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Significance of differential allelic expression in phenotypic plasticity and evolutionary potential of microbial eukaryotes

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Background: Differential allelic expression (DAE) plays a key role in the regulation of many biological processes, and it may also play a role in adaptive evolution. Recently, environment-dependent DAE has been observed in species of marine phytoplankton, and most remarkably, alleles that showed the highest level of DAE also showed the fastest rate of evolution.

Methods: To better understand the role of DAE in adaptive evolution and phenotypic plasticity, we developed a 2-D cellular automata model "DAEsy-World" that builds on the classical Daisyworld model.

Results: Simulations show that DAE delineates the evolution of alternative alleles of a gene, enabling the two alleles to adapt to different environmental conditions and sub-functionalize. With DAE, the build-up of genetic polymorphisms within genes is driven by positive selection rather than strict neutral evolution, and this can enhance phenotypic plasticity. Moreover, in sexually reproducing organisms, DAE also increased the standing genetic variation, augmenting a species' adaptive evolutionary potential and ability to respond to fluctuating and/or changing conditions (*cf.* genetic assimilation). We furthermore show that DAE is likely to evolve in fluctuating environmental conditions.

Conclusions: DAE increases the adaptive evolutionary potential of both sexual and asexually reproducing organisms, and it may affect the pattern of nucleotide substitutions of genes.

Keywords: differential allelic expression; daisyworld model; adaptive evolution; phenotypic plasticity

Author summary: In diploid organisms, the differential expression of the two alleles of a gene gives individuals more opportunities to adapt to fluctuating environmental conditions, which is particularly beneficial for clonally reproducing species.

INTRODUCTION

The study of molecular evolution has traditionally focussed on nucleotide variation within exons, but phenotypic diversity is also underpinned by differences in regulatory sequences that can affect gene expression [1]. Conversely, much genetic variation is cryptic, and the phenotypic effect of this cryptic genetic variation can be conditional on the genetic background (*e.g.*, dominance and epistasis), as well as the environment [2]. Cryptic genetic variation can be released under novel or stressful conditions, potentially fueling a selective response. Classic population genetic theory dating back as early as the 1940s acknowledged the importance of this "store of concealed genetic variability" that is invisible under normal (optimal) environmental conditions [3]. This cryptic genetic variation may turn beneficial under new circumstances. In contrast to the "standing variation",

which consists of additive genetic variation that is immediately available to selection, such cryptic variation has been dubbed "crouching variation" [4]. Cryptic genetic variation can be released by changes in gene expression, and this is perhaps most pronounced for genes that respond to the biotic or abiotic environment [5,6]. The interactions between the expression of genes and the environment underpin phenotypic plasticity, enabling organisms to (adaptively) respond to environmental changes [7]. This is central to the Baldwin effect, which postulates that individuals with better phenotypic plastic response have a higher chance to survive and produce offspring, which in turn can dictate the course of evolution [8,9]. An increased level of *cis*-regulatory variation has been linked with weaker purifying selection and less frequent positive selection [10]. This has implications for the preservation of this cryptic genetic variation, potentially enabling it to be preserved within a population to allow for allele-specific enhancement (ASE) variation depending on environmental condition.

Microorganisms with complex genomes (*e.g.*, eukaryotes) that are exposed to environmental fluctuations have evolved phenotypic plasticity to modulate the diverse environmental conditions. Such phenotypic plasticity may be particularly important for microorganisms in the temperate and polar oceans, given that these environments are extremely heterogeneous, both at the microscopic and macroscopic scale [11–13]. Furthermore, these environments are exposed to multiple stressors [14], and in some cases, rapidly changing due to global warming [15–17]. Also, the dynamic interactions between these organisms create new resources and niches, enabling their co-existence. Not surprisingly, the biodiversity of microbes in the marine environment is exceptionally high [18], and this is evident both at the level of allelic variation and expression variation [19].

Mock *et al.* [19] examined the genome evolution of a cold-adapted diatom from the Southern Ocean, *Fragilariopsis cylindrus*, and found that almost a quarter of the diploid genome consisted of genetic loci with highly diverged alleles. The alleles are highly diverged because they reside in a population with a huge effective population size, which is estimated to be in the tens of millions. Consequently, the alleles coalesce in the distant past, which means they have had time to accumulate mutations causing them to diverge. In addition, the alleles also appear to be under positive selection, which accelerates evolution and further increases the allelic divergence. The loci with diverged alleles showed differential allelic expression (DAE) depending on environmental conditions, including darkness, low iron, freezing, elevated temperature and increased CO_2. Most strikingly, the fastest evolving alleles also showed the most pronounced DAE. Positive correlations between expression variation and sequence divergence of alleles has also been observed in other species [20], and this is often taken as evidence for relaxed stabilizing selection and reduced canalization. However, one alternative interpretation is that DAE and allelic divergence underpin phenotypic plasticity, and hence, this could be an adaptation evolved to cope with extreme fluctuating conditions (*cf.* the Baldwin effect [9]). Arguably, DAE facilitates the accumulation of beneficial mutations by allowing the allelic lineages (or haplotypes) to evolve independently from each other. Each allele is being expressed under a particular environmental condition, such that natural selection can molt the nucleotide variation so that the allele functions optimally in the condition under which it is expressed. DAE thus assists with the "fine-tuning" of adaptations to specific environmental conditions. An investigation of DAE at the population scale (psADE) [21] has shown the presence of a partial genetic control, thereby allowing the extent of DAE to be under the control of natural selection.

