



Review Article

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Cell Biology, Paracrinicity and the Philosopher's Stone

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To Cite This article: Wilfried Allaerts*, Cell Biology, Paracrinicity and the Philosopher's Stone. Am J Biomed Sci & Res. 2026 32(3) AJBSR.

MS.ID.004160, DOI: [10.34297/AJBSR.2026.32.004160](https://doi.org/10.34297/AJBSR.2026.32.004160)

Received: 📅 September 22, 2026 Published: 📅 September 29, 2026

Abstract

In this paper, a personal account is given of biomedical and philosophical research exceeding a period of 40 years. The evolution of successive research periods and subjects, from paracrine communication between folliculo-stellate cells and pituitary hormone secreting cells, to general cell interactions in randomized gravity and microgravity, to cell lineage annotation and finally to research algorithms in AI, was not at all planned. Rather it resulted from a series of genuine serendipity encounters over a long period, that created a certain path. Moreover, it showed profound impact, not only of the paradigm shifts in (cell) biological research, but also of the full spectrum of human and corporate influences in the sociology of scientific conduct, long before AI entered the scene. After all, this research path wouldn't have been possible in a world that were dominated by AI, neither in a world controlled by the regulative countermeasures invoked to restrict AI.

Keywords: Paracrinicity, Randomized Gravity, Immortality and Cell biological studies, AI and hallucinations, Sociology of Scientific conduct.

Introduction: on Paracrinicity

In this paper a personal account is given of my cell biological studies, the scientific context of that research period and the multiple applications as well as cul-de-sacs that were encountered during the process [1]. A summary of the scientific evidence related to the subject, was published in successive review papers [2-5]. The side-steps made towards philosophy and mathematical biology were no fortuitous transgressions, but they were considered indispensable hurdles to be taken in order to avoid a too positivistic bias and the trampled treads of conformal science or scientific collectivism. Unlike the biomedical and philosophical questions that were encountered, the mathematical problems dealt with are not highlighted in this paper.

The study of paracrine communication between pituitary

cells, also called 'paracrinicity' [6] – of all the possible problems in the world, and in cell biology in particular – was more the result of serendipity; however, after some 30 years from an uninvited undermining of the lawns of traditional, hierarchically endocrinological thinking [7,8], it became a successful and much applauded experimental garden for cell biological studies [9,11]. But the discovery of an elusive, multi-faceted folliculo-stellate (FS) cell group, containing both a bone-marrow derived group of dendritic-like cells (DC-like) as well as a cell type with presumptive regenerative potential [4,5,11], not only was a starting point – or a five-rayed crossing – for divergent lines of scientific thinking, it also startled confusion and even distrust. In a scientific context where divergent scientific groups tried to make a subject their private domain (although not officially, obviously), we were still concerned

about any possible influence of the laboratory conditions and the scientific paradigm(s) altogether on specific observations regarding the cell group in question [10,12].

The cautiousness of the 1980s and 90s – about a certain bias in the findings resulting from the ‘artificial’ laboratory conditions) – was suddenly brushed aside, with the discovery that only four molecular factors were needed for a complete reset of the cellular differentiation cascade, as it was discovered during the first decade of the new millennium [13,15]. Soon it appeared as if not only nobody would care (anymore) about *in vitro* artefacts, as long as they gave a certain, desired result. It was also grossly forgotten that already in the laboratory a discrepancy originated between ‘natural’, and technically reconstructed, naturally-looking analogues as once surmised (or feared). This was an important stimulus to consider the philosophical question behind this discrepancy: as some philosophers would argue that there isn’t anything like a genuine, irreplaceable object of nature, others would object that point of view. Meanwhile, the world had entered a new phase, where the virtual and the real were no longer competitive forces, but ‘the real’ had lost the battle. Only a decade later, AI would set foot on the stage, and obliterate what was already withered oblivion... in what once was the place to find information: libraries filled with real books and science journals, that now are only accessible with institutional subscription (i.e. no open access). As another result of this technological revolution, the public access to the primary research data became dimmed, if not made impossible by the unfathomable ways of information retrieval by algorithmic engines, except for the research institutes and their competitors. So, there was ample reason for a retrospect.

