary conditions. At the time of a new astrobiological input, the state of life on Earth will have been the product of all previous workings of the fundamental mechanisms upon and through the sequence of previous astrobiological inputs. With a new input, the system will further evolve, based on the input, the mechanisms and the previously achieved state.

As the paper argues, the causal elements taken to be involved in biological evolution need to radically modified beyond the neo-Darwinian consensus. This is achieved by grasping and conceptually articulating to each other findings and models in previously widely disparate domains such as astrobiology and molecular immunology. The new synthesis suggests that the concrete history of life on Earth will necessarily reveal facts about, and mappings amongst, biological groupings significantly different from those imposed by reading the evidence solely in the light of Neo-Darwinism. Just as the promise of Nicholas Copernicus' first proposal in 1543 was only fully realized several generations later on the basis of Kepler's adducing of laws and possible causal mechanisms for planetary motion and Galileo's discovery of dramatic confirmatory empirical evidence, so the Hoyle-Wickramasinghe panspermia model can now be fleshed out and articulated by means of two generations of findings in astrobiology and molecular biology. In each case the initial claims were potentially revolutionary and quite brilliantly executed in themselves. But in each case it was necessary for wider and deeper empirical and theoretical foundations to be laid under the original claim-foundations making use of factual and theoretical materials not necessarily available at the time of the founders' inaugural claims.

Finally, let us take an even wider view and speculate about the kinds of challenges the new synthesis poses to a range of political, cultural and religious beliefs. Revolutionary theories almost always have such a penumbra of wider consequences. The paper hints at this, without of course being able to enter into any detail. For example, amongst the wider scientifically literate public, the dominant popular versions of neo-Darwinism are threatened, along with the many cultural, philosophical and public policy claims that have been leveraged from it. For religious believers of all stripes, the new synthesis, even more than orthodox Darwinism, demystifies the history of life on Earth and embeds it in a history of cosmic events, that is, the history of the Universe at large. Finally, as intellectual historians and historians of science have long recognized, there is a central question that has energized both biological and socio-political theorizing since the early 19th century; that is, even before Darwin. That question concerns 'Man's place in nature'- where 'nature' meant 'the immediate terrestrial environment'. The new synthesis re-invents and extends that question: We will now be inquiring about humankind's place in, and relations to, the entire cosmos, and, in particular, we will be viewing humankind's situation as the result of a concatenation of cosmic processes and events that have impacted the Earth in a decidedly ruptural and randomly causative manner. " (Note: The Evolutionary Physiologist Denis Noble of Oxford has also used the argument from boundary and initial conditions (Chapter 6 of Dance to the Tune of Life (2017) and was first used first used in Noble (2011).

#### References

- Aaskov, J., et al., 2006. Long- term transmission of defective RNA viruses in humans and Aedes mosquitoes. Science 311, 236–238.
- Abe, F., et al., 2013. Extending the planetary mass function to Earth mass by microlensing at moderately high magnification. Mon. Not. Roy. Astron. Soc. 431 (4), 2975–2985.
- Aiewsakun, P., Katzourakis, A., 2017. Marine origin of retroviruses in the early Palaeozoic Era. Nat. Commun. 8, 13954. https://doi.org/10.1038/ncomms13954.
- Albertin, C.B., et al., 2015. The octopus genome and the evolution of cephalopod neural and morphological novelties. Nature 524, 220–224.
   Allen, D.A., Wickramasinghe, D.T., 1981. Diffuse interstellar absorption bands be-
- Allen, D.A., Wickramasinghe, D.I., 1981. Diffuse interstellar absorption bands between 2.9 and 4.0 μm. Nature 294, 239–240.
- Altwegg, K., et al., 2016. Prebiotic chemical amino acid and phosphorus in the coma of comet 67P/Churyumov-Gerasimenko. Sci. Adv 2, e1600285, 27 May. Arcot, S.S., et al., 1996. Alu fossil relics - distribution and insertion polymorphism.
- Genome Res. 6, 1084–1092. Bach, D., 2008. Characterization of APOBEC3G binding to 7SL RNA. Retrovirology 5,
- 54. https://doi.org/10.1186/1742-4690-5-54.
- Bell, E.A., et al., 2015. Potentially biogenic carbon preserved in a 4.1 billion-year-old zircon. Proc. Natl. Acad. Sci. U.S.A. 112, 14518–14521.
- Bergmann, S., et al., 2006. The hemocyanin from a living fossil, the cephalopod Nautilus pompilius: protein structure, gene organization, and evolution. J. Mol. Evol. 62, 362–374.
- Bianciardi, G., et al., 2012. Complexity analysis of the viking labelled Release experiments. Intl J. Aeronautical & Space Sci. 13, 14–26. https://doi.org/10.5139/ IJASS.2012.13.1.14.