Variation in gene expression has been shown to also play a role in human evolutionary adaptation [22]. Local enrichment in the expression level of genes responsible for responding to, for example, UV-induced DNA damage in equatorial regions points to the importance of regulatory variation in allowing for fine-tuned responses to the local environment. This has been further shown in studies of ASE between different human populations, in which local environmental pressures such as pathogens or diet have been linked to variation in enhancement [23].

The evolutionary implications of DAE can be studied using an Individual Based Model (IBM) in which the evolutionary forces are simulated explicitly so that the individuals can evolve *in silico* and adapt to changing environmental conditions. This enables a direct comparison between DAE and non-DAE strategies under different environmental scenarios and reproductive strategies. In addition, given that marine phytoplankton have a significant impact on biogeochemical cycles [24], studying the impacts of feedback loops between the simulated organisms and the environment is relevant to understand the impact on global change scenarios. The original model designed to study the effects of coupling between life and its environment is the Daisyworld model [25]. It is based on James Lovelock's Gaia theory of the Earth as a self-regulating homeostatic system. Although its central premise that living organisms can have major effect on the climate system is no longer controversial, evolutionary biologists have often ignored the Gaia theory, questioning how a self-regulating biosphere can arise when natural selection acts to maximize the individual fitness of a diverse set of organisms [26]. Various different guises of Gaia have been proposed, and

of those, Homeostatic Gaia appears to be the most acceptable model for evolutionary biologists [26]. More recently, some have argued that biogeochemical cycles and other homeostatic processes that might confer stability are the units of selection [27], whilst others argue for ecosystem-level selection for environmental regulation [28]. The effects of phenotypic plasticity and DAE on environmental homeostasis (*cf.* Homeostatic Gaia) have, however, not been explored despite their likely importance during adaptive evolution of organisms to rapid environmental change and perturbations.

Here, we test the hypothesis that DAE delineates evolutionary trajectory of the alternative alleles, enabling each allele to climb its respective fitness peak in the heterogeneous adaptive landscape, as typically observed in the marine environment. Furthermore, we test whether DAE enables phenotypic plasticity, and whether it can accelerate the rate of evolution by delineating the evolutionary trajectory of alleles. We thus examine whether both processes (*i.e.,* phenotypic plasticity and allelic sub-functionalisation) enhance the adaptive evolutionary potential of marine microbes. Both these processes are independent of environmental feedback or Gaia. In addition, given the importance of marine phytoplankton in biogeochemical cycling, we also examine the consequences of DAE on the environmental resilience of organisms and their feedback with the global environment (*cf.* Gaia [29,30]). We make use of *in silico* simulations of an individual based model in the form of an enhanced 2D cellular automata building on previous work of Daisyworld [31,32] in order to test these hypotheses. We note that the conclusions we draw about the evolution of phenotypic plasticity and allelic sub-functionalisation are independent of the environmental feedback assumed in Gaia. Only the effects of DAE on local and global temperature, and the perseverance of populations are integral to Gaia.

RESULTS

Basic characteristics of the DAEsy-World model

First, we show the output of simple simulations at a single point in time to illustrate the effect of DAEsies on local and global temperature (Fig. 1). The figure shows a 50×50 grid without DAEsies (panel A) and with DAEsies (panel B), and the environmental temperature without DAEsies (panel C) and with DAEsies (panel D). In this figure, the background colour without DAEsies is shown as the mid grey value. DAEsies in panel B have different colours affecting their albedo, which in turn affects the local and global temperature. Note the colour gradient ranges from dark (at the top, representing the polar region

