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Polyploid *Arabidopsis* species originated around recent glaciation maxima

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Polyploidy may provide adaptive advantages and is considered to be important for evolution and speciation. Polyploidy events are found throughout the evolutionary history of plants, however they do not seem to be uniformly distributed along the time axis. For example, many of the detected ancient whole-genome duplications (WGDs) seem to cluster around the K/Pg boundary (~66 Mya), which corresponds to a drastic climate change event and a mass extinction. Here, we discuss more recent polyploidy events using *Arabidopsis* as the most developed plant model at the level of the entire genus. We review the history of the origin of allotetraploid species *A. suecica* and *A. kamchatica*, and tetraploid lineages of *A. lyrata*, *A. arenosa* and *A. thaliana*, and discuss potential adaptive advantages. Also, we highlight an association between recent glacial maxima and estimated times of origins of polyploidy in *Arabidopsis*. Such association might further support a link between polyploidy and environmental challenge, which has been observed now for different time-scales and for both ancient and recent polyploids.

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Introduction

Polyploidy is a widespread phenomenon, especially in the plant kingdom, and is known to affect evolutionary dynamics and species diversification by increasing genetic variation and genomic complexity [1,2*,3].

Furthermore, whole genome duplications (WGDs) are often associated with key innovations [4], where the evolution of the flower and seeds form perhaps the most fascinating examples [5]. Recent advances in sequencing technologies revealed WGDs in many extant plant lineages, and allowed to observe a striking coincidence of WGDs with the Cretaceous–Paleogene (K/Pg) boundary (approximately 66 Mya), caused by the K/Pg extinction event, resulting from drastic climate change [6,7]. Some other periods of environmental instability seem to coincide with WGDs in plants as well. Close to one third of the lineages of the grass tribe *Andropogoneae* are allopolyploids, which originated from a minimum of 34 independent events coinciding with the expansion of the C₄ grasslands in the Late Miocene (11.6–5.3 Mya), when more efficient photosynthesis became important due to an earlier decrease in CO₂ level [8]. And although accurate dating of (very) ancient WGDs is difficult and should be interpreted with caution, it has been suggested that some old WGDs in gymnosperms might correlate with the Permian–Triassic extinction (~250 Mya) [9]. While polyploids may have a greater adaptive potential due to their increased genetic variation, which could play an important role in the establishment of both autopolyploids and allopolyploids [2*], it has also been argued that a correlation between WGDs and environmental upheaval or changing environmental conditions could be explained by a more neutral scenario, where external stressors cause an increase in the rate of unreduced gamete formation, leading to the origin and possible establishment of polyploids [10–13]. Unreduced gametes have somatic chromosome numbers (2*n*) due to meiotic impairment, to which both genetic and environmental factors can contribute. Production rates of male unreduced gametes (which is easier to measure experimentally, compared to female gametes) were estimated to be lower than 2% for most of the accessed natural plant populations, with significant variation among species [14,15]. Asexual and predominantly selfing species produce more unreduced gametes compared to the outcrossers, suggesting relaxed and/or weaker selection on meiosis effectiveness in the former [15]. Stressful environmental conditions like cold, heat, drought and low nutrition can increase production of 2*n* gametes [10,11,16]. Temperature stress, for example, was shown to impair normal microtubule functioning during meiotic cell cycle which lead to higher production of unreduced pollen [12,13]. Interestingly, gibberilic acid hormone, controlling many

aspects of plant physiology including response to abiotic stress, was also shown to induce diploid pollen formation [15]. Taken together, it is reasonable to assume that external stress can increase the formation of unreduced gametes and thus promote polyploidy.