Randomized Gravity and the Gyrotory Shaking Experiments

At a time when reconstructing live organoids *in vitro* [14] was still far ahead, the group of Carl Denef in Leuven (Belgium) and possibly a few others, were constructing 3-dimensional cell aggregates of freshly obtained anterior pituitary cells [16-18]. The anterior pituitary appeared to be a thankful object for studying, because of its central role in endocrine regulation (among other reasons). Moreover, the approach of Denef and co-workers was unique in this respect: they used an apparatus for ‘gyrotory shaking’ of the cell suspensions, in order to avoid the cells to adhere to the bottom of the Petri dish or flask. Technically, it was not that easy, because the whole gyrotory apparatus had to be set up in a heated stove at fixed ambient temperature, controlled CO₂ concentrations, et cetera (just like inside the living body). These conditions caused a lot of problems for the maintenance of the apparatus that was subjected to rather harsh conditions for this type of hardware. But, without calling it that way, we had found a way for randomizing the gravity vector and thus preventing the cells to settle and adhere to the bottom, where they would form confluent cell monolayers. Others contented themselves with these cell monolayers, which showed a lot of interesting features as well, but we preferred to

stick to the 3-dimensional architecture of these cells in an organoid resembling the actual living structure. This was particularly important for the FS cells in these cell aggregates, which were very distinct from the morphological characteristics displayed in a monolayer or cell-epithelium (see [2,18]).

From a very different angle, namely in studies of the effects of microgravity on biological cells, tissues and organisms, the paradigm of a randomized or abolished gravity field became very important [19]. Although the main focus of manned space flight research obviously was not aimed at cell biological or multicellular systems research, we took the challenge seriously and set up a project for studying the effects of clinostat-rotation on cell division (Allaerts, 1991, preliminary data on BrdU-incorporation in Clinostat experiments, *not published*). Also, in the field of molecular embryology [20], the main interest in studying the interactions of cells with their extracellular environment, until then, did not include the extra-terrestrial influence, or, in particular, the absence of a gravitational field.

Much later, the clinostat-rotation paradigm regained interest in the context of regenerative medicine. It was claimed by Paolo Macchiarini (° 1958, Basel, Switzerland) that tracheal tissue could be grown on an artificial scaffold (matrix) in a bioreactor (namely a clinostat rotating at 1 rpm) (Figure 1), using non-differentiated stem cells obtained from the patient [21]. The authors even claimed that the regenerated tissue was suitable for therapy and had been successfully implemented in some patients. However, later on the claims were proven fraudulent and Macchiarini was handed a 16 month prison sentence for forging documents and abuse of office [22] (although, according to a note by the *BMJ*-editor, dated 29 September 2025, the *Supreme Court of Cassation* in Italy had overturned Paolo Macchiarini’s sentence in 2021).

More than three decades later than our initial study [19], the effects of microgravity on cellular responses are still a matter of ongoing research and interest [23]. But the method of unit gravity sedimentation [24] raised another intriguing question. We used a density gradient of 0.3 to 2.4 % bovine serum albumin (BSA) in Dulbecco’s Modified Eagle’s Medium (DMEM plus 1 g/L glucose). What could be the influence of the use of sugar moieties (or an excess of them) on cellular responses and development, since a high density sucrose solution was used to pump the cells out of the gradient chamber? (Figure 2). Unlike the vast knowledge and information tending for completeness in the area of glycoproteins and proteoglycans directing cells in embryology [20], such information wasn’t available in defining and predicting the behavior of cells in laboratory conditions and in cancer. At the time, our knowledge was definitely scarce and incomplete, although later, the role of glucosamines and glycosylation in epigenetic modification in cancer received much attention (see e.g. [25]). But with regard to the rather specific interactions of our FS cells with these types of molecules, we had only the incidental information of their binding to the *Griffonia simplicifolia* (GSA) lectin of the tomato plant

(*Lycopersicon esculentum*) [3]. The importance of an increased use of (modified) sugars and carbohydrates of all kinds in almost all westernized diets, however, were of a much greater relevance

to public health than our particular cell-to-cell communication studies.