with low solar radiation) to light DAEsies (at the bottom, representing the equator which has the most intense solar radiation). Without DAEsies, there is a marked temperature gradient (panel C). The temperature is however homogenized, fluctuating around 25°C when the surface is populated by DAEsies (panel D). These results are consistent with Daisy-World models (reviewed by Wood *et al.* in [32]).
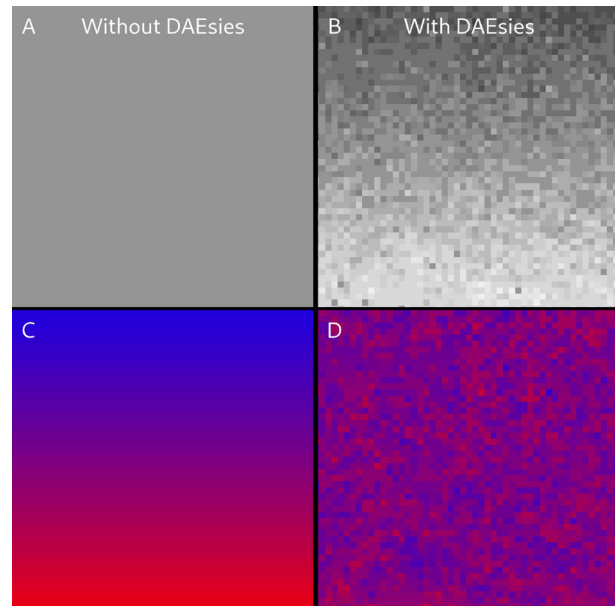

Figure 1. Simulation output showing the 50 × 50 grid at a single point in time. Panels (A) and (C) show the simulation results without DAEsies, and panels (B) and (D) the simulations with DAEsies. Panel (C) shows the gradient in temperature as a consequence of differences in luminosity. Red indicates hot (the equator at the bottom part of panel), and blue indicates cold (the pole at top). Panel (B) shows the distribution of DAEsies, with dark DAEsies at the pole and lighter DAEsies at the equator. Panels (C) and (D) show the environmental temperature. In the presence of DAEsies, the temperature gradient showed in Panel (C) is homogenised in Panel (D).

Effects of DAE on fitness

Next, we examine the effect of DAE on temperature, population stability and fitness in a scenario where luminosity is fluctuating with increasing frequency until the DAEsy population goes extinct (Supplementary Fig. S1). We examine whether DAE leads to the functional divergence of alleles of the simulated temperature-preference locus, and we compare sexually and clonally reproducing DAEsies. Note that without DAE, both alleles are equally expressed (*i.e.*, $h = 0.5$), and that

with DAE, the "fittest" allele closest to the environmental temperature is expressed 80%, and the alternative allele 20% ($h = 0.2$). Figure 2 shows that clonal reproduction with DAE results in the most diverged alleles and phenotypic plasticity. Although clonal DAEsies possess the most diverged alleles that cover the widest temperature range, sexually reproducing DAEsies with DAE are even better able to adapt to rapidly fluctuating environmental conditions, showing the longest survival times (Fig. 3). Both the mode of reproduction (sexual vs. clonal), and the presence or absence of DAE explained significant variation in population resilience (GLM: $F_{1,396} = 290.5$, $p < 0.0001$, and $F_{1,396} = 559.3$, $p < 0.0001$). Interestingly, there is a significant interaction between the mode of reproduction and DAE (GLM: $F_{1,396} = 63.3$, $p < 0.0001$), which showed that clonally reproducing DAEsies benefit more from DAE than their sexual counterparts (Fig. 3). This is understandable; given that without allele segregation and reassortment during sexual reproduction, the clonal DAEsies rely on (slow) mutation accumulation and DAE for their adaptive response to environmental change. DAE extends the environmental envelope that clonal DAEsies can tolerate without reassortment of their alleles. Furthermore, sexually reproducing DAEsies with DAE are the most efficient in moderating global temperature fluctuations (Fig. 4).
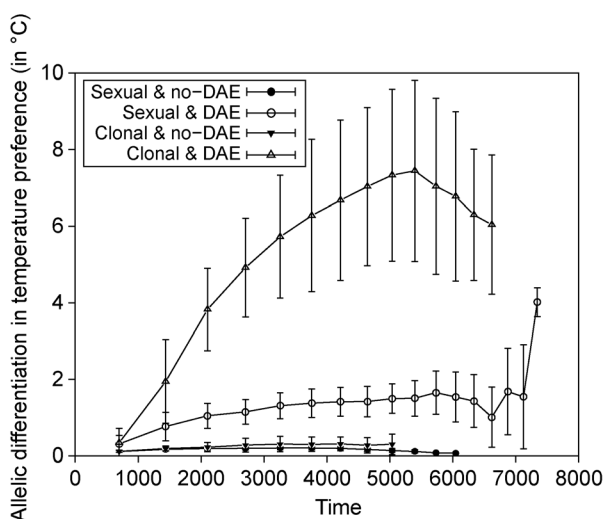

Figure 3. The mean (±StDev) time to population extinction and the actual data points (crosses) for different modes or reproduction (sexual and clonal) for DAEsies with and without DAE under a scenario of luminosity with increasing rapid fluctuations. Sexually reproducing DAEsies with DAE are the most resilient to extinction in this scenario.

