



Cellular differentiation as a candidate “new technology” for the Cambrian Explosion

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Abstract

Almost all of the modern animal phyla appear to originate in a relatively compressed interval of time known as the Cambrian Explosion. Although several factors have been identified that may have enabled the Cambrian Explosion, there remains the question of the final trigger. The development of cellular differentiation, the capacity of a cellular lineage to become specialized permanently in response to external signals, is proposed as the trigger. Cnidaria and eukaryotic slime molds, which pre-date the Cambrian, have specialized cellular functions but their cells do not appear to differentiate irreversibly. With differentiation, cellular roles can be fixed during embryogenesis. Fixed cellular roles may have enabled more complex and more competitive organisms, perhaps by facilitating multi-scale structures in organs or increasing the stability and reliability of network systems including synaptic connections. A candidate evolutionary pathway to cellular differentiation is proposed.

Introduction

For reasons that have remained unclear, almost all of the modern animal phyla arrive in the fossil record during a geologically short period of about twenty million years, starting about 540-545 million years ago (Baker, 2006; Valentine, Jablonski, and Erwin, 1999). The Cambrian Explosion has been a unique and troubling anomaly in the history of life.

Various attempts have been made to explain the Cambrian Explosion. Rapid change following a long period of quasi-stasis suggests the existence of a triggering or enabling event, either external to organisms or incorporated in organisms. It has been noted that the oxygen content of the atmosphere was slowly rising (Thomas, 1997). This was likely an enabler, and has been suggested as a trigger by Ohno (1997),

but it fails to explain why the development of new body types was so abrupt. Other proposed enablers include the development of complex multicellular animals (metazoans) during the previous Ediacaran period, and the disappearance of the worldwide ice sheets that preceded that period.

Around the time of the Cambrian Explosion, the geological record indicates several shifts in the ratio of various isotopes that are differentially concentrated by metabolism, which implies that biological productivity changed around that time. However, it has been unclear whether this was a result of some unknown environmental factor that may have contributed to or triggered the Cambrian Explosion, or whether it was simply a result of the shifting populations caused by the Cambrian Explosion (Brasier, Corfield, Derry, Rozanov, and Zhuravlev, 1994).

In the absence of any clear external trigger, it is reasonable to look for a biological capability that may have triggered the explosion – a capability, newly developed, which allowed or promoted the development of diverse and disparate life forms that were previously not favored, or perhaps not even possible. For example, the development of eukaryotic cells might have represented a candidate trigger; however, there is clear fossil evidence of eukaryotes at least several hundred million years prior to the Cambrian Explosion (Marshall, 2006). Some apparently bilateral animals have been found 40-55 million years before the Cambrian (Chen, Bottjer, Oliveri, Dornbos, Gao, Ruffins, and Li, 2004), so the development of bilaterian body plans probably was not the final trigger.

It has been suggested that the development of eyes triggered the Cambrian Explosion (Parker, 2003). However, if the Cambrian Explosion was triggered by the development of a new biological capability, then we should not expect to find that capability in animals that pre-date the Cambrian by many millions of years, such as the Cnidarians. Modern jellyfish have Hox genes and some have eyes, which suggests that neither of those innovations was the trigger.

Butterfield (2007) describes the increasing impact of coevolution during the Ediacaran and early Cambrian periods. A new and highly advantageous biological capability would make the animal lineage that developed it highly competitive. Instead of coevolving with existing Ediacaran fauna, the improved animals might quickly drive many Precambrian lineages into extinction and fill their niches with rapidly diversifying body plans. A reasonable comparison for the rate of disruption might be the introduction of rats and other invasive species to an island ecosystem. It may be worth noting that animals which first appear in the Cambrian strata are all bilaterian (even starfish have bilateral embryos), while Precambrian fauna included radially symmetrical animals. This line of reasoning also suggests that we may be able to identify a trigger by looking for differences between Cambrian and Precambrian animals.

Cellular differentiation

Cells in modern animals are, for the most part, differentiated: locked irrevocably into particular roles, and incapable of producing tissue types outside these roles. Cases of dedifferentiation have been observed in the animal kingdom, notably in the regeneration process of salamanders (Echeverri, Clarke, and Tanaka, 2001), but these are notable exceptions to the rule. The mechanisms of cellular differentiation are a topic of ongoing research. Specialization, in which cells exhibit variable behavior and somatic roles in response to chemical control signals, must be distinguished from differentiation, in which cells become near-irreversibly locked into a particular functional role.

Examples of specialization without differentiation can be found in descendants of Precambrian animals. For example, the polyps of modern jellyfish include highly specialized cells, but jellyfish can reproduce by polyp defecation, demonstrating that the descendants of polyp cells are capable of taking on all necessary roles for a complete animal. Thus, jellyfish cells would be considered as specialized, but not differentiated. Hox and parahox genes, which organize cellular behavior into structures as complex as

eyes, appear to pre-date the Cambrian, since they have been found in Cnidarians (Finnerty and Martindale, 1999); however, the existence of Hox genes is a separate question from the permanent pattern of expression of Hox or other genes in differentiated cells. It should be emphasized that in these examples, the specialized cells retain full flexibility. Indeed, the ability to lock in patterns of cellular function via differentiation could have evolved only after specialized patterns of cellular function were established.

It is useful to explore how cellular differentiation could have evolved incrementally from pre-existing mechanisms. Methylation is discussed here to provide an example of a plausible mechanism, and not as the definitive answer; histone acetylation is another means of altering gene expression. Recent research on human stem cells has found distinct patterns of methylation that change as the cells differentiate (Bibikova et al, 2006), and studies of mouse embryonic stem cells vs. differentiated cells show patterns of difference in histone methylation (Bernstein et al, 2006). This implies that differentiation may be implemented, at least in part, by epigenetic modification. Thus, comparable changes in epigenetic patterns during embryogenesis are predicted in all animals that emerged in the Cambrian, but not in the Cnidarians.

