

How to make a domesticate

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1 **Summary**

2 Crop domestication is an adaptive process that transforms a wild plant into a domesticated
3 species that can be reared and maintained for human use. Though there are hundreds of
4 thousands of flowering plant species, only a small fraction has ever been domesticated. Suc-
5 cessful domestication is likely influenced by a number of key plant characteristics, including
6 its life history, the usefulness of a crop for early societies, and the maintenance of a large
7 effective population size. Although many studies have sought to identify individual loci with
8 large effects on domestication traits, we argue that relevant phenotypes are likely controlled
9 by a large number of loci, most of relatively small effect. Most of these alleles were prob-
10 ably selected from standing genetic variation present in the wild ancestor rather than new
11 mutations. Both archaeological evidence and quantitative genetics suggest that the process
12 of domestication was in most cases gradual, likely lasting several millennia. We end by
13 discussing how these findings from the past may inform future efforts to domesticate new
14 species.

15 **Main text**

16 The Neolithic Revolution brought about the transition from hunting and gathering to a
17 sedentary lifestyle, laying the foundation for the development of modern civilizations. The
18 primary innovation that facilitated these changes was the domestication of plants and ani-
19 mals. Plant domestication is a process which started approximately 10,000 years ago and has
20 thereafter been repeated independently in many locales around the world [13]. Here, we offer
21 a perspective that seeks to predict what factors influence the success of domestication, how
22 many genes contributed to the process, where these genes originated and the implications for
23 *de novo* domestication.

24 **What is a domesticate?**

25 Defining domestication is not straightforward, and it is likely that no one concept fits all
26 species. Here, we define domestication as the process of adaptation to agro-ecological envi-
27 ronments and human preferences by anthropogenic selection. The advantage of this definition
28 is that it views domestication as a process rather than a binary trait, allowing for a spec-
29 trum of domestication from the simple tolerance or cultivation of wild plants (e.g., hops
30 and many herbs) to semi-domesticated crops showing a number of agronomic adaptations
31 (e.g., amaranth, flax and olive) and fully domesticated crops such as maize, barley and soy-
32 bean. These examples demonstrate that domestication is often gradual, ongoing and without
33 easily-defined start and end points. While much of the initial selection by humans was likely
34 unintentional [3], fully domesticated species have also adapted to intentional selection as well.
35 Part of the reason why domestication may be difficult to define is that it generally does
36 not act upon a single trait but instead leads to a suite of morphological and physiological
37 modifications that may differ among taxa. These changes typically affect traits related to
38 production and human preferences (e.g., taste, seed and fruit size), and together are referred
39 to as the domestication syndrome [10]. The domestication syndrome frequently overlaps be-
40 tween crops with similar purposes, but may differ dramatically between those with distinct
41 purposes. In cereals, for example, the domestication syndrome includes larger seeds as well
42 as reduced seed shattering and dormancy, but these traits were likely of lesser importance

43 for plants domesticated for leaves or fiber. In addition to traits common to the domestica-
44 tion syndrome, many domesticates may also exhibit unique phenotypic changes as well as
45 adaptations that have allowed them to spread outside of their initial geographic region of
46 origin.

47 **Which plants were domesticated?**

48 Successful and widespread crops comprise only a tiny fraction of angiosperms species. From
49 the over 250,000 described angiosperms only about 2,500 crops have been partially or fully
50 domesticated [16], and of these only a dozen provide more than 90% of human staple food.
51 In the following we discuss potential explanations for the selection of a species to be domes-
52 ticated, including geography, life history, and genetics.

53 The domestication and adoption of crops was likely influenced by a number of regional and
54 cultural factors. At least 15 centers of plant domestication have been robustly identified by
55 archaeological and other work, each giving rise to a different assemblage of domesticates.
56 Often several complementary crops were domesticated alongside in a single center of do-
57 mestication. For instance, energy rich cereals such as wheat and barley were domesticated
58 together with the protein rich legumes lentil and chickpea in the fertile crescent, a pattern
59 mirrored by rice and soybean in Southeast Asia or maize and common bean in the Americas.
60 This suggests that domestication followed similar patterns independently in distinct regions
61 by various cultures and that a major determinant of the success of domesticates was the util-
62 ity a plant offered to early societies. And while geography undoubtedly influenced the early
63 spread of domesticates [4], successful domesticates nonetheless hail from diverse geographical
64 and cultural origins.