Figure 2. The allelic divergence for sexual and clonally reproducing DAEsies with and without DAE expressed as the mean (±StDev) difference in temperature preference between the alleles. Simulated is a scenario of luminosity with increasing rapid fluctuations. Clonal reproduction with DAE results in the most diverged alleles, which implies that these organisms are genetically best adapted to cope with extreme conditions through phenotypic plasticity. However, sexually reproducing DAEsies with DAE are most resilient.
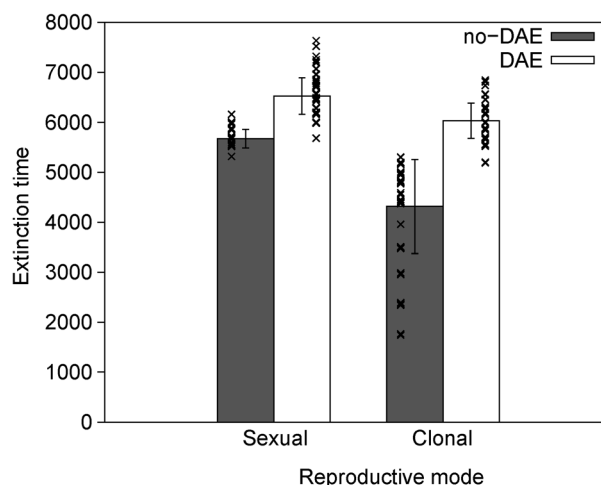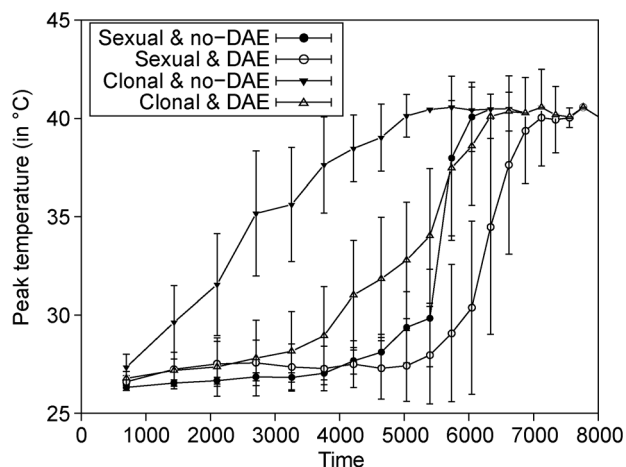

Figure 4. The effect of mode of reproduction (clonal vs. sexual) and DAE on the mean (±StDev) peak temperature in a scenario with an increasing frequency of temperature oscillation. Sexual DAEsies with DAE are the most efficient in moderating global temperature fluctuations.

Evolution of DAE

To examine under which environmental conditions DAE is likely to be adaptive, we allowed the dominance coefficient (h) to evolve. At the start of the simulations, the alleles are additive (i.e., equally expressed with $h =$

0.5), and reproduction is sexual. The simulations show that under fluctuating luminosity, DAEsies with DAE evolve a dominance coefficient of $h = 0.13 \pm 0.04$ (Fig. 5).
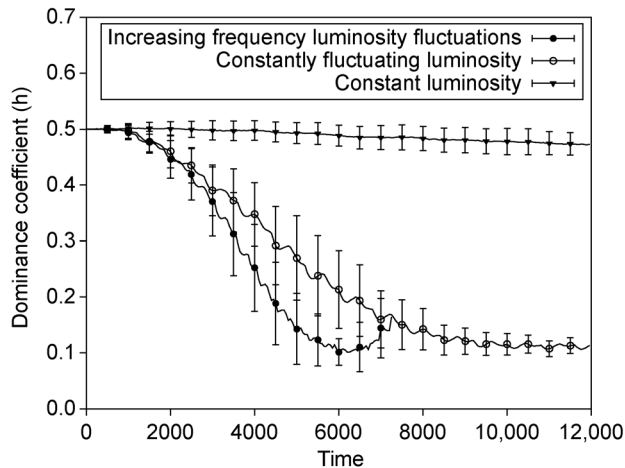

Figure 5. Adaptive change of the mean ($\pm$StDev) dominance coefficient (h) in sexually reproducing DAEsy populations in different luminosity regimes. The adaptive change in h, and hence DAE, evolves in environments with fluctuating luminosity and temperature.