In this review, we provide yet another line of support for a putative link between the origin and establishment of polyploids and environmental change, based on recent research on the evolutionary history of polyploids within the genus *Arabidopsis*. Since the *Arabidopsis* genus became an accepted model for plant comparative genomics, and for studying processes of speciation and adaptation [17–19], there is an extensive amount of genomic resources available, including reference genomes for *A. thaliana* [20], *A. lyrata* [21] and *A. halleri* [22], over a 1000 resequenced genomes of *A. thaliana* [23], as well as genus-wide resequencing data [24]. *Arabidopsis* includes 27 diverse lineages, which differ in ecology, karyotype, genome size, ploidy and mating-system [24,25]. The genus includes both types of polyploids: autopolyploid and allopolyploid and we will briefly discuss the evolutionary history and potential selective advantages of some of them in this short review.

A. suecica

The allotetraploid *A. suecica* ($2n = 4x = 26$) is a hybrid between *A. thaliana* ($2n = 10$) and *A. arenosa* ($2n = 4x = 32$). Most likely, *A. thaliana* provided an unreduced maternal gamete that was fertilized by a diploid paternal gamete from a tetraploid *A. arenosa* (Figure 1a) [26]. One of the most attractive features of *A. suecica* as a model to study allopolyploidy is the high divergence between the parental species (about 6 Mya), which allows clear separation of homeologous sequences. Until recently, *A. suecica* has been considered a rare example of an allopolyploid that originated from a single hybridization event [26]. However, a recent study has challenged this view, showing high levels of shared polymorphisms with both parental species throughout the genome [27*]. Given that natural accessions of *A. thaliana* are mostly homozygous, due to earlier transitions from outcrossing to selfing [21,28,29], such an extensive shared variation with *A. suecica* can be explained only by multiple founding events contributing to the formation of the hybrid [27*]. Nevertheless, severe bottleneck signatures are easily registered along the genome of *A. suecica* as loci with reduced genetic diversity. Diversity at the loci inherited from one founder was used to estimate the time of origin (expected coalescence time) for *A. suecica*, which resulted to be around 16 Kya (with a 95% confidence interval of 14.1–18.4 Kya) (Figure 1b) [27*]. *A. suecica* is currently distributed in the Fennoscandinavian region [30]. However, at the time of its origin [27*], these currently occupied territories were still mostly covered with the ice sheet. This fact, plus considering the distribution of the genetically closest *A. thaliana*