Bieler, K., et al., 2015. Abundant molecular oxygen in the coma of comet 67P/

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Churyumov–Gerasimenko. Nature 526, 678–681. https://doi.org/10.1038/ nature15707.

Biver, N., et al., 2015. Ethyl alcohol and sugar in comet C/2014 Q2 (Lovejoy). Sci. Adv. 1, e1500863, 23 October 2015.

- Bostrom, N., 2014. Superintelligence: Paths, Dangers, Strategies. Oxford University Press, Oxford, UK.
- Brasier, M., 2012. Secret Chambers. Oxford University Press. ISBN 9780199644001. Buhr, F., et al., 2016. Synonymous codons direct co-translational folding towards
- different protein conformations. Mol. Cell 61, 342–351. Campbell, J.H., Perkins, P., 1988. Transgenerational effects of drug and hormonal treatments in mammals: a review of observations and ideas. In: Boer, G.J., Feenstra, M.G.P., Mirmiran, M., Swaab, D.F., van Haaren, F. (Eds.), Progress in
- Brain Research, vol. 73, pp. 535–553. Capaccione, F., et al., 2015. The organic-rich surface of comet 67P/Churyumov-Gerasimenko as seen by VIRTIS/Rosetta. Science 347 (6220).
- Carlini, D.B., et al., 2000. Actin gene family evolution and the phylogeny of coleoid cephalopods (Mollusca: cephalopoda). Mol. Biol. Evol. 17, 1353–1370.
- Chen, Y.-H., et al., 2015. Phosphatidylserine vesicles enable efficient en bloc transmission of enteroviruses. Cell 160, 619–630. https://doi.org/10.1016/ j.cell.2015.01.032.
- Chiu, Y.-L., Greene, W.C., 2006. APOBEC3 Cytidine Deaminases: distinct antiviral actions along the retroviral life cycle. J. Biol. Chem. 281, 8309–8312. https:// doi.org/10.1074/jbc.R500021200.
- Chivian, D., et al., 2008. Environmental genomics reveals a single-species ecosystem deep within the Earth. Science 322, 275–278.
- Christener, B.C., et al., 2014. A microbial ecosystem beneath the West Antarctic ice sheet. Nature 512, 310–313. https://doi.org/10.1038/nature13667.
- Clube, S.V.M., et al., 1996. Giant comets, evolution and civilization. Astrophys. Space Sci. 245, 43–60.
- Combe, M., et al., 2015. Single-cell analysis of RNA virus infection identifies multiple genetically diverse viral genomes within single infectious units. Cell Host Microbe 18, 424–432. https://doi.org/10.1016/j.chom.2015.09.009.
- Cordaux, R., Batzer, M.A., 2009. The impact of retrotranspositions on human genome evolution. Nat. Rev. Genet. 10, 691–703.
- Cosic, I., 1994. Macromolecular bioactivity: is it resonant interaction between macromolecules? Theory and applications. IEEE Trans. Biomed. Eng. 41, 1101–1114.
- Cosic, I., Cosic, D., 2016. The treatment of crigler-najjar syndrome by blue light as explained by resonant recognition model. EPJ Nonlinear Biomedical Physics 4, 9. https://doi.org/10.1140/epjnbp/s40366-016-0036-6.
- Cosic, I., et al., 2015. Is it possible to predict electromagnetic resonances in proteins, DNA and RNA? EPJ Nonlinear Biomedical Physics 3, 5. https://doi.org/10.1140/ s40366-015-0020-6.
- Cosic, I., et al., 2016. Environmental light and its relationship with electromagnetic resonances of biomolecular interactions, as predicted by the Resonant Recognition Model. Int. J. Environ. Res. Publ. Health 13 (7), 647, https://doi.org/ 10.3390/ijeprh13070647.
- Cossetti, C., et al., 2014. Soma-to- germline transmission of RNA in mice xenografted with human tumour cells: possible transport by exosomes. PLoS One 9, e101629.
- Coulson, S.G., Wickramasinghe, N.C., 2000. IR spectrometry of coals. In: Celnikier, L.M., Tran Thanh Van, J. (Eds.), Frontiers of Life, Proceedings of the XIIth Recontres de Blois, pp. 233–236.
- Coulson, S.G., Wickramasinghe, N.C., 2003. Frictional and radiation heating of micron-sized meteoroids in the Earth's upper atmosphere. Mon. Not. Roy. Astron. Soc. 343, 1123–1130.
- Coulson, S.G., et al., 2014. On the dynamics of volatile meteorites. Mon. Not. Roy. Astron. Soc. 445, 3669–3673.
- Crick, F.H.C., Orgel, L.E., 1973. Directed panspermia. Icarus 19, 341–346.
- Dawkins, R.L., 2015. Adapting Genetics: Quantal Evolution after Natural Selection Surviving the Changes to Come. Nearurban Publishing, Dallas, TX. ISBN 978-0-9864115-1-9.
- Dawkins, R.L., et al., 1999. Genomics of the major histocompatibility complex: haplotypes, duplication, retroviruses and disease. Immunol. Rev. 167, 275–304.
- Deamer, D., 2011. First Life: Discovering the Connections between Stars, Cells, and How Life Began. University of California Press, Berkeley, USA.
- Devanapally, S., et al., 2015. Double-stranded RNA made in C. elegans neurons can enter the germline and cause transgenerational gene silencing. Proc. Natl. Acad. Sci. U.S.A. 112, 2133–2138. https://doi.org/10.1073/pnas.1423333112.
- Diehl, W.E., et al., 2016. Tracking interspecies transmission and long-term evolution of an ancient retrovirus using the genomes of modern mammals. eLife 5, e12704.
- Dodd, M.C., et al., 2017. Evidence for early life in Earth's oldest hydrothermal vent precipitates. Nature 543, 60–65.
- Doria, M., et al., 2009. Editing of HIV-1 RNA by the double-stranded RNA deaminase ADAR1 stimulates viral infection. Nucleic Acids Res. 37, 5848–5858.
- Eckwahl, M.J., et al., 2016. Host RNA packaging by retroviruses: a newly synthesized story. mBio 7 (1). https://doi.org/10.1128/mBio.02025-15 e02025–15.
- Eldredge, N., Gould, S.J., 1972. Punctuated equilibria : an alternative to phyletic gradualism. In: Schopf, T.J.M. (Ed.), Models in Paleobiology. Freeman Cooper, San Francisco, pp. 82–115.
- Erwin, J.A., et al., 2016. L1-associated genomic regions are deleted in somatic cells of the healthy human brain. Nat. Neurosci. 19, 1583–1591. https://doi.org/10.1038/ nn.4388.