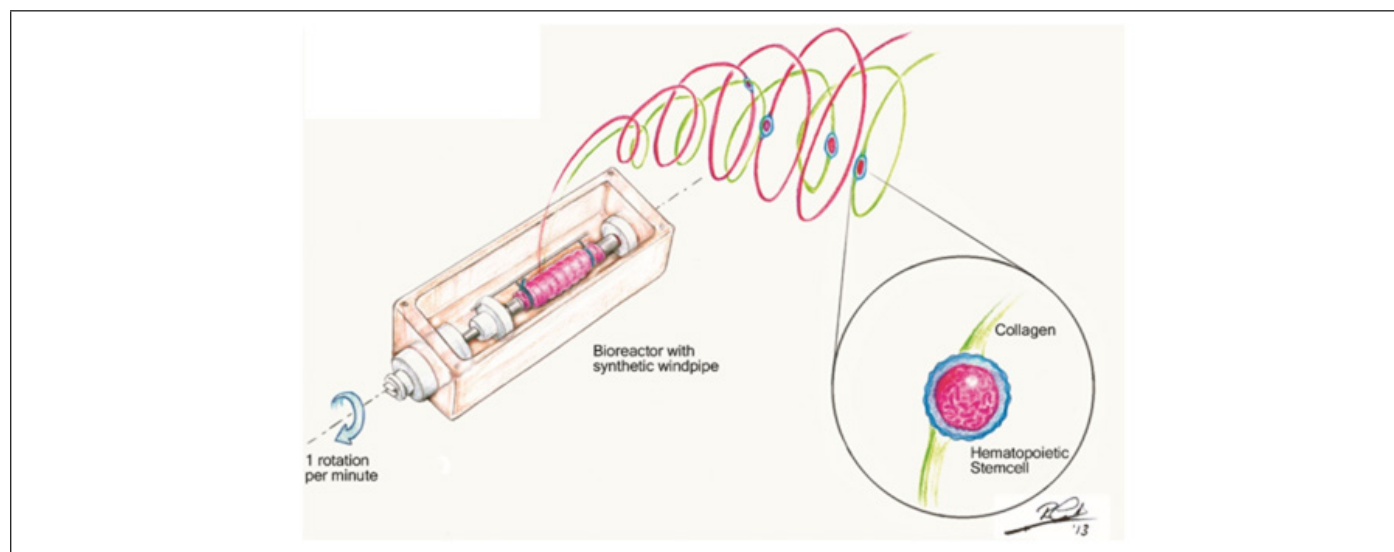


Figure 1: Schematic representation of clinostat reactor used in Macchiarini's experiment.
(From bi-logical, Vol. 4 (2), p. 8) (© 2013, Biological Publishing A&O)