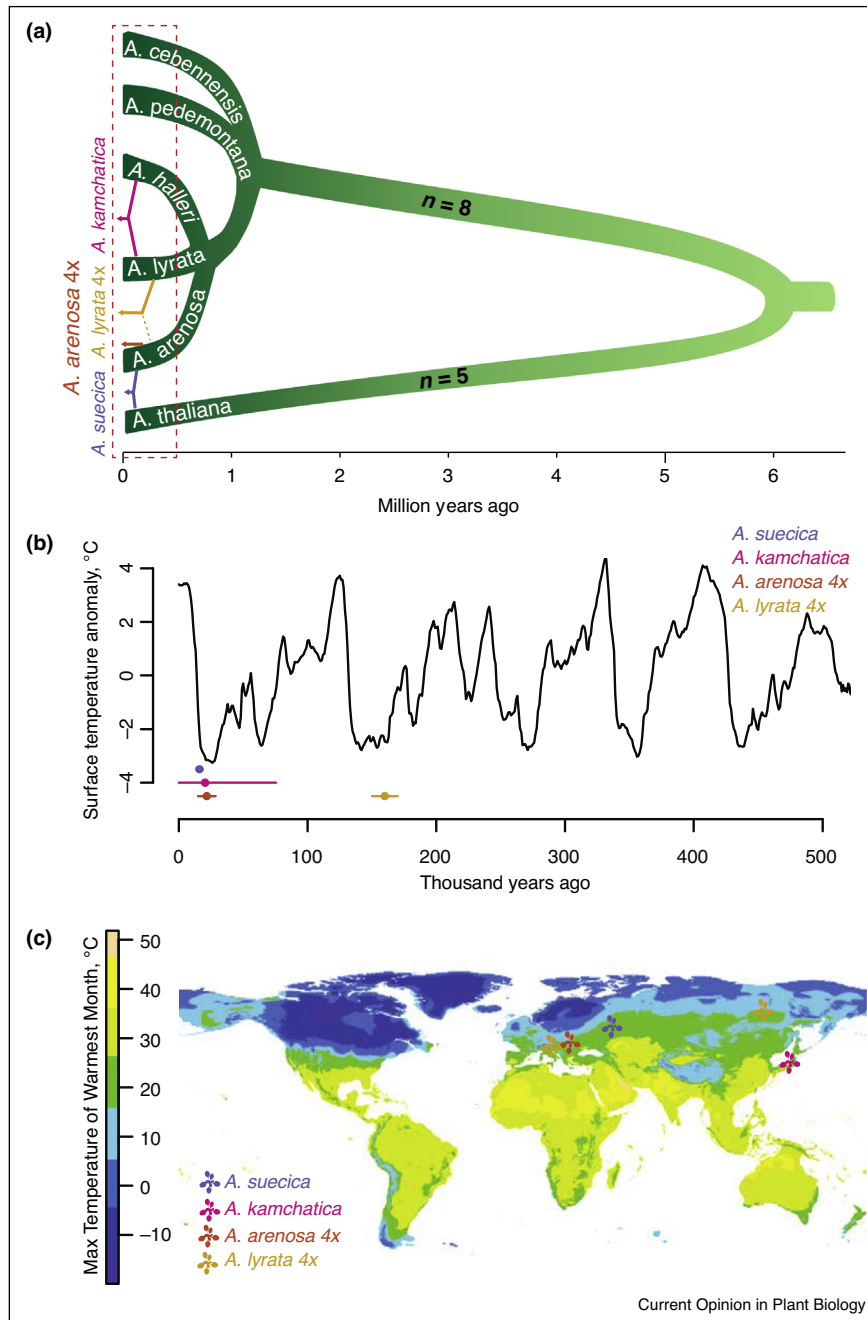
accessions, suggested that *A. suecica* was formed in Eastern Europe or central Eurasia (Figure 1c) [27*]. Subsequent shifts of the occupied territory might be explained by the retreat of the glacial ice from the Fennoscandinavian region and rise in temperature in the original territories. *A. suecica* is a selfer, which is ensured by the dominance of the S-locus inherited from selfing *A. thaliana* over the S-locus inherited from outcrossing *A. arenosa*, together with the degradation of the male-specificity *SCR* gene from the *A. arenosa* part of *A. suecica* [27*].

A. kamchatica

A. kamchatica ($2n = 4x = 32$) originated through hybridization of a diploid *A. lyrata* ($2n = 16$) and a diploid *A. halleri* ($2n = 16$) (Figure 1a). The genetically closest lineages to *A. kamchatica* are the Siberian *A. lyrata* subsp. *petraea* (also called *A. petraea* subsp. *umbrosa* or *A. umbrosa*) and the East Asian *A. halleri* subsp. *gemmifera* [31–34]. Genetic diversity studies of *A. kamchatica* suggests a polytopic origin around Japan with a later migration to the North-East of Russia and the North-West of North America. The current distribution of *A. kamchatica* is limited to East Asia and North America [32–34]. Four chloroplast haplotypes shared between *A. kamchatica* and *A. halleri* indicate multiple founder events of the hybrid [33]. Two characterized lineages, *A. kamchatica* subsp. *kamchatica* and *A. kamchatica* subsp. *kawasakiana*, differ in seed morphology and habitat [35]. While the former is an arctic-alpine perennial plant distributed in East Asia and North America at different altitudes, the latter is annual and found in sandy habitats along the seashore and at Lake Biwa in Japan [36]. Probably, different founding pairs of *A. lyrata* and *A. halleri*, as well as population fragmentation during the postglacial period leading to strong genetic drift and fixation of different genotypes [33,36], contributed to the population structure of *A. kamchatica*.

