when these are found. Why do predictions sometimes attenuate rather than sharpen perception, for example, why can we not tickle ourselves? These findings of attenuated, rather than enhanced, processing of the expected are prominent in action control literatures but in fact are also found elsewhere [17,19]. Similar temporally-tuned methods to those employed by Gandolfo and Downing [2] may prove useful in disentangling the precise nature of mechanisms operating across the sensory hierarchy [20].

In conclusion, Gandolfo and Downing's [2] new work contributes to a lively debate about the role of prior knowledge in shaping what we perceive. Their findings provide compelling evidence that expectations alter perception through influences realised in specific sensory areas before the sensory events are presented, and contribute to an emerging view that a common set of domain-general principles may account for the effects of prediction across a host of disciplines.

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Evolution: The Flowering of Land Plant Evolution

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Two new studies that consider the timing of origin of angiosperms are poles apart in their estimates. However, their partisan molecular and palaeontological perspectives may hold the key to establishing a unified evolutionary timescale for flowering plants.

More than 90% of living land plants are angiosperms (flowering plants) and so it is difficult to conceive of a world without them. Angiosperms are not merely decorative, effecting incalculable ecosystem services, encompassing most commercial crop species while also serving as global climate engineers [1]. But there was a world before angiosperms, though no one can quite agree when it ended because of a long-standing controversy concerning the timing of origin of the living clade of (crown) angiosperms. For over a century, repeated sampling of the fossil record has failed to find evidence of crown-angiosperms before the Cretaceous, which began about 145 million years ago, yet almost from their introduction, molecular clock analyses have estimated a much more ancient origin, perhaps

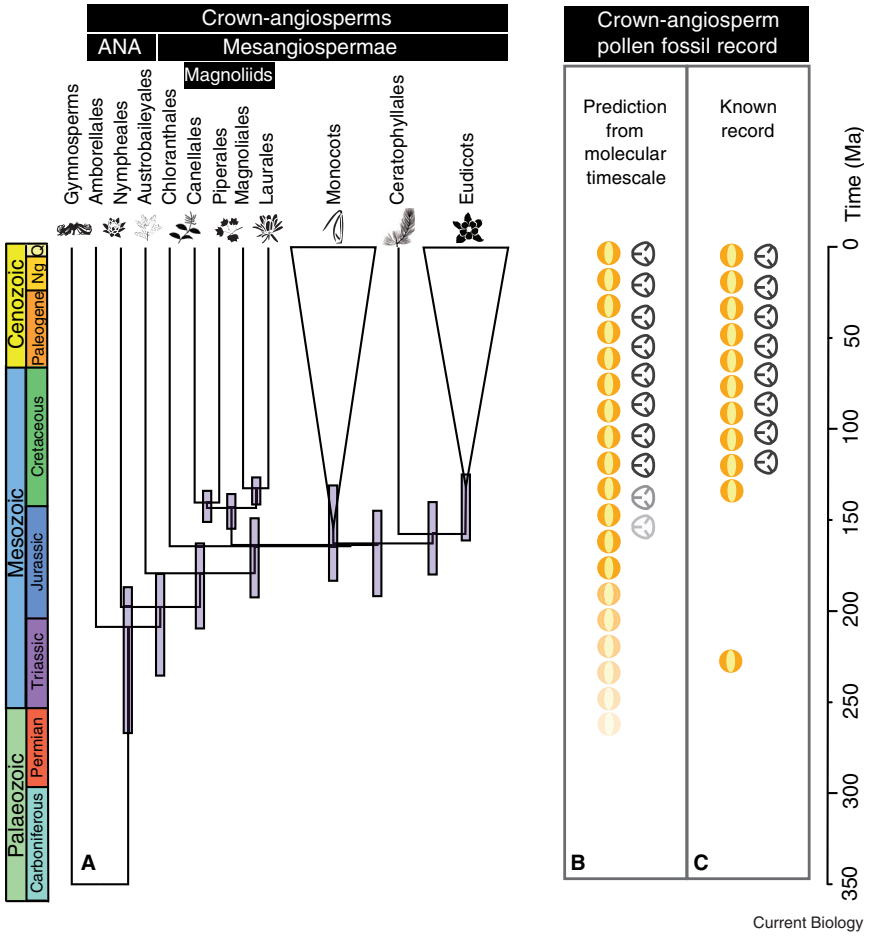

Figure 1. Comparison of molecular timescale angiosperm evolution to the predicted and actual fossil record.