Flew, A., 2007. There Is a God : How the World's Most Notorious Atheist Changed

His Mind. Harper Collins, New York.

- Fox, D., 2014. Antartica's secret garden. Nature 512, 244-246.
- Frank, L.A., Sigwarth, J.B., 2001. Detection of small comets with a ground-based telescope. J. Geophys. Res. 106, 3665–3683.
- Franklin, A., et al., 2004. Human DNA polymerase-η, an A-T mutator in somatic hypermutation of rearranged immunoglobulin genes, is a reverse transcriptase. Immunol. Cell Biol. 82, 219–225. https://doi.org/10.1046/j.0818-9641.2004.01221.x.
- Gibson, C., et al., 2011. The origin of life from primordial planets. Int. J. Astrobiol. 10, 83–98. https://doi.org/10.1017/S1473550410000352. https://arxiv.org/abs/ 1004.0504.
- Gillon, et al., 2016. Temperate earth size planets transiting a nearby ultracool dwarf star. Nature 533, 221–224.
- Gold, T., 1989. New ideas in science. J. Sci. Explor. 3 (2), 103–112. http://amasci.com/ freenrg/newidea1.html.
- Gold, T., 1992. The deep hot biosphere. Proc. Natl. Acad. Sci. U.S.A. 89, 6045–6049. Gold, T., 1999. The Deep Hot Biosphere: the Myth of Fossil Fuels. Copernicus. Springer Verlag, New York.
- Gorczynski, R.M., Steele, E.J., 1980. Inheritance of acquired immunologic tolerance to foreign histocompatibility antigens in mice. Proc. Natl. Acad. Sci. U.S.A. 77, 2871–2875.
- Gorczynski, R.M., Steele, E.J., 1981. Simultaneous yet independent inheritance of somatically acquired tolerance to two distinct H-2 antigenic haplotype determinants in mice. Nature 289, 678–681. https://doi.org/10.1038/289678a0.
- Gould, SJ., Eldredge, N., 1977. Punctuated equilibria: the tempo and mode of evolution reconsidered. Paleobiology 3, 115–151.
- Grebennikova, T.V., Syroeshkin, A.V., Shubralova, E.V., et al., 2018. The DNA of bacteria of the World Ocean and the Earth in cosmic dust at the International Space Station. Sci. World J. In press.
- Harris, M.J., et al., 2002. The detection of living cells in the stratosphere. Proc.SPIE Conf. 4495, 192–198.
- Harris, R.S., Liddament, M.T., 2004. Retroviral restriction by APOBEC proteins. Nat. Rev. Immunol. 4, 868–877.
- Haynes, R., 1980. The boggle threshold. Encounter 92-96. Aug 1980.
- Hiel, C.S., et al., 2014. Functional activity of plasmid DNA after entry into the atmosphere of Earth investigated by a new biomarker stability assay for Ballistic Spaceflight Experiments. e112979 PLoS One 9.
- Hoover, R.B., 2005. Microfossils, biominerals, and chemical biomarkers in meteorites. In: Hoover, R.B., Rozanov, A.Y., Paepe (Eds.), Perspectives in Astrobiology. RR IOS Press, Amsterdam, pp. 43–65.
- Hoover, R.B., 2011. Fossils of cyanobacteria in Cl1 carbonaceous meteorites: implications to life on comets, Europa and Enceladus. J. Cosmology 16, 7070–7111.