To examine whether DAE enhances a species' evolutionary potential and ability to cope with directional environmental change (*e.g.*, global warming), we compared the population size (N) of sexually and clonally reproducing DAEsies with and without DAE. To simulate global environmental warming, luminosity fluctuated and increased in intensity (Supplementary Fig. S1). Figure 6 shows that species with DAE have a larger population size and higher tolerance to climatic warming. Surprisingly, and in contrast to the results of increasingly rapid fluctuations, clonally reproducing DAEsies survived for slightly longer than sexually reproducing DAEsies under a scenario of global warming. This can be partially explained by the more extremely diverged alleles of clonal DAEsies, resulting in a superior phenotypic plasticity compared to their sexual counterparts (Supplementary Figs. S2 and S3). In addition, in contrast to clonal organisms, sexually reproducing DAEsies were challenged finding a mate when the population size was dwindling, which contributed to their extinction (*cf.* Strong Allee effect [33]).

Furthermore, we observed that under constant luminosity, the phenotype of DAEsies (both their colour as well as their temperature preference) could shift dramatically, but only for the DAE simulations (Fig. 7A, B). Such tipping points are associated with DAEsies finding a new
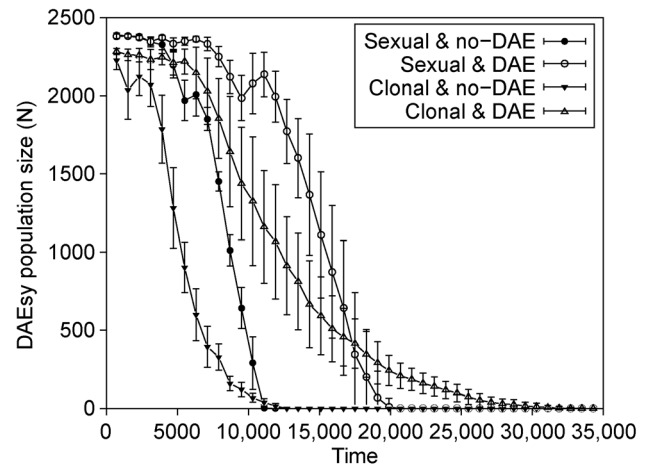

Figure 6. The mean ($\pm$StDev) population size at the peak temperatures of clonally and sexually reproducing DAEsies with and without DAE under a scenario of global warming (*i.e.*, fluctuating luminosity with increasing intensity). The population is most resilient to extinction in clonally reproducing DAEsies with DAE.

temperature optimum (a couple of degrees higher or lower than the start temperature of 25°C, and $1.6 \pm 0.7\%$ darker or lighter than the intermediate grey value). The spontaneous change can be understood by studying Fig. 8, in which we calculated the fitness contours for different allelic divergence and dominance values (h) in clonal DAEsies with DAE in the scenario without oscillations in luminosity. Initially, the allelic divergence is low, and so there is no selective advantage to evolve lower h values. Hence, the optimal h has a wide range (indicated by the dark blue in the top panels of Fig. 8). Over time, selection (and genetic drift) causes the divergence of alleles, which enables DAEsies to better adapt to the local environmental conditions by phenotypic plasticity. However, drift can also produce a stochastic change in mean albedo. DAEsies with small h are superior in expressing the best-adapted allele, as evidenced by the shift in optimal h value in Fig. 8. Due to the small (stochastic) change in mean albedo, selection gradually replaces the maladapted temperature-preference allele. This in turn leads to a directional change in temperature, and hence, a tipping point. We only observed these spontaneous variations in h value, temperature preference and global temperature in clonal DAEsies, presumably because these had the greatest allelic divergence of temperature-preference alleles that can reinforce the initial stochastic change in albedo.