Comparison of (A) molecular timescale of angiosperm evolution (summarized from Li *et al.* [3]) to (B) the pollen record it predicts, and (C) the known pollen record (B–C after Coiro *et al.* [4]). Note that the outlying Triassic record of monosulcate pollen in (C) has not been investigated ultrastructurally and so it is not possible to discriminate stem- versus crown-angiosperm interpretations. The fading colours and grey scale of the pollen in (B) reflect the uncertainty associated with the estimates for the timing of the origin of crown-angiosperms and eudicots in (A).

more than a 100 million years earlier [2]. Two new studies, by Li *et al.* [3] and Coiro *et al.* [4], together indicate that there is no evidence of a looming détente despite improved molecular clock methods, denser and deeper sampling of plant genomes and a more refined understanding of the plant fossil record. However, a solution may lie in the nature of their disagreement.

Mismatches between molecular clock estimates and the fossil record are hardly news, following infamous controversies over the timing of diversification of mammals, birds, animals and land plants, among others. However, in most cases they have diminished in scale, both as a consequence of the development of more realistic models of rate variation and a more sober approach to the interpretation of the fossil evidence used to calibrate molecular clocks to geological time [5]. However, these advances have not had the same impact on attempts to infer the timescale of angiosperm evolution.

The new study by Li et al. [3] is unparalled in scope, sampling 80 genes from the chloroplasts of 2881 species, including most families and all orders, which they use to estimate the evolutionary relationships of angiosperms (Figure 1A). Other studies have used more genes, but the impact of broader taxonomic sample has been a concern. Their phylogenetic results largely corroborate convention and their evolutionary timescale estimates crown-angiosperms to have appeared in an interval extending back in time from the Early Jurassic, through the Triassic, and deep into the Permian (187–267 Ma). The staggering scale of this 47–127 million year mismatch with a fossil record starting at 140 Ma, is no surprise at all. Indeed, it is something that seasoned clock watchers have come to expect from molecular estimates of angiosperm evolutionary history and the authors consider it high time that we take them seriously, formalizing at least a 'Jurassic Gap' interpretation of the fossil record.

Mismatches between molecular clock estimates and the fossil record should be the expectation since molecular clocks estimate the timing of genetic divergence, while the fossil record remains blind to this episode until descendent lineages have acquired morphologically distinct characteristics that can be fossilized. However, it is the scale of such mismatches that invoke the ire of palaeo folk. Palaeobotanists are united in a vociferous defense of the veracity of the angiosperm fossil record for good reason. Fossil stem-angiosperms are known from at least as far back as the Triassic, providing evidence for the assembly of the crown-angiosperm body plan. Nevertheless, repeated claims of Jurassic crown-angiosperm macroremains have failed to withstand scrutiny [4,6].

An absence of evidence is not evidence that crown-angiosperms were absent from Jurassic (or earlier) floras, but palaeobotanists take confidence in their interpretation of the fossil record because they rely on more than the simple presence and absence of fossils.

The fossil record is not a random sample of historical biological diversity, but a decidedly non-random archive structured by local and global tectonic processes that result in the differential preservation of environments across geological time [7]. Knowledge of this structure provides for a qualified interpretation of the fossil record, one in which fossil occurrences are predictable [8]. To be sure, fossil representatives of lineages can be absent because they were present but simply not preserved and, indeed, some ancient plant lineages (e.g., bryophytes) have a truly appalling fossil record. However, the same cannot be said of angiosperms,

where individual plants can yield millions of pollen grains that are all-but indestructible. Absence of crown-angiosperm pollen fossils from Jurassic strata that otherwise preserve the pollen and seeds of stem-angiosperms and gymnosperms surely tells us they are absent because crown-angiosperms had not yet evolved.