65 In addition to its geographic origin, a plant's life history may also influence the process of
66 domestication. Annual plants have been very successful as domesticates, likely both because
67 many annuals were ruderal species already adapted to disturbed environments and because
68 the shortened generation time speeds up response to selection. Several crops show increased
69 rates of self-fertilization compared to their wild ancestors, and self-fertilization also facili-
70 tates the maintenance of desired genotype combination and lessens inbreeding depression.
71 Nonetheless, the complexity of adaptation during domestication and the polygenic nature of

72 many domestication traits suggests that at least some outcrossing likely played an important
73 role even in primarily self-fertilizing species, providing an influx of new variation and the
74 opportunity to combine favorable alleles on different genetic backgrounds. Asexual repro-
75 duction plays an important role in many perennial crops such as sweet potato, cassava and
76 banana, and may allow a sort of “instant domestication” by immediately fixing particular
77 combinations of traits while maintaining heterozyosity and avoiding inbreeding depression.
78 But clonal propagation dramatically increases the effective generation time, and many mod-
79 ern crops that are propagated clonally probably reproduced sexually during much of their
80 domestication history [2].

81 Genetic factors have also likely contributed to the success of some domesticates. The advan-
82 tages of polyploidy in domestication likely include increased maintenance of genetic diversity,
83 increased recombination products, or increased opportunities for novel adaptations via home-
84 ologous genes [17]. Overall, polyploidy appears to have played a direct role in the success of
85 some crops such as wheat and even though most domesticates are considered diploid many,
86 such as maize, are relatively recent polyploids and may still benefit from similar advantages.
87 A number of studies have demonstrated that domesticated species display an overall de-
88 crease in genetic diversity compared to their wild ancestors, consistent with pronounced
89 demographic change during domestication. Early human agriculturalists likely sampled only
90 a fraction of plants from natural populations, often leading to genetic bottlenecks associated
91 with the selection of favorable phenotypes. Such population bottlenecks, combined with
92 strong selection for adaptive traits, undoubtedly reduced the effective size of plant popu-
93 lations and resulted in increased genetic drift and decreased diversity within populations.
94 Species with a larger effective population size at the onset of domestication should be more
95 resilient to such changes, maintaining more diversity upon which subsequent selection can
96 act and thus increasing the likelihood of successful domestication. Consistent with this idea,
97 successful crops exhibit greater genetic diversity than most wild plants surveyed [11], sug-
98 gesting that larger effective population size may have played a role in these species’ success as
99 domesticates. Changing population size during the initial phase of domestication may have
100 also led to an accumulation of slightly deleterious alleles [18], and this “cost of domestication”
101 may have proven limiting for species with initially small effective population size.

102 **How many genes contribute?**

103 At the genetic level, it is clear that selection and demographic change during the process
104 of domestication have resulted in the reduction of genetic diversity across the genome in
105 most crops. But how many loci were actually targeted by selection? While early crossing
106 experiments in maize suggested that as few as four or five loci of large effect could explain
107 differences in ear morphology between maize and its wild ancestor teosinte [1], genome-
108 wide scans of domestication often identify hundreds of loci targeted by selection. Mapping
109 studies seeking to characterize the specific quantitative trait loci (QTLs) contributing to
110 adaptive domestication traits have identified numerous large-effect loci for traits such as seed
111 shattering or branching, but most studies of this nature are under-powered to identify loci of
112 smaller effect. Moreover, even large effect loci usually explain only a fraction of the differences
113 between wild and domesticated taxa: QTL mapping of the classic domestication locus *tb1*, for
114 example, reveals that the additive effect of the locus is likely less than 20% of the difference
115 in lateral branching between maize and teosinte [6]. Thus, rather than acting to fix a single
116 large-effect locus, selection during domestication has likely acted predominantly on polygenic
117 variation, moving the phenotype mean and reducing but not eliminating genetic variation
118 (Figure 1). Consistent with this idea, recent work in maize has identified substantial variation
119 in domesticated maize for traits selected for during domestication, predominantly driven by
120 loci with small, additive effects [19] as expected for a trait under stabilizing selection to
121 maintain the population mean. This idea is also supported by archaeological evidence in
122 many crops, where even traits with known QTL of large effect — such as seed size in rice —
123 show continual change in the archaeological record [7].