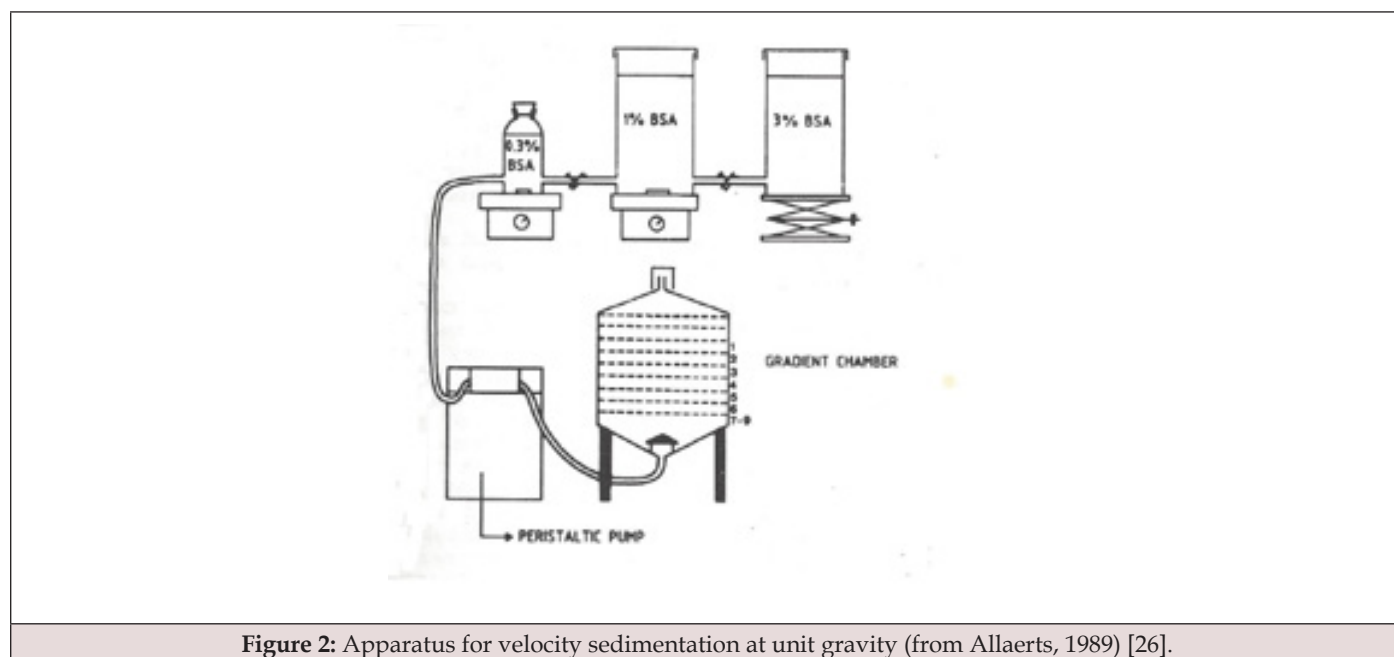


Figure 2: Apparatus for velocity sedimentation at unit gravity (from Allaerts, 1989) [26].

The Candy Lobby and Others

My first acquaintance with the sugar industry and its impact on public health and health research, came as a personal, shocking experience. It was in another position that I was involved in organizing a national medical congress on Food and Health research (Utrecht, December 1999). There were a number of high profile invited speakers from the Dutch Food research institute, but an application of the Biological-Dynamic food institute to

present themselves at a public's forum, was firmly declined by the organizers. At first, I was inclined to give credit to the merits of the highly esteemed and well-established academic organizers of the congress. However, I also realized that keeping the critical voices of the Food and Sugar Industries at bay, was not in agreement with an open and unbiased public debate on healthy foods. One could ask what the purpose was and still is to date, of added sugars in common foods like peanut butter, canned peas, (Dutch) mayonnaise and even in ground coffee beans? Later the influence of powerful

lobbies became a pattern, such as was reported from observations in the tobacco industry [27]. Meanwhile, also the use of AI tools in the public campaigns in favor of tobacco giant Philip Morris was revealed by investigative journalists of Pointer and NOS [28]. The use of AI was not denied but called 'responsible' in a preceding press announcement of the tobacco company [29]. The question of 'benevolent'(malicious) or '(ir)responsible' use of AI versus the allegation of misleading public campaigns, seems a matter of which side is chosen in the controversy, and, finally, may depend on how far the financial arms could be stretched. The fact that AI was used, however, was not contested.