DISCUSSION

Environmental fluctuations in the oceans expose marine microorganisms to a wide range of extremely challenging
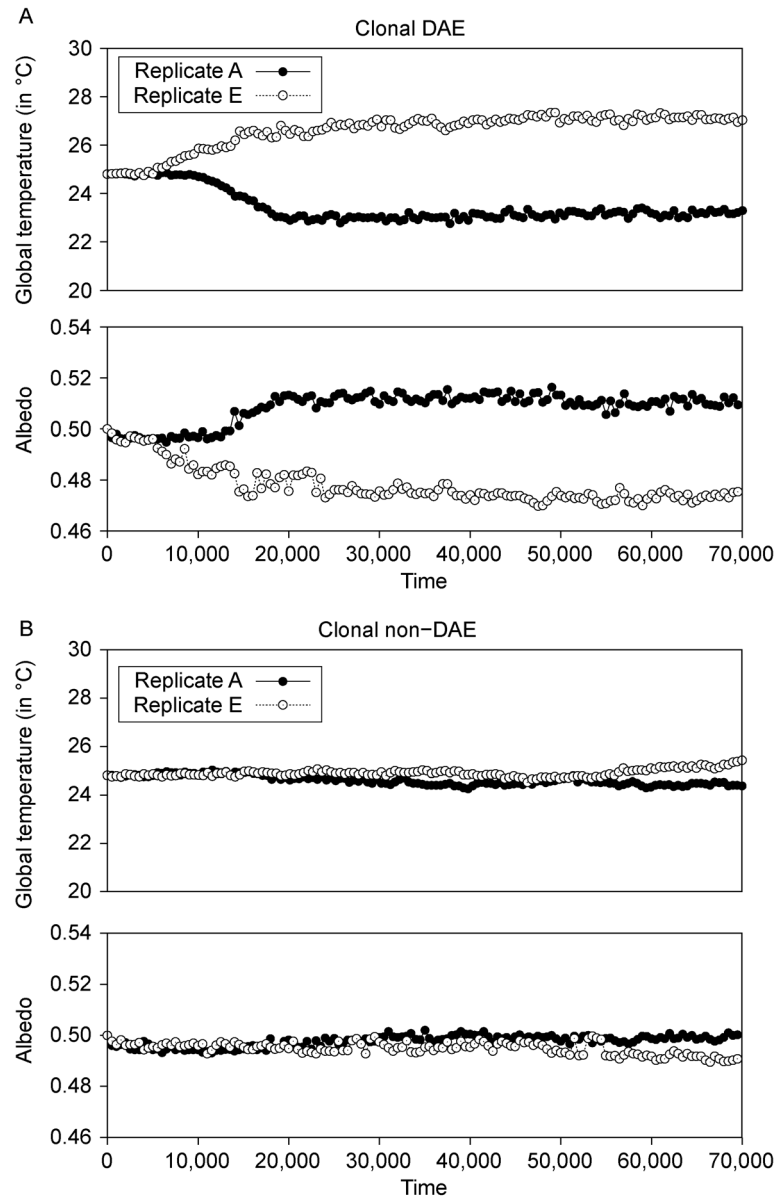
Figure 7. The mean colour and mean temperature preference of DAEsy populations with DAE (A) and without DAE (B) under constant luminosity. Model A and E are two replica runs, which converge to different equilibrium temperature preferences and colours in the DAE scenario after around 10,000 time steps. Rather than homeostasis, there is stochastic change in equilibrium value of the mean phenotype of the DAEsy population (*i.e.*, a "tipping point").

conditions which rapidly change across the seasons, especially in temperate and polar oceans [15–17]. Suspended in currents, subducted by vertical mixing and exposed to a wide temperature range (*i.e.*, > 20°C to below the freezing point of sea water), these surface ocean microbes are subjected to a highly dynamic environment. Given that extreme seasonal changes can occur within the lifespan of a single organism, these ocean microbes need to possess significant phenotypic plasticity to thrive. Mock *et al.* [19] showed that many loci in the genome of a

polar diatom *F. cylindrus* possess highly diverged alleles that are differentially expressed depending on the environment. Here, we test the hypothesis that environment-dependent, DAE of functionally diverged alleles underpins this phenotypically plastic response. Rather than being a consequence of relaxed stabilizing selection and reduced canalization, we propose that DAE is an adaptation evolved to cope with extremely varying conditions, which allows for the sub-functionalization of alleles. To examine this hypothesis, we designed and
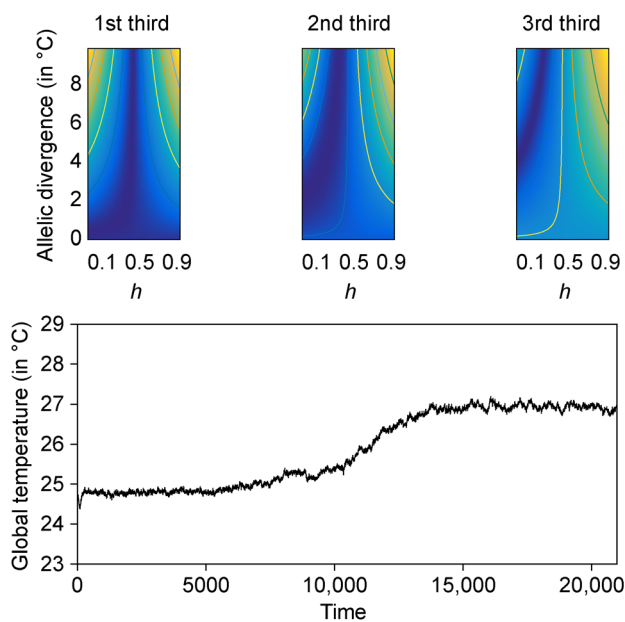
Figure 8. Interaction between changes in dominance coefficient (h), allelic divergence, and ambient temperature in asexual DAEsies with DAE in constant luminosity. From left to right, the top three panels summarise the data between time-steps 1–7000, 7001–14,000 and 14,001–21,000. The colour gradient corresponds to an estimated match between the genotype and the ambient temperature, with dark blue values indicating a good match and yellow a poor match. The allelic divergence increases over time (shift in dark blue). In addition, the optimal h value shifts from additivity ($h = 0.5$) at the start of the simulations to lower dominance values ($h = 0.2$–0.3) at the end. In turn, this affects the ambient temperature (bottom figure).