- Hope-Simpson, R.E., 1978. Sunspots and flu: a correlation. Nature 275, 86.
- Hoyle, F., Wickramasinghe, N.C., 1976. Primitive grain clumps and organic compounds in carbonaceous chondrites. Nature 264, 45.
- Hoyle, F., Wickramasinghe, N.C., 1977a. Polysaccharides and the infrared spectra of galactic sources. Nature 268, 610–612.
- Hoyle, F., Wickramasinghe, N.C., 1977b. Identification of the 2200A interstellar absorption feature. Nature 270, 323.
- Hoyle, F., Wickramasinghe, N.C., 1978a. Calculations of infrared fluxes from galactic
- sources for a polysaccharide grain model. Astrophys. Space Sci. 53, 489–505. Hoyle, F., Wickramasinghe, N.C., 1978b. Life Cloud. J.M. Dent Ltd, London.
- Hoyle, F., Wickramasinghe, N.C., 1979. Diseases from Space. J.M. Dent Ltd, London.
- Hoyle, F., Wickramasinghe, N.C., 1981. Evolution from Space. J.M. Dent Ltd, London.
- Hoyle, F., Wickramasinghe, C., 1982. Why Neo-Darwinism Does Not Work. University College Cardiff Press. ISBN 0 906449 50 2.
- Hoyle, F., Wickramasinghe, N.C., 1985. Living Comets. Univ. College, Cardiff Press, Cardiff.
- Hoyle, F., Wickramasinghe, N.C., 1986. The case for life as a cosmic phenomenon. Nature 322, 509–511.
- Hoyle, F., Wickramasinghe, N.C., 1991. The Theory of Cosmic Grains. Kluwer, Dordrecht.
- Hoyle, F., Wickramasinghe, N.C., 1993. Our Place in the Cosmos : the Unfinished Revolution. J.M. Dent Ltd, London.
- Hoyle, F., Wickramasinghe, N.C., 1997. Life on Mars? : the Case for a Cosmic Heritage. Clinical Press Ltd, Bristol.
- Hoyle, F., Wickramasinghe, N.C., 2000. Astronomical Origins of Life: Steps towards Panspermia. Kluwer, Dordrecht.
- Hoyle, F., et al., 1982. Infrared spectroscopy over the 2.9-3.9µm waveband in biochemistry and astronomy. Astrophys. Space Sci. 83, 405–409.
- Hoyle, F., et al., 1984. The spectroscopic identification of interstellar grains. Astrophys. Space Sci. 98, 343–352.
- Hu, W.-S., et al., 2012. HIV-1 reverse transcription. Cold Spring Harb Perspect Med 2 a006882, 22 pages.
- Jablonka, E., Lamb, M.J., 1995. Epigenetic Inheritance and Evolution: The Lamarckian Dimension. Oxford University Press, Oxford.
- Jablonka, E., Lamb, M.J., 2005. Evolution in Four Dimensions: Genetic, Epigenetic, Behavioral, and Symbolic Variation in the History of Life. MIT Press, Boston. ISBN 0-262-10107-6.
- Jones, R.B., et al., 2013. LINE-1 retrotransposable element DNA accumulates in HIV-1- infected cells. J. Virol. 87, 13307–13320.
- Jönsson, K.I., et al., 2008. Tardigrades survive exposure to space in low Earth orbit. Curr. Biol. 18, R729–R731.
- Kapitonov, V., Jurka, J., 1996. The age of Alu subfamilies. J. Mol. Evol. 42, 59–65.
- Katzourakis, A., 2013. Paleovirology: inferring viral evolution from host genome

sequence data. Phil. Trans. Roy. Soc. Lond. 368, 20120493.