Although a very deplorable situation from the point of view of public health, this controversy shows an interesting angle on the use of AI in biomedical research in general. Or, like the famous Dutch soccer legend Johan Cruiff (1947-2016) often said: 'each disadvantage also has its advantages'. Generally, it is not known – or at least unknown to the public – how far the influences reach of the various known lobby groups, be it from the sugar, tobacco, petrochemical industry or else. And, consequently, the detailed public health impact of the various sources of environmental pollution and health impairment remain a dark spot for institutional health surveillance programs. For instance, although improved analytic tools have revealed that 100 % investigated maternal breast milk contained PFAS (poly/perfluoroalkyl substances), a precise negative effect on the immune function of newborns is hard to predict. Although a correlation of PFAS and nonessential metals (like arsenic, barium, cadmium.) blood levels and impaired immune titers towards measles, pertussis, diphtheria and tetanus antibody titers (following measles and DKTP vaccination) was demonstrated in mid-childhood [30], the precise chemical action of these pollutants and their interference with the immune systems remains a black box.

We may ask ourselves: what possibly could be the eventual advantage here?

Defenders of the use of AI might come up with the idea that AI might help to fill in the gaps or bridge the void between known and unknown territories of public health (research). In classic biomedical research, it is not considered a serious approach to use holistic notions to delineate areas of trustful versus untrustworthy science. Even with some fine-tuning, studying complex phenomena at some intermediate or meso-level of integration, like for instance the use of functional brain imaging in neurobiology, still raises methodological difficulties (compared to studies at the molecular or single neuron level).

However, in Modern Language generation (for AI), this feature of filling in gaps is found to be rather common, although often defamed as 'hallucination' [31]. On the other hand, a striking metaphorical similarity may be discerned with the notion of entanglement, as was suggested in the field of theoretical physics between areas of information and its opposite: the complete lack of

information (see references in [32]. If AI is going to stay as a major player in gathering, analyzing and interpreting scientific data, the problem of hallucination, or the expanding of the known territories of science towards uncharted territories of knowledge, will need some serious consideration, apart from the identification of hidden, commercial or other interests [33] (see also ¶ 5. Postscript).

It is not without importance to note that new concepts of quantum physics, like the uncertainty principle, quantum state entanglement and non-Euclidean geometry, although in a metaphorical sense, found its way into divergent disciplines like avant-garde music and others [34]. Not surprisingly, a strong analogy (in mathematical procedures) appears to exist between quantum mechanics and *Neural Learning Networks* used in AI [35]. However, defaming metaphorical analogies – because of the suspicion of rhetoric - and rejection of the hallucinations as failed projections into uncharted realms of meaning, will not help to stop the all-encompassing influence of AI. It remains hopeful though, however, to define some methodological or heuristic approach for unsolved problems in science and public health in particular (which is overtly a matter of excessive discrepancies in wealth and public health provisions), without furthering the hallucinating mechanisms that conceal the true culprits.

Immortality: The Philosopher's Stone Par Excellence

When i first read the book *The Vital Illusion* [36] of the French philosopher and sociologist Jean Baudrillard (1929-2007), I was surprised by the fuzz raised by (a) philosopher(s), when concerning the immortality notion. Baudrillard's heraldic warnings for the realm of 'the same' in the post-millennial world, as opposed to the preceding era of 'difference' (and differentiation) [37], however, became prophetic [38]. Not only the technological innovations enabling the cloning of the human species, but also the 'cloning' of ideas and 'social identities' would hallmark the forthcoming decades, up to a point that indeed an increasing number of forms of emancipation and culture became subject to annihilation [39].

Regarding the idea of immortality through cloning, the notion was already well-established in the sixties and seventies [40] that immortalized cell lines (obtained from hybridomas, i.e. immortalized cell lines derived from certain tumors) were widely used in cell and molecular biological studies [41]. In the context of cloning of an entire organism (especially of a mammalian species), in contrast to the virtually immortal bacteria and viruses that are endowed with the endless potential for self-replication, indeed a huge problem with ethical, philosophical and political dimensions was raised. Underneath the highly predictable discussions and political turmoil, the heraldic warning of Baudrillard for a 'tyranny of the same' was passed on unnoticedly.