developed a 2-D cellular automata model building on the Daisyworld model of Wood *et al.* [31]. Our DAEsy-World model simulates organisms (DAEsies) coping with spatiotemporal heterogeneity in temperature, and it enables us to compare the phenotypic and evolutionary response of organisms with and without DAE.

The simulations showed that in a fluctuating environment, DAE results in the evolution of functionally diverged alleles adapted to different temperature optima. The ability to express a specific allelic variant thus helps to fine-tune adaptation to the environment. Alleles of the same gene are able to become sub-functionalized, climbing different fitness peaks in the adaptive landscape, thus broadening the range of environmental conditions that organism can tolerate. Allelic divergence was most pronounced in the clonally reproducing DAEsies, and these were better adapted to cope with extreme conditions through phenotypic plasticity than clonal DAEsies without DAE. Clonal DAEsies with DAE also showed a

higher level of allelic divergence than their sexually reproducing counterparts; without the disruptive effects of recombination, alleles in clonal organisms remain in the same genetic background, which allows these alleles to climb their fitness peaks uncompromised by reassortment after sexual reproduction. In contrast, Mendelian segregation after sexual reproduction could leave the offspring with two alleles both adapted to the same extreme condition, and this segregation load dampens adaptive evolution. Interestingly, clonally reproducing DAEsies benefitted significantly more from DAE than sexually reproducing DAEsies when the fitness was expressed in terms of population resilience. This implies that DAE might be more likely to evolve in organisms with asexual reproduction. The general conclusions hold true and are independent on environmental feedback.

Irrespective of the mode of reproduction (clonal or sexual), DAE enhanced the adaptive evolutionary potential by the sub-functionalization of alleles. In sexual DAEsies, the response to selection could be interpreted as a form of "genetic assimilation", as hypothesised by Waddington [34]. According to Waddington [34], if an organism is exposed to extreme conditions to which it adapts, the adapted character may become canalized such that the trait also appears in the absence of the extreme condition. In our simulations, the DAEsies in fluctuating environment have evolved alleles to cope with the extreme conditions (*i.e.*, high and low temperature). Once the environment changed directionally (*e.g.*, due to global warming), these DAEsies reproduced offspring, some of which inherited two "high temperature" adapted alleles. These offspring displayed a higher temperature tolerance than their parents, and the trait became canalized (*i.e.*, showed little or no phenotypic plasticity). DAE and phenotypic plasticity thus enable the initial survival of the organism under fluctuating environmental conditions [35]. In addition, DAE helps to provide a genetic substrate that can augment the adaptive response to selection through genetic assimilation when the population is pushed beyond its normal environmental range. Again, this conclusion is not dependent on environmental feedback.

Simulations furthermore showed that if a mechanism exists to independently express alleles in response to environmental demands, DAE will evolve diverged alleles and phenotypic plasticity in organisms exposed to a fluctuating environment. Even if the alleles were initially completely additive ($h = 0.5$) and equally expressed, the h will evolve so there is a more extreme bias in allele expression, resulting in a wider temperature tolerance range. However, under stable environmental conditions, there was little bias in allelic expression as both alleles occupied the same fitness peak, and the trait remained canalized. As before, the evolution of differ-

ential allelic expression in fluctuating environments is not dependent on environmental feedback.

DAE also had a significant effect on homeostasis of DAEsy-World and Gaia. As expected, the increased resilience of organisms with DAE increased the ability of the system to self-regulate, census Gaia [30,32]. However, unexpectedly, in a stable environment, DAE occasionally resulted in a tipping point whereby the optimum temperature and colour of the simulated DAEsies shifted up or down, reaching a new equilibrium. We believe this is the result of feedback between the h and the temperature. As the model starts to diverge from the start temperature, a change in h allows for improved survival by upregulating the expression of the best-matching temperature allele. As a consequence, the maladapted allele is being replaced. In other words, DAE begins to actively change the system (*i.e.*, the global temperature, the mean albedo and the value of the temperature preference allele), up until the point at which the equilibrium h value is reached. It is likely that any deviation away from the start temperature could trigger this runaway process, resulting in a tipping point, rather than homeostasis *per se*.