Previously, it has been suggested that there exists a diploid form of *A. kamchatica* in Taiwan [37,38]. However, later flow cytometric studies failed to confirm such ploidy variation within *A. kamchatica* [39], and, based on the geographical distribution, rather suggested that the diploid plants correspond to *A. lyrata* subsp. *petraea* [34]. General interspecific reticulation in *Arabidopsis* and, in particular, ancient gene flow between *A. halleri* and *A. lyrata* in East Asia [24] could potentially explain phylogenetic inconsistencies and the mosaic genome of *A. lyrata* subsp. *petraea* in the previous study [38]. This secondary contact between *A. halleri* and *A. lyrata* could also prevent the accumulation of genomic incompatibilities between the two species and therefore assist the establishment of the allotetraploid *A. kamchatica*. The time of origin of *A. kamchatica*, in terms of divergence from its parental species, was estimated using nucleotide divergence and synonymous substitution rates of four nuclear loci. Employing a mutation rate given by Koch *et al.* [40], the mean divergence time was estimated at

Figure 1



(a) Schematic representation of relatedness between *Arabidopsis* lineages and polyploid origins (colored arrows). The dashed rectangle denotes the last 500 000 years when polyploids originated and for which we provide the temperature reconstruction data [93] in panel b. **(b)** *A. suecica* (cherry blue color), *A. kamchatica* (deep cerise color) and tetraploid *A. arenosa* (tenne color) originated around the last glacial maximum (LGM); tetraploid *A. lyrata* (gamboge color) originated approximately at the second to last glaciation. **(c)** Approximate geographical origins of polyploid *Arabidopsis* lineages are marked with the colored rosette shape symbols. Heatmap background represents the maximal temperature of the warmest month around the LGM [94], to give an idea of the ice margins during the glaciations.

20 417 years (with a 95% confidence interval of 0–75 460 years) (Figure 1b) [41]. Demographic modeling using whole-genome sequence data would probably narrow the current boundaries of *A. kamchatica*'s time of

origin. Transition to selfing in *A. kamchatica* occurred multiple times with the common feature of degradation of male specificity genes [41,42].

Tetraploid *A. lyrata* lineages The *A. lyrata* species complex has a circumpolar distribution with five taxa described at the species and subspecies level, two of which contain tetraploids. Both diploid and tetraploid populations exist in European *A. lyrata* subsp. *petraea*, where tetraploids are mainly restricted to the foothills of the eastern Austrian Alps and few localities in the Czech Republic. Diploids exist in distinct habitats in the same area (Figure 1a and c) [43–45]. A potential allotetraploid origin (with *A. arenosa* as the proposed hybridization partner) was suggested based on the lower-than-expected genome size of tetraploids compared to diploids of the same taxon [31]. Further investigations detected introgression from *A. arenosa* into *A. lyrata*, with the highest fraction of the *A. arenosa* genome in the southern populations and lower fractions in the northernmost populations [45]. Gene flow seems to be directional, as only *A. lyrata* plastid types are found in hybrids. In contrast to *A. kamchatica* and *A. suecica*, tetraploid *A. lyrata* do not have disomic inheritance [45], and are predominantly self-incompatible [46]. The crown age of these populations, and therefore their putative origin, has been dated to around 160 000 years ago, based on the divergence time estimation of complete plastid genomes, coinciding with the end of the second to last glaciation (Figure 1b) [47]. These tetraploid *A. lyrata* populations putatively survived the last glaciation cycle in their current distribution range, a known refuge area for mountain plant species [48]. Whether tetraploid *A. lyrata* originated from allo-tetraploidization or auto-tetraploidization is unclear. A recent study suggested that gene flow became possible after polyploidization of *A. lyrata* led to a breakdown of post-zygotic barriers [49]. However, partial genetic assignment to *A. arenosa* has been detected in all studied populations of tetraploid *A. lyrata* to date [45,47]. Some evidence for polyploidy, based as chromosome counts mentioned in older literature [50] and a microsatellite pattern indicative of tetraploidy, was detected in another *A. lyrata* taxon, *A. petraea* subsp. *septentrionalis*, which is distributed from Western Russia to the Lena river in Siberia [25]. However little is known about its time or mode of origin. Reports of tetraploid *A. lyrata* in North America (Alaska and Western Canada) can most likely be attributed to *A. kamchatica*.