124 **From whence beneficial alleles?**

125 A long standing question in the study of evolution is whether domestication is limited by
126 genetic variation and thus forced to wait for *de novo* mutations to generate beneficial varia-
127 tion. Relative to other study systems domestication offers the advantage that the direct wild
128 ancestor of domesticated species is often known and can be assayed for the relevant variation.
129 Observations of convergent evolution, in which multiple crops show similar genetic changes

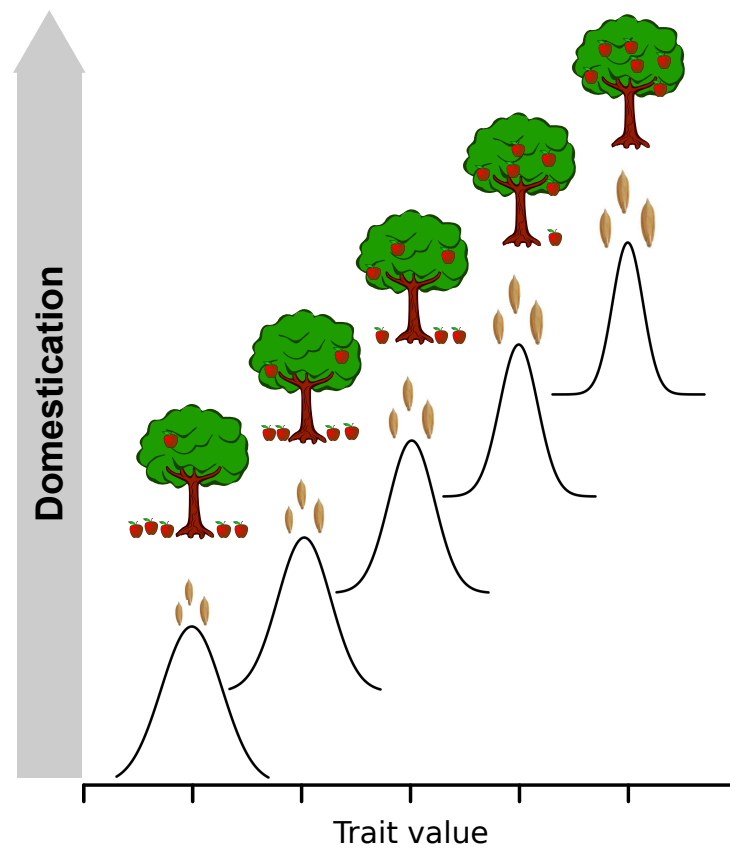


Figure 1: Schematic process of the evolution of domestication traits, such as fruit abscission in apples or seed size in rice. Most traits are quantitative, showing variation in both wild and domesticated taxa. Adaptation from this standing genetic variation often results in gradual change over time, reflected in steadily decreasing variation for the trait.

130 for similar traits, suggests that the potential targets of selection may be limited for at least
131 some traits. One such example is the *Sh1* gene, important in the reduction of seed shattering
132 in rice, maize and sorghum [14]. And while it is difficult to rule out the existence of domes-
133 tication alleles at low frequencies in natural populations, causal mutations for some traits —
134 such as the nonsynonymous mutation in *teosinte glume architecture 1* that contributes to the
135 reduction in hard fruitcases observed in maize — have never been observed in wild plants
136 and appear to have been selected from *de novo* mutations.

137 Given the polygenic nature of most domestication traits, however, it seems unlikely that
138 adaptation to domestication could occur if it required new mutations at each of many loci.
139 Although domestication phenotypes such as reduced shattering or lack of seed dormancy are
140 likely deleterious in wild populations, alleles controlling these traits can be maintained at low
141 population frequencies, especially for loss-of-function mutations in outcrossing plants where
142 such alleles can be masked in a heterozygous state. Because most traits are polygenic and
143 may be under stabilizing selection in both wild and domesticated populations, it is also likely
144 that the fitness consequences of an individual allele are not constant through time and may
145 depend considerably on genetic background. Because selection is unlikely to reduce diversity
146 around alleles already present on multiple haplotype backgrounds and alleles segregating in
147 the population may not be present in the parents of individual mapping populations, the
148 available evidence likely underestimates the importance of standing genetic variation, and
149 these challenges are only magnified as the number of genes contributing to a trait increases.
150 Standing genetic variation is not limited to variants that affect phenotypes in the wild ances-
151 tor, however. Crossing studies have revealed substantial genetic variation for phenotypes not
152 present in the wild ancestor. Such cryptic variation is seen for ear phenotypes in the maize
153 ancestor teosinte that itself does not have an ear [5]. Selection on these variants may be
154 substantially less, exposed only in certain environments or until sufficient phenotypic change
155 is effected by alleles at other loci, but they may nonetheless be an important source of large
156 effect alleles that would otherwise be rare in the wild. Related wild taxa, which may have
157 novel traits or have adapted to novel environments, provide yet another source for potentially
158 adaptive variation. Adaptive introgression from wild relatives appears to have been impor-
159 tant for a number of crops, facilitating local adaptation and even agronomic improvement in

160 a number of species including apple, maize, tomato, and sunflower.

