

# How epigenetic evolution can guide genetic evolution

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The expression level of a gene in future generations can be modified both by genetic mutations and by the attachment of methyl groups to the DNA. Since the DNA methylation pattern along a genome is inherited, methylation patterns constitute a significant epigenetic inheritance mechanism that is subject to evolution by natural selection. The variation rate of methylation patterns is generally higher than that of DNA which suggests that evolution of methylation patterns might be more rapid than that of genetic evolution. But, common consequences of methylation, such as reduced expression of methylated genes, could also be produced by genetic changes and these would have higher heritability. The question we address in this work is how the evolution of epigenetic methylation-dependent phenotypes might interact with the evolution of genetic DNA-determined phenotypes.

There is no biological mechanism known to directly transfer methyl groups into equivalent DNA changes. However, in principle an indirect mechanism could cause evolved methylation patterns to enable the subsequent evolution of equivalent genetic patterns in a manner analogous to the Baldwin effect (Baldwin, *Am. Nat.*, 30:441-451, 1896; Jablonka et al, *TREE*, 13:206-210, 1998). The Baldwin effect describes how non-heritable acquired characteristics can influence the evolution of equivalent genetic characteristics without any direct Lamarckian inheritance of acquired characters. This occurs because the ability to acquire or learn a new behaviour changes the selective pressures acting on genetic changes. Specifically, genetic changes that support this behaviour, e.g. by reducing learning time by making a small part of the behaviour genetically innate, may be selected for when the learning mechanism is present even though these same genetic changes may not be selected for when the learning mechanism is absent. Over generations, the modified selection pressures so produced can cause genetic assimilation of a phenotype that was previously acquired, even to the extent of making the acquisition mechanism subsequently redundant. Thus a learned behaviour can guide the evolution of an equivalent innate behaviour (Hinton & Nowlan, *Complex Systems*, 1: 495-502, 1987).

In the Baldwin effect a rapid mechanism of lifetime adaptation guides the relatively slow genetic evolution of the same behaviour. By analogy, Jablonka et al have suggested that “genetic adaptations may be guided by heritable induced or learnt phenotypic adaptations”. Here we hypothesise that “inherited epigenetic variations may be able to ‘hold’ an adapted state for long enough to allow similar genetic variations to catch up”, as they put it, even if the epigenetic variations are not induced or learnt but simply evolved by natural selection on methylation patterns. We assume that an individual may only express one phenotype in its lifetime, but that a given genome will persist relatively unchanged on a timescale that allows its methylome to adapt by natural selection. Thus, in contrast to the Baldwin effect, in this case two mechanisms of evolution by natural selection are coupled — one acting at a different variation rate from the other. We present a simple model to illustrate how a rapidly evolving methylome can guide a slowly evolving but highly-heritable genome. This is used to show that methylome evolution can enable genetic evolution to cross fitness valleys that would otherwise require multiple genetic changes that were each selected against. This finding suggests that the relatively rapid evolution of methylation patterns can produce novel phenotypes that are subsequently genetically assimilated in DNA evolution without direct transfer or appeal to induced phenotypes. This can enable the genetic evolution of new phenotypes that would not be found by genetic evolution alone, even if methylation is not significant in the ultimate phenotype.