- Kopparapu, R.K., 2013. A revised estimate of the occurrence rate of terrestrial planets in habitable zones around Kepler M-Dwarf. Astrophys. J. 767. L8.
- Kuhn, T.S., 1970. The Structure of Scientific Revolutions, second ed. Univ. Chicago Press, Chicago,
- Lane, N., 2015. The Vital Question: Energy, Evolution, and the Origins of Complex Life. W.W. Norton & Company, London.
- Levin, G.V., 2007. Modern myths of Mars. Int. J. Astrobiol. 6, 95-108.
- Levin, G.V., 2013. Implications of Curiosity's findings for the viking labelled Release experiment and life on Mars. Instruments, methods, and missions for astrobiology XVI. In: SPIE Proc., 8865, 8865-8862.
- Levin, G.V., 2015. The curiousness of Curiosity. Astrobiology 15, 101-103. https:// doi.org/10.1089/ast.2014.1406.
- Levin, G.V., Straat, P.A., 1976. Viking Labeled Release biology experiment: interim results. Science 194, 1322-1329.
- Levin, G.V., Straat, P.A., 2016. The case for extant life on Mars and its possible detection by the Viking Labelled Release Experiment. Astrobiology 16, 798-810.
- Levison, H.F., et al., 2010. Capture of the Sun's Oort cloud from stars in its birth cluster. Science 329, 187–190. https://doi.org/10.1126/science.1187535.
- Leya, T., et al., 2017. Algae Survive outside Space Station. AlgaeIndustryMagazine.Com, 7th February, 2017. http://www.algaeindustrymagazine. com/algae-survive-outside-space-station/.
- Liscovitch-Brauer, et al., 2017. Trade-off between transcriptome plasticity and genome evolution in cephalopods. Cell 169, 191–202.
- Lin, X., 2012. MicroRNAs and unusual small RNAs discovered in Kaposi's Sarcoma-Associated Herpesvirus virions. J. Virol. 86, 12717-12730. https://doi.org/ 10.1128/IVI.01473-12.
- Lindley, R., 2010. The Soma: How Our Genes Really Work and How that Changes Everything! CYO Foundation. ISBN1451525648, POD book Amazon.com.
- Lindley, R., 2013. The importance of codon context for understanding the Ig-like somatic hypermutation strand-biased patterns in TP53 mutations in breast cancer. Cancer Genet. 206, 222-226.
- Lindley, R.A., Steele, E.J., 2013. Critical analysis of strand-biased somatic mutation signatures in TP53 versus Ig genes. In: Genome -wide Data and the Etiology of Cancer ISRN Genomics, vol. 2013. Article ID 921418, 18 pages.
- Lindley, R.A., et al., 2016. Association between targeted somatic mutation (TSM) signatures and HGS-OvCa progression. Cancer Med 5, 2629-2640.
- Liu, Y., 2007. Like father like son. EMBO Rep. 8, 798-803.
- Liu, Y., Li, X., 2016a. Darwin's Pangenesis as a molecular theory of inherited diseases. Gene 582, 19-22. https://doi.org/10.1016/j.gene.2016.01.051.
- Liu, Y., Li, X., 2016b. Darwin and Mendel today: a comment on "Limits of imagination: the 150th Anniversary of Mendel's Laws, and why Mendel failed to see the importance of his discovery for Darwin's theory of evolution". Genome 59, 75-77. https://doi.org/10.1139/gen-2015-0155.
- Louis, G., Kumar, A.S., 2006. The red rain phenomenon in Kerala and its possible extraterrestrial origin. Astrophys. Sp.Sci. 302, 175-187.
- Lutz, F.E., Grisewood, E.N., 1934. Reactions of Drosophila to 2537A radiation. Am. Mus. Novit. 706. March 1934.
- Mattick, J.S., 2012. Rocking the foundations of molecular genetics. Proc. Natl. Acad. Sci. U. S. A. 109, 16400-16401.
- McCafferty, P., 2008. Bloody red rain again! Red rain in meteors and myth. Int. J. Astrobiol. 7, 9–15.
- McLure, C.A., et al., 2013. Genomic evolution and polymorphism: segmental duplications and haplotypes at 108 regions on 21 chromosomes. Genomics 102, 15-26.
- Miyake, N., et al., 2010. Identification of micro-biofossils in space dust. J. Cosmology 7, 1743–1749
- Muotri, A.R., et al., 2007. The necessary junk: new functions for transposable elements. Hum. Mol. Genet. 16 (2), R159-R167. https://doi.org/10.1093/hmg/ ddm196.
- Napier, W.M., et al., 2007. The origin of life in comets. Int. J. Astrobiol. 6, 321-323.
- Noble, D., 2011. A Theory of Biological Relativity: No Privileged Level of Causation Interface Focus Royal Society Publishing. https://doi.org/10.1098/rsfs.2011.0067. Published 9 November 2011.
- Noble, D., 2013. Physiology is rocking the foundations of evolutionary biology. Exp. Physiol. 98 (8), 1235–1243.
- Noble, D., 2017. Dance to the Tune of Life. Cambridge University Press. ISBN 1-107-17624-9.
- Noble, D., et al., 2016. New Trends in Evolutionary Biology: Biological, Philosophical and Social Science Perspectives. The Royal Society, London, 6-9 Carlton House Terrace, London, SW1Y 5AG Nov 7 -9, 2016. Editors-Organisors. https:// royalsociety.org/science-events-and-lectures/2016/11/evolutionary-biology/
- Oliver, K.R., Greene, W.K., 2012. Transposable elements and viruses as factors in adaptation and evolution: an expansion and strengthening of the TE-Thrust hypothesis. Ecol. Evol. 2 (11), 2912-2933. https://doi.org/10.1002/ece3.400.
- Paules, C.I., et al., 2017. The pathway to a universal influenza vaccine. Immunity 47, 599-603.
- Paz-Yaacov, N., et al., 2010. Adenosine-to-inosine RNA editing shapes transcriptome diversity in primates. Proc. Natl. Acad. Sci. U.S.A. 107, 12174-12179.
- Pflug, H.D., Heinz, B., 1997. Analysis of fossil organic nanostructures: terrestrial and extraterrestrial. SPIE Proc. Instrum. Methods Missions Investigation Extraterr. Microorg.. 86, 3111. https://doi.org/10.1117/12.278814. July 11, 1997.
- Pirakitikulr, N., et al., 2016. The coding region of the HCV genome contains a network of regulatory RNA structures. Mol. Cell 61, 1-10.