161 **How long did it take?**

162 The timing of crop domestication is tightly linked to human history, though how and why
163 foragers became farmers is still a matter of some controversy. Domestication plausibly began
164 when hunters and gatherers living in semi-permanent settlements planted desirable plants,
165 eventually creating ecologically novel garden and field niches for those plants that fostered
166 the planting-harvesting-replanting cycle required for domestication. And while Darwin de-
167 scribed domestication as an example of accelerated evolution [3], determining the duration
168 of a continuous process such as domestication is difficult and attempts to do so remain con-
169 troversial, with studies from multiple angles coming to different conclusions. Population
170 genetic analyses, for example, find that individual large-effect alleles could fix very rapidly,
171 and early experimental studies in the field suggest that single domestication traits could
172 change dramatically in as little as 30 years [12]. In stark contrast to these results, however,
173 archaeological remains indicate that important traits such as seed and infructescence size or
174 seed shattering remained variable over millennia, changing only incrementally over time [7].
175 Although these results appear contradictory, we argue that they are in fact consistent with a
176 model of selection on a polygenic trait. Loci with the largest effects should experience rapid
177 changes in allele frequency, perhaps moving the population mean considerably over shorter
178 periods of time. But because large effect loci explain a minority of the phenotypic difference
179 between wild and domesticated taxa, phenotypic change would continue to be observed for
180 long periods of time.

181 Archaeological remains provide valuable insights into phenotypic change, even though most
182 early crop remains are small and allow inference of only a few phenotypes of interest. The
183 addition of DNA extracted from archaeological samples, however, offers the opportunity
184 to better understand the timing of selection during domestication. Comparison of known
185 domestication genes in maize and barley, for example, have shown the intermediate domes-
186 tication state of 5,000-6,000 year old samples [9]. The current outlook is that the above
187 studies, while powerful, may only be scratching the surface of the overall potential of the role
188 of ancient DNA in crop domestication. Recent methodological developments allow study of

189 polygenic traits in ancient samples by looking for coordinated shifts in allele frequency across
190 loci associated with phenotypic variation in extant samples [15]. We predict that effective
191 interrogation of ancient samples, using these and other approaches, will rapidly allow a much
192 more detailed analysis of the duration and process of selection for many important crops.

193 **Where to go next?**

194 We have proposed that domestication is best thought of as an adaptive process instead of
195 a binary trait, often resulting in gradual change without clear-cut phases. This process is
196 complex, and we have argued that successful domestication depends on a number of intrinsic
197 and extrinsic factors, including life history, utility, polyploidy, and large effective population
198 sizes. Nonetheless, more careful consideration of the relative importance of these factors
199 and how they act in concert could provide a useful basis for considering which plants might
200 make good candidates for domestication and better understanding why domestication of some
201 plants appears to have failed. While it may be ultimately difficult to identify the origin of
202 every functional allele and most work to date has focused on alleles of large effect, we argue
203 that most traits are polygenic and that much of the variation important for domestication
204 existed as standing variation already segregating in wild populations. If domestication in-
205 deed proceeded via polygenic adaptation from standing genetic variation, this implies that
206 breeding, rather than modification of a handful of genes, may prove a more efficient means
207 for future domestication efforts.

208 The experimental reproduction of domestication [8] of wild species is likely a challenging
209 endeavor and has yet to be accomplished. The fact the many crops have been independently
210 domesticated multiple times suggests the idea is plausible, though in most cases multiple
211 domestications were facilitated by gene flow among cultivated populations. *De novo* domes-
212 tication of a new wild species may in fact be considerably more difficult, due in part to the
213 complex genetic basis of domestication traits, limitations of life history, and the lengthy time
214 required. Nevertheless, some recently adopted crops like sugar beet have shown dramatic
215 adaptation in only the last few hundred years, and we argue that the early stages of such
216 efforts may be reached rather quickly with careful selection of candidate species and modern
217 breeding methods such as genomic selection and high throughput phenotyping.

218 Finally, we believe that better integrating the considerations discussed above into studies
219 of crop domestication will facilitate our understanding of plant adaptation to anthropogenic
220 environments and help clarify the utility of studying domestication as an example of experi-
221 mental evolution — an idea championed by Darwin nearly 150 years ago [3].

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