This is a key point made in a recent study by a Coiro *et al.* [4], who provide a temporal and spatial review of the pollen fossil record through the Jurassic–Cretaceous interval, demonstrating a graduated emergence of crown-angiosperm diversity. Given the richness and consistency of the pollen fossil record, it is not surprising that the earliest crown-angiosperm pollen appears earlier than the oldest macroremains. However, the pollen record exhibits anything but the sudden emergence of crown-angiosperm diversity that the macrofossil record suggests. Rather, the evolutionary grades of pollen encountered in the early Cretaceous record match precisely the order predicted by molecular phylogenies of their living relatives, with monosulcate pollen of the early diverging ANA-grade plants (*Amborella*, Nymphaeales, and Austrobaileyales), magnoliids, Chloranthaceae and monocots occurring in older strata than tricolpate pollen of early branching eudicots, and then the tricolporate pollen grains of more derived eudicots. This correlation between fossil stratigraphic order and phylogenetic branching order strongly suggests that the fossil evidence is more signal than noise.

Cleverly, Coiro and colleagues explore the predictions of molecular clock analyses like the one conducted by Li *et al.* [3], inferring the nature of ancestral pollen based on the characteristics of living lineages and a molecular timescale of angiosperm evolution. Their results require the presence of ANITA-grade pollen deep in the Triassic and eudicot-grade pollen from the latest Jurassic (Figure 1B); these expectations are not met (Figure 1C). Mapping fossil occurrences onto palaeogeographic reconstructions they demonstrate an early Cretaceous expansion to global distribution of crown-angiosperm pollen. Perhaps most importantly, they demonstrate that the early endemic distribution and earlier absence of crown-angiosperm pollen is not merely a consequence of non-preservation since there are records of gymnosperm and stem-angiosperm pollen and seeds, extending deep into the geological record. These records are important since they demonstrate that the environmental, ecological and preservational conditions were ripe for the preservation of crown-angiosperms — they are absent because they had not yet evolved.

Coiro and colleagues accept that there remains scope for a Late Jurassic origin of crown-angiosperms — that the fossil record might even require it — but this still leaves a yawning mismatch with molecular timescales that infer a full Jurassic Gap. The discordance likely arises from three main factors: the perfunctory nature of most molecular clock analyses; the way in which the results of molecular clock analyses are interpreted; and the way in which fossil evidence is interpreted to calibrate molecular clock analyses.

Molecular clock methods are now so parameter-rich that it is possible to obtain just about any desired result and so fossil age constraints are essential. Most molecular analyses follow a simple pipeline that does not explore the impact of rate model, gene sample, partition strategy, competing phylogenetic hypotheses, or the degree to which fossil calibrations approximate the true time of divergence. Each of these factors (and more) can have a profound impact on the ensuing evolutionary timescale [9] and very often there is no objective criterion to choose among them. For this reason, it is more appropriate to integrate the results of experiments that explore parameter space (e.g., [10]) which may lead to results that are less precise than we might want — but more likely to yield the accuracy we need.

The results of molecular clock analyses are probabilistic, estimating a distribution of clade ages that are commonly summarized by a point estimate, such as a mean or median. However, simulation studies indicate that point estimates are usually wrong, while the span of the distribution of age estimates usually encompasses the true clade age [11]. Molecular clock analyses have recovered estimates for the crown age of angiosperms that encompass the late Jurassic interval that Coiro and colleagues predict as the origin time of crown-angiosperms (e.g., [12]). In this sense, the perception of mismatch between molecular clock estimates and the fossil record is more an issue of interpretation rather than fundamental incongruence.