- Priscu, J.C., Christner, B.C., 2004. Earth's icy biosphere. In: Bull, A. (Ed.), Microbial Diversity and Bioprospecting. ASM Press, Washington, D.C., pp. 130–145. Chap
- Qu, J., 2016. Is sunspot activity a factor in influenza pandemics? Rev. Med. Virol. 26,
- 309–313. https://doi.org/10.1002/rmv.1887.
  Rauf, K., Wickramasinghe, C., 2010. Evidence for biodegradation products in the interstellar medium. Int. J. Astrobiol. 9, 29–34.
  Refsland, E.W., Harris, R.S., 2013. The APOBEC3 family of retroelement restriction
- factors. Curr. Top. Microbiol. Immunol. 371, 1-27. https://doi.org/10.1007/978-3-642-37765-5 1
- Rothenfluh, H.S., 1995, Hypothesis: a memory lymphocyte specific soma-togermline genetic feedback loop. Immunol. Cell Biol. 73, 174–180.
- Ruff, S.W., Farmer, J.D., 2016. Silica deposits on Mars with features resembling hot spring biosignatures at El Tatio in Chile
- Nat. Commun. Now. 7, 13554. https://doi.org/10.1038/ncomms13554.
- Rvan, F., 2009, Virolution, Collins, London,
- Sanjuan, R., 2010. Mutational fitness effects in RNA and single-stranded DNA viruses: common patterns revealed by site-directed mutagenesis studies. Phil Trans R Soc B 365, 1975–1982. https://doi.org/10.1098/rstb.2010.0063.
- Sanjuan, R., 2012. From molecular genetics to phylodynamics: evolutionary relevance of mutation rates across viruses. PLoS Pathog. 8 (5), e1002685. https:// doi.org/10.1371/journal.ppat.1002685.
- Sanjuan, R., Domingo-Calap, P., 2016. Mechanisms of viral mutation. Cell. Mol. Life Sci. 3, 4433-4448. https://doi.org/10.1007/s00018-016-2299-6.
- Sanjuan, R., et al., 2004. The distribution of fitness effects caused by singlenucleotide substitutions in an RNA virus. Proc. Natl. Acad. Sci. U.S.A. 101, 8396-8401. https://doi.org/10.1073/pnas.0400146101.
- Sanjuan, R., et al., 2010. Viral mutation rates. Virology 84, 9733-9748. https:// doi.org/10.1128/JVI.00694-10.
- Sharma, U, et al., 2015. Biogenesis and function of tRNA fragments during sperm maturation and fertilization in mammals. Science 351, 391-396.
- Shi, M., et al., 2016. Redefining the invertebrate RNA virosphere. Nature 540, 539-543. https://doi.org/10.1038/nature20167.
- Shivaji, S., Chaturvedi, P., Begum, Z., et al., 2009. Janibacter hoylei sp. nov., Bacillus isronensis sp. nov. and Bacillus aryabhattai sp. nov., isolated from cryotubes used for collecting air from the upper atmosphere. Int. J. Syst. Evol. Microbiol. 59, 2977-2986
- Smith, W.E., September 26, 2013. 2013. Life is a cosmic phenomenon: the "Search for Water" evolves into the "Search for Life". In: Hoover, R.B., Levin, G.V., Rozanov, A.Y., Wickramasinghe, N.C. (Eds.), Proc. SPIE 8865, Instruments, Methods, and Missions for Astrobiology XVI. San Diego, California, United States. https://doi.org/10.1117/12.2046862.