Tetraploid *A. arenosa* lineage(s) *A. arenosa* includes both diploid and tetraploid lineages (Figure 1a). While tetraploid *A. arenosa* is spread mainly in central, eastern and western Europe, the diploids are limited to the Balkans, the Pannonian Basin, the Carpathians, and the Baltic Sea coast [25,51,52]. Based on genetic diversity assessment, *A. arenosa* seems to be an obligate outcrosser, and it has the highest genetic diversity among *Arabidopsis* species [24,53]. Demographic modeling of 20 populations of different ploidy sampled in Central Europe suggested an origin of tetraploid *A. arenosa* from a single population close to the Northern Carpathians about 15 000–19 000 generations ago (Figure 1b and c) [54]. Generations

probably correspond to one to two years, since *A. arenosa* lineages vary in life cycle from being perennial to annual, but even perennials flower every year [54,55]. Later, tetraploid lineages split and colonized the rest of Europe through different routes of migration [54]. The demography of *A. arenosa* has recently been described by Yant and Bomblies [56].

Tetraploid *A. thaliana* accessions

Within the *A. thaliana* lineage, very few natural tetraploid accessions have been reported so far: Stoc (Stockholm, Sweden), Wa-1 (Warschau, Poland), Ciste-2 (Italy), and Bla-5 (Spain) [57–59]. These accessions have been characterized by some morphological differences compared to the diploids and by having a stable cytotype [57,58,60]. A recently conducted study on the demography and the post-glacial spread of *A. thaliana* accessions classified the Wa-1 accession as a non-relict one, which suggests its relatively recent origin after the last glacial maximum [61].

Polyploidy and adaptation

Climatic oscillations during the Pleistocene have probably driven speciation by the repeated geographic isolation and merging of refugia areas [62,63], whereas secondary contacts between species from different refugia may have led to hybridization [64]. The establishment of new species in changing environments may require overcoming specific challenges, in which polyploidy may be advantageous. For example, polyploid Arctic plants seem to colonize new territories more successfully compared to diploids [65]. Polyploids often show increased adaptive potential and environmental robustness, although the exact mechanisms remain elusive [2,66]. An increased number of alleles in polyploids may buffer against undesirable changes, and/or allow for neo-functionalization or sub-functionalization of duplicated copies. To what extent WGD itself, in case of autopolyploids, or hybridization events in case of allopolyploids, play a major role in enhanced adaptation is still the topic of much debate and might be highly variable for different events or species [2,67,68].

It has been reported that the allotetraploid *A. suecica* can more effectively assimilate carbon and produces starch compared to its progenitors. Interestingly, the strength of such hybrid vigour increased with intensity of light, which suggests environmental regulation of heterosis in *A. suecica* [69]. *A. halleri* (one of the parental species of *A. kamchatica*) tolerates high concentrations of toxic metals in soil and hyperaccumulates heavy metals such as cadmium (Cd) and zinc (Zn) [70]. Apart from allowing to occupy toxic ecological niches, hyperaccumulation can act as a defense mechanism against herbivory [71,72]. *A. kamchatica* can grow on both metalliferous and non-metalliferous soils and accumulates Zn at levels closer to those found in *A. halleri* than in *A. lyrata*, probably due

to cis-regulatory differences and extra metal ion transporter genes [73].