Ultimately, it is naive to perceive molecular timescales and the fossil record as competing and adversarial. The diverse family of molecular clock methods attempt in their different ways to integrate fossil constraints on the age of living clades with phylogenetic hypotheses, molecular distances, and evolutionary models. To be sure, molecular timescales are hypotheses and they must be tested, such as through the discovery of incompatible fossil evidence. However, rejection in such circumstances merely indicates that their underlying fossil evidence was incorrect — inspiring new analyses based on improved fossil sampling — rather than inspiring despair with the entire enterprise (e.g., [13]). Indeed, fossil calibrations are the soft underbelly of most molecular clock methods since they require fossils to not only inform the minimum age of living clades, but also constrain their maximum age. Inference of a 'Jurassic Gap' in the fossil record of crown-angiosperm evolutionary history is rooted largely in the loose maximum constraints on the age of this clade. An improved evolutionary timescale for crown-angiosperms requires more precise (but no less accurate) fossil constraints. These may not be achievable for many of the infamous molecular clock–fossil record mismatches, but the uniquely rich and dense fossil record of seed plants may hold the key. Coiro and colleagues provide objective evidence for tightening these constraints and their implementation will doubtless lead to a dramatically diminished Jurassic Gap.

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Development: How Tadpoles ROC Tail Regeneration

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Specialized epidermal cells are essential for the complex tissue regeneration required to replace tails and limbs, but their exact identities and molecular roles remain murky. Recent work in *Xenopus* has identified an epidermal cell population critical for tail regeneration, providing intriguing new directions for the field.

Full regeneration of an appendage is an amazing feat, yet one that few animals are able to successfully perform. Even fewer are able to regenerate throughout their entire lives, namely species of Urodele amphibians such as the axolotl. Other animals, such as frogs, retain the ability to regenerate as immature tadpoles, but soon transition to a regeneration-incompetent state [1]. This transition period provides a remarkable opportunity to compare regenerative and non-regenerative states within the same species. Recent work reported in *Science* by Aztekin *et al.* [2] examines transcriptional differences of this precise phenomenon at the single-cell level.

Generally, across species, appendage regeneration occurs in a prescribed set of stages. In the hours following loss of an appendage, a specialized wound epidermis forms and covers the plane of injury. Following this, progenitor cells underneath the wound epidermis begin to proliferate, eventually forming a mass known as a blastema. Once the animal's blastema reaches a critical mass, the cells begin to differentiate, eventually re-forming the structure and tissue composition of the previous appendage.

Two recent studies in axolotl leveraged single-cell transcriptomics to define cellular heterogeneity during limb regeneration [3,4], and wound epidermal cells were specifically explored over several time points in one [3]. However, a focused interrogation of the earliest time points might reveal some of the most immediate cellular changes in epidermis. These changes may be critical for downstream regenerative success since blastema growth has been known to be dependent on wound epidermis formation for several decades [5]. The recent study by Aztekin *et al.* [2] seeks to better understand the earliest hours following appendage loss in *Xenopus* tadpoles. This study examines over 13,000 cells at multiple time points during formation of wound epidermis in regeneration-competent and regeneration-incompetent frog embryos.

The authors compared cell types between uninjured tails, tails undergoing successful regeneration, and tails from older tadpoles that were amputated but cannot regenerate. They found an intriguing population present only in uninjured samples and samples from embryonic tadpoles undergoing successful regeneration. These cells were missing from the samples taken near the amputation plane of mature tadpoles that can no longer regenerate. Deeper examination showed this population expressed multiple key genes (*Wnt5a*, *Fgf10*, *Msx1*, etc.) previously implicated in the regenerative response [6]. Through a combination of these factors, this population of cells was defined as "regeneration-organizing cells," or ROCs (Figure 1). After identifying the location of the population as along the midline edge of the epidermis, the authors generated a reporter line whereby ROCs are identified through their co-expression of *Lef1* and *Tp63*. Using these animals, ROCs are observed to relocate from their midline