- Snyder, D.P., 2015. The origins of megacryometeors: troposphere or extraterrestrial? Cosmology 19, 70-86 (Cosmology.com).
- Spadafora, C., 2008. Sperm-mediated "reverse" gene transfer: a role of reverse transcriptase in the generation of new genetic information. Hum. Reprod. 23, 735-740. https://doi.org/10.1093/humrep/dem425.
- Steele, E.J., 1979. Somatic Selection and Adaptive Evolution : on the Inheritance of Acquired Characters, first ed. University of Chicago Press, Chicago. Williams-Wallace, Toronto, 1979; 2nd Edit.
- Steele, E.J., 2014. Reflections on ancestral haplotypes: medical genomics, evolution and human individuality. Perspect. Biol. Med. 57, 179-197.
- Steele, E.J., 2015. Ancestral Haplotypes: Our Genomes Have Been Shaped in the Deep Past. Nearurban Dallas, Tx, ISBN 978-0-9864115-0-2.
- Steele, E.J., 2016a. Origin of congenital defects: stable inheritance through the male line via maternal antibodies specific for eye lens antigens inducing autoimmune eye defects in developing rabbits in utero. In: Levin, M., Adams, D.S. (Eds.), Ahead of the Curve -Hidden Breakthroughs in the Biosciences Chapter 3. Michael Levin and Dany Spencer Adams IOP Publishing Ltd 2016, Bristol, UK.
- Steele, E.J., 2016b. Somatic hypermutation in immunity and cancer: critical analysis of strand-biased and codon-context mutation signatures. DNA Repair 45, 1-24. https://doi.org/10.1016/j.dnarep.2016.07.001.
- Steele, E.J., Dawkins, R.L., 2016. New Theory of HIV Diversification : Why it May Never Be Possible to Make a Protective Vaccine viXra.org 1612.0346. http:// viXra.org/abs/1612.0346.
- Steele, E.J., Lindley, R.A., 2017. ADAR deaminase A-to-I editing of DNA and RNA moieties of RNA: DNA hybrids has implications for the mechanism of Ig somatic hypermutation. DNA Repair 55, 1-6.
- Steele, E.J., Lloyd, S.S., 2015. Soma-to-germline feedback is implied by the extreme polymorphism at IGHV relative to MHC. Bioessays 37, 557-569.
- Steele, E.J., Gorczynski, R.M., Pollard, J.W., 1984. The somatic selection of acquired characters. In: Pollard, J.W. (Ed.), Evolutionary Theory: Paths into the Future. John Wiley, London, pp. 217–237.
- Steele, E.J., Lindley, R.A., Blanden, R.V., 1998. In: Davies, Paul (Ed.), Lamarck's Signature : How Retrogenes Are Changing Darwin's Natural Selection Paradigm. Allen & Unwin, Frontiers of Science: Series. Sydney, Australia, 1998.
- Strugnell, J., Nishiguchi, M.K., 2007. Molecular phylogeny of coleoid cephalopods (Mollusca: cephalopoda) inferred from three mitochondrial and six nuclear loci: a comparison of alignment, implied alignment and analysis methods. J. Molluscan Stud. 73, 399-410.
- Strugnell, J., et al., 2005. Molecular phylogeny of coleoid cephalopods (Mollusca: cephalopoda) using a multigene approach; the effect of data partitioning on resolving phylogenies in a Bayesian framework. Mol. Phylogenet. Evol. 37, 426-441