A recent study [74] on North American populations of *A. kamchatica* showed a higher freeze tolerance compared to *A. thaliana*. Cold tolerance of *A. kamchatica* varied along the latitudinal distribution of the examined populations with mid-latitude populations exhibiting highest tolerance. Armstrong *et al.* [60] suggested that the higher genetic diversity of the mid-latitude populations probably facilitated adaptation to cold. However, it is unclear whether *A. kamchatica* is better adapted to cold than its parental species. For example, *A. lyrata* subsp. *petraea* can be found in the most northern territories compared to the rest of the genus. Both *A. lyrata* subsp. *petraea* and *A. kamchatica* subsp. *kamchatica* are perennial and overwinter under insulate snow cover, probably experiencing similar conditions. Interestingly, synthetic allopolyploids between *A. lyrata* and *A. halleri* showed upregulation of cold-response genes from the *A. lyrata* contributor under cold stress conditions [75]. The range of altitudinal distribution and clinal variation of flowering time in *A. kamchatica* suggest adaptive changes along altitudes, however the genetic basis of such is yet to be uncovered [76,77].

Autotetraploid *A. arenosa*, as well as some diploid lineages of *A. lyrata*, colonized extreme ecological niches such as serpentine barrens [78,79**]. Apparently, such adaptation was not completely independent and some adaptive alleles introgressed from *A. lyrata* populations to *A. arenosa* [79**]. Introgression in the opposite direction, from *A. arenosa* to tetraploid *A. lyrata*, was hypothesized to have allowed *A. lyrata* to escape its narrow niche, restricted to limestone in Austria and to colonize siliceous bedrock [45,47*]. Interestingly, tetraploid lineages of *A. arenosa* that colonized railways switched to rapid cycling due to loss of vernalisation requirement, also show high tolerance to temperature stress [80]. The natural autotetraploid *A. thaliana* accession Wa-1 was described to have a higher resistance to salinity [59] and powdery mildew [81].

While polyploidy may be advantageous in some circumstances, it also comes with mechanistic challenges during cell divisions due to the increased number of chromosomes [82,83]. *A. arenosa* became a primary model for studying the effects of autotetraploidy on meiotic chromosomal segregation [56*,83,84], where genes regulating crossover interference, chromosomal pairing and segregation were shown to be under selection in the autotetraploid lineages [84]. In the case of allotetraploid *A. suecica* with disomic inheritance [85], synthetic lines also appear to be less stable [66,85,86], suggesting adaptation of natural accessions, where a quantitative trait locus was found to regulate meiotic stability [86]. The exact mechanism of adaptive changes in both cases is yet to be

described, as well as the persistence of adaptation to polyploidy in other systems.

Conclusions and outlook

The recent accumulation of large population-scale genomic sequence data from different *Arabidopsis* diploids and polyploids allowed the reconstruction of their evolutionary history, and seems to suggest that *Arabidopsis* polyploids originated and got established during the two latest peaks of the Quaternary glaciation (see Figure 1). If true, such pattern adds to the observation that polyploidy and WGDs might be correlated with periods of environmental challenge or change [6]. In fact, there are several other examples, for instance of Alpine and Carpathian plants, where polyploids are believed to have originated during Pleistocene glacial cycles [87–89]. The nature of such association remains largely unclear, but maybe large-scale evolutionary field experiments could provide more direct answers. For example, field transplant experiments with *Achillea borealis* (Asteraceae) showed a five-fold fitness advantage of hexaploids over tetraploids in dune habitats [90]. A three year transplantation experiment of the *Claytonia perfoliata* complex revealed local adaptation among cytotypes, although no polyploid advantage in general was observed [91]. On the other hand, adaptive advantages of polyploids under drought conditions have been shown in an 18 year old field trial with *Acacia senegal* [92]. Conducting more field experiments, in addition to controlled experiments in the lab, on different plant models, although very challenging, would help to understand whether polyploidy can indeed be advantageous under harsh conditions or during times of environmental upheaval. In the face of current climate change and global warming, research in this area should become even more significant.

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