Random epigenetic DNA methylation occurs in bacteria, where it is used to control gene expression over multiple generations, as a sort of genetic “tuning knob” or meta-evolutionary strategy (Caporale, 2003). Random changes to methylation patterns can alter gene expression patterns, allowing genes to be turned off without degrading their sequence; presumably this is useful in allowing bacterial populations to adjust to cyclical conditions with long time scales.

In contrast to the random epigenetic changes in bacteria, whatever modifications are involved in the differentiation process happen at a specific time, in response to specific signals (for example, signaling molecules during embryogenesis), and with specific results. The development of a single mechanism capable of inducing epigenetic change at particular points in the genome, and at a particular point in time, in response to specific signals, would have been enough to implement near-irreversible differentiation. For example, a mechanism to create epigenetic changes on command might have evolved from a mechanism that preserves epigenetic patterns during DNA copying.

Consequences and implications

A specialized but non-differentiated cell would take on whatever role was called for by the signals it was receiving. The regenerative properties of Hydra show how easily specialized cells can switch roles. Technau and Scholz (2003) note that the endodermal and ectodermal cells in Cnidarians can adopt different fates, at least in the polyp form. A high degree of behavioral flexibility implies that an organism made of such cells would need to maintain constant chemical gradients, at some energy cost, in order to preserve its structure. Intricate organ structures would require sharp-edged gradients, costing even more energy.

Cellular slime molds and jellyfish demonstrate that diverse, intricate, collective, and cooperative cellular behavior can be maintained by signaling (Holstein, Hobmayer, and Technau, 2003). However, there would be a tradeoff between intricacy of structure, reliability of structure, and energy required to maintain it. Additionally, any shift in the spatial signal map (for example, caused by physical damage elsewhere in the organism) could cause cells to transform into other types of cells, disrupting or breaking network structures to the detriment of tissues depending on them.

By contrast, given a capacity for true differentiation, a cell could stay in its assigned role indefinitely without energy being expended to “remind it” of its proper function. When cells can be made to differentiate irreversibly via external chemical signals, the mechanisms of embryogenesis can be applied

at multiple size scales to produce structures of almost unlimited complexity. A brief expenditure of signaling energy, sufficient to establish sharp gradients and intricate patterns for as little as a few minutes, would be sufficient to create permanent and reliable structures within the organism. This could allow the development of more intricate and large-scale structures and networks, such as vascular systems. In particular, preserving reliable function of individual neurons would enable long-term synaptic learning. Either the development of more advanced organs or the development of synaptic learning would presumably have given a substantial advantage to the organism.

If cellular differentiation is so advantageous, why did it not evolve earlier? This dovetails with the question of why the Cambrian Explosion was delayed by many millions of years. A possible answer can be found in the fact that the descendants of a differentiated cell will all be differentiated, and thus limited. Therefore, the organism would no longer be able to reproduce by repurposing any convenient clump of cells, because any differentiated cells in that clump would need special handling. This implies that, in order to make use of differentiated cells system-wide, the organism might need to modify its reproductive pattern; differentiation might not be very useful until the reproductive adaptations appeared, and might even be selected against. A viable combination of differentiation and appropriate reproductive apparatus might take quite a while to evolve. Differentiation might also be difficult to evolve because an imprecise molecular mechanism, one that caused many epigenetic changes rather than targeting specific points in the genome, could easily have unreliable or damaging impacts.

The differentiation conjecture requires that all post-Cambrian animals descended from a single organism, presumably bilaterally symmetrical. (Although, as previously mentioned, starfish appear to be radially symmetrical, their embryos are bilateral.) This would imply that recognizable ancestors of modern animals will not be found among the Ediacarans. This parallels the arguments of Seilacher (e.g. Seilacher, Grazhdankin, and Legouta, 2003) that most of the Ediacaran fauna are not the ancestors of any modern animals.

Although it is always risky to look for confirmation of a new hypothesis in previously available data, it may be worth noting that the features of Ediacaran animals – flat bodies, apparent lack of organs, only simple patterns of spatial organization, and appearance of being “quilted” together (certainly not segmented in any metameric way)” (Gould, 2002) – might result from the constraints implied by dynamic and unstable assignment of cellular function. The “quilting” might result from poorly controlled growth or specialization of cells. Conversely, the Tommotian organisms – the first to appear in the Cambrian Explosion – may have had more sharply defined internal structures, and perhaps may also have had internal transport structures that provided nutrient transport through three-dimensional volumes (Gould, 1989).

Conclusion

The Cambrian Explosion, and the fossil record surrounding it in time, have raised many difficult questions about evolution. An understanding of why the Cambrian Explosion happened when it did, and why it was so rapid once it began, would begin to answer major questions about the mechanisms of evolution and the origins of complex animal life.

The abruptness of the Cambrian Explosion – the rapid production of nearly all modern animal forms – is indirectly answered by the differentiation conjecture. The development of finely ramified organs, perhaps in conjunction with synaptic learning, would represent a significant broadening of the evolutionary space; in addition, Cambrian animals would have been able to outcompete Ediacaran animals, driving many of them extinct and opening still more niches. The development of motile target-seeking predation, which apparently was rare or non-existent in Ediacaran times, would have fueled an arms race, which has been recognized by Gould and Butterfield, among others, as a driver of rapid evolution.

Although environmental factors surely set the stage for the Cambrian Explosion, cellular differentiation, as a capability developed by a particular lineage of organisms which then diversified rapidly, is a strong candidate for the final trigger.

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