Strugnell, J., et al., 2006. Divergence time estimates for major cephalopod groups:

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evidence from multiple genes. Cladistics 22, 89–96.

Telesnitsky, A., Wolin, S.L., 2016. The host RNAs in retroviral articles. Viruses 8, 235. https://doi.org/10.3390/v8080235, 15 pages.

- Temin, H.M., 1974. On the origin of the RNA tumor viruses. Annu. Rev. Genet. 8, 155–177.
- Tepfer, D., Leach, S., 2017. Survival and DNA damage in plant seeds exposed for 558 and 682 Days outside the international space station. Astrobiology 17, 205–215. Tegmark, M., 2014. Our Mathematical Universe. Random House, New York.
- Tian, C., et al., 2007. Virion packaging determinants and reverse transcription of SRP RNA in HIV-1 particles. Nucleic Acids Res. 35, 7288–7302. https://doi.org/ 10.1093/nar/gkm816.
- Vanysek, V., Wickramasinghe, N.C., 1975. Formaldehyde polymers in comets. Astrophys. Space Sci. 33, L19–L28.
- Villarreal, L.P., 2004. Can viruses make us human? Proc. Am. Phil. Soc. 148, 296–323.
- Wainwright, M., Wickramasinghe, N., Narlikar, J., Rajaratnam, P., 2003. Microorganisms cultured from stratospheric air samples obtained at 41km. FEMS Microbiol. Lett. 218, 161–165.
- Wainwright, M., et al., 2014. Recovery of cometary microorganisms from the stratosphere. Astrobiol Outreach 2 (1). https://doi.org/10.4172/2332-2519. 1000110.
- Wainwright, M., et al., 2015a. Biological entities isolated from two stratosphere launches-continued evidence for a space origin J. Astrobiol Outreach 3 (2). https://doi.org/10.4172/2332-2519.1000129.
- Wainwright, M., et al., 2015b. Masses staining positive for DNA-isolated from the stratosphere at a height of 41 km. Astrobiol Outreach 3 (2). https://doi.org/10. 4172/2332-2519.1000130.
- Wickramasinghe, N.C., Rycroft, M., 2018. Transport of submicron dust including bacteria from the Earth's surface to the high ionosphere. Adv. Astron. Astrophys. In press.
- Walker Jr., J., Wickramasinghe, C., 2015. Big Bang and God an Astro-theology. Palgrave Macmillan, US.
- Wallis, M.K., 2007. Exotic amino acids across the K/T boundary cometary origin and relevance for species extinction. Int. J. Astrobiol. 6, 303–306.
- Wallis, J., et al., 2013. The Polonnaruwa meteorite oxygen isotope, crystalline and biological composition. J. Cosmol. 21, 10004–10011.
- Wallis, M.K., Wickramasinghe, N.C., 2015. Rosetta images of Comet 67P/Churyumov-Gerasimenko: inferences from its terrain and structure. J. Astrobiol Outreach 3 (1). https://doi.org/10.4172/2332-2519.1000127.
- Wesson, P., 2011. Necropanspermia. Observatory 131, 63-66.
- Wickramasinghe, N.C., 1974. Formaldehyde polymers in interstellar space. Nature

252, 462-463.

- Wickramasinghe, N.C., 2010. The astrobiological case for our cosmic ancestry. Int. J. Astrobiol. 9, 119–129.
- Wickramasinghe, C., 2011. Viva panspermia. Observatory 131, 130–134.
- Wickramasinghe, N.C., 2012. DNA sequencing and predictions of the cosmic theory of life. Astrophys. Space Sci. 343, 1–5.
- Wickramasinghe, N.C., et al., 2012. Life-bearing primordial planets in the solar vicinity. Astrophys. Space Sci 341, 295–299.
- Wickramasinghe, Chandra, 2015a. The Search for Our Cosmic Ancestry. World Scientific, Singapore.
- Wickramasinghe, Chandra, 2015b. Vindication of Cosmic Biology. Tribute to Sir Fred Hoyle (1915-2001). Edit. Chandra Wickramasinghe, World Scientific, Singapore.
- Wickramasinghe, D.T., Allen, D.A., 1986. Discovery of organic grains in Comet Halley. Nature 323, 44–46.
- Wickramasinghe, C., Smith, W.E., 2014. Convergence to panspermia. Hypothesis 12 (1), e9,. https://doi.org/10.5779/hypothesis.v12i1.358.
- Wickramasinghe, N.C., Steele, E.J., 2016. Dangers of adhering to an obsolete paradigm: could Zika virus lead to a reversal of human evolution? J. Astrobiol. Outreach 4 (1). https://doi.org/10.4172/2332-2519.1000147.
   Wickramasinghe, N.C., Tokoro, G., 2014a. Life as a cosmic phenomenon: 1 the socio-
- Wickramasinghe, N.C., Tokoro, G., 2014a. Life as a cosmic phenomenon: 1 the socioeconomic control of a scientific paradigm. J. Astrobiol.Outreach 2 (2). https:// doi.org/10.4172/2332-2519.1000113.
- Wickramasinghe, N.C., Tokoro, G., 2014b. Life as a cosmic phenomenon: 2.The panspermia trajectory of Homo sapiens. J. Astrobiol Outreach 2 (2). https://doi. org/10.4172/2332-2519.1000115.
- Wickramasinghe, N.C., et al., 1996. Eruptions of comet hale-bopp at 6.5AU. Astrophys. Space Sci. 240, 161–165.
- Wickramasinghe, J.T., et al., 2009. Liquid water and organics in Comets: implications for exobiology. Int. J. Astrobiol. 8, 281–290.
- Wickramasinghe, J.T., et al., 2010. Comets and the Origin of Life. World Scientific, Singapore.
- Wickramasinghe, N.C., et al., 2015. Rosetta studies of Comet 67P/Churyumov–Gerasimenko: prospects for establishing cometary biology. J. Astrobiol. Outreach 3 (1). https://doi.org/10.4172/2332-2519.1000126.
- Wickramasinghe, N.C., et al., 2017. Sunspot cycle minima and pandemics: the case for vigilance? ? J. Astrobiol. Outreach 5 (2). https://doi.org/10.4172/2332-2519. 1000159.
- Yohn, C.T., Jiang, Z., McGrath, S.D., Hayden, K.E., Khaitovich, P., et al., 2005. Lineagespecific expansions of retroviral insertions within the genomes of african great apes but not humans and orangutans. PLoS Biol. 3, e110.