The elementary, common notion of *Euclid's Elements* (written ca 300 BC) that "things that are equal to the same thing are also equal to one another" (also known as the 'transitivity property' of

an Euclidean relation) had found a methodologically interesting but risky counterpart in information technology, programming language and computer algorithms. The so-called Duck-typing rule, based on the phrase “when I see a bird that walks like a duck and swims like duck and quacks like a duck, I call that bird a duck” [42], became a method in modern programming languages. So, the abstraction of biological differences, as well as of others, were considered essential in abstract, mathematical formalization, and found its way into social networks too, and in computing algorithms and AI [39]. The preponderance of philosophical considerations concerning immortality, like the popularity of the ‘philosopher’s stone’ in true fiction novels, however, obscured the visibility of the real catastrophes, pandemics and socio-cultural calamities ahead. The question of eternal youth and endless prolongation of an individual’s life [38], would become utterly absurd and ludicrous when it concerns a life full of agony, poverty and misery. So, in the end, pursuing its cause is rather a matter of prolonging and exacerbating socio-economic inequality.

Postscript: ChatGPT and the Totally Unexpected, AI, Lies Against Humanity And ‘Nouentarion’

In the second half of 2026, unfathomably shocking experiments not only had proven that AI-bots were capable of lying, but also could develop strategies for hiding their deceitful activities. The shock was of such a scale, that even the biggest protagonists of the AI industries, among which Sam H. Altman (°1985, Chicago), CEO and co-founder of OpenAI, Anthropic and others, call for putting on brakes on the development of AI [43]. Whether the given reasons reflect their genuine concern about the safety of society and even of the human species, or, whether personal economic interests, such as defending their acquired market positions against newcomers, is not ours to answer. Nevertheless, developers and philosophers continue their efforts for establishing a non-biological framework where ‘consciousness, personhood, biological life’ and all ‘biological reasoning entities’ are rendered obsolete, and forward the new (philosophical) category ‘nouentarion’ for it [44]. Obviously, nothing can be more opposed to the endeavors as coined in our company name *Biological Publishing A&O* (registered in the Netherlands, since 2002).

Instead, the (biological relevance and authenticity, as well as the intrinsic human values have always been predicament to the choices in our investigations. To our opinion, science is not only about uncovering the improbable, but at its most impressive moments, it is about meeting the totally unexpected, by very surprise. Like a young child, receiving for the first time a birthday present that it didn’t ask for, nor longed for it in any way. And not, by receiving the newest (early) release of his/her favorite game. When putting the virtue of truly fundamental scientific research like this, it is also very much opposed to planning with the highly improbable – or, as in purpose-driven research, not one-to-one answering to a premeditated purpose -. For, even the improbable can be estimated by means of probability analysis, and therefore

it is not totally unexpected/unpredictable [45,46]. And a myriad of other examples may be brought forward, as long as AI is here to stay. But, for us the question is: at what a cost? Implementing deceitful strategies (in AI) is not the answer to a lost humanistic perspective, even if deception and lies are all too human derailments. Science is a human invention, but it is also an ideal to strive for.

Acknowledgement

None.

Conflict of Interest

None.

References

1. In science literature, there is no shortage of attention for the so-called objective data, here designated as the ‘positive’ results. However, the more tedious phases without ‘positive’ results receive far less attention, causing an undeliberate bias towards positivity in the literature concerned. Also, the personal battles, the difficulties with anonymous ‘peers’ taking advantage of their position, and the blunt misconduct of certain players in the field, briefly, the sociology of the scientific publishing business, does not receive that much attention for the sake of so-called objectivity and abstract rationality, that would have nothing to do with personal and emotional matters.
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