What does this mean for the Gaia theory? Various variants of Gaia have been proposed, some of them tend to be rejected by evolutionary biologists as implausible (*e.g.*, Optimizing Gaia, and Geophysiological Gaia), whereas others (*i.e.*, Homeostatic Gaia) are considered to be more plausible (reviewed by Free & Barton [26]). Homeostatic Gaia may arise when restrictions of environmental conditions to a habitable range are accomplished through the feedback from the biota. In such scenario, environmental homeostasis could occur rarely, which is known as the Lucky Gaia model (*i.e.*, Earth is highly improbable). Alternatively, according to the Probable Gaia model, environmental stasis is a statistically likely outcome. In both cases, the interactions between life and the environment is a by-product of evolved traits that may lead to global stability [26]. Our DAEsy simulations show that different solutions for homeostasis can be found when diverged alleles are differentially expressed (*i.e.*, DAE), thus rendering Lucky Gaia a slightly more probable proposition.

CONCLUSION

Differential allelic expression is a potentially important mechanism by which organisms can enhance their phenotypic plastic response and adaptive evolutionary potential. A positive correlation between DAE and allelic divergence may not just be a consequence of relaxed stabilizing selection and decanalization, but rather point to an evolutionary mechanism that enables organisms to cope with fluctuating environmental conditions. DAE may be particularly important for marine eukaryotic microorganisms that are unable to escape unfavourable conditions through a behavioural response. These organisms have a complex multidimensional adaptive landscape caused by significant spatiotemporal heterogeneity of their environment. This landscape can be better explored by natural selection through DAE, with alleles of the same gene becoming sub-functionalized and occupying different fitness peaks. We propose that DAE in marine eukaryotic microorganisms allows for the sub-functionalization of alleles through the build-up of genetic polymorphisms within some genes driven by positive- and balancing selection, rather than by genetic drift alone. Assuming feedback from biota can restrict environmental conditions to a habitable range (*cf.* Homeostatic Gaia), DAE may enable organisms to explore and find different solutions to reach homeostasis.

MATERIALS AND METHODS

Using the Daisy-World model of Wood *et al.* [31] as a prototype, we develop a 2-D cellular automata model with a heterogeneous environment and environmental dependent alleles included explicitly. Our model is called DAEsy-World, emphasising the central question of our research, *i.e.*, the role of differential allelic expression of balanced polymorphism in evolution and feedback loops. DAEsy-World consists of a 50×50 grid that is populated by DAEsies with two traits, *i.e.*, albedo (grey-scale) and growth temperature. Both traits can evolve and are each coded by a single gene with two alleles. Individuals can reproduce offspring depending on their fitness, which is defined by the absolute difference between ambient temperature and the individual's growth temperature. When reproducing, alleles are transmitted to the offspring either clonally (in which case the offspring has the same genotype as its parent, baring mutations), or sexually (in which case the alleles of the two genes are transmitted independently of each other, *i.e.*, there is no linkage). In other words, recombination was set to $r = 0.5$. The mutation rate was set to $\mu = 0.05$, which falls within the range of the mutation rate of polygenic traits [36]. Gene flow is defined by the distance between the parent DAEsy and its offspring, and the distance in the simulations was $m = 3$. Albedo and growth temperature are non-additive traits, each with a dominance coefficient (h). For albedo, the two alleles are expressed based on the value of h, irrespective of temperature (*i.e.*, no DAE). However, growth temperature has two possible modes: DAE and non-DAE. In the non-DAE case, the alleles are expressed at random, irrespective to their fit to the environmental temperature. In the DAE mode, the most optimal allele

(*i.e.*, the allele closest to the environmental temperature) is expressed with *h*, and the least optimal allele expressed as 1–*h*.

Finally, the model simulated different climatic change scenarios: (1) a constant luminosity, (2) a stably fluctuating luminosity, (3) a constant luminosity with increasing rapid fluctuations, and (4) a fluctuating luminosity with a linearly increasing intensity (Supplementary Fig. S1). This fourth scenario simulates global environmental warming. Temperatures of a square at timestep *t* are calculated based on the position (*x*,*y*) in the grid using the following equation:

$$T_t(x,y) = 0.7\left(259 + \sqrt[4]{\frac{S \times Y \times R \times (1-a)}{4\sigma}}\right)$$

$$+ 0.3 \times T_{t-1}(x,y),$$

where $S = 1366$ is the insolation, *Y* is the intensity of insolation based on distance from the pole that ranges from 0.8 (at the pole) to 1.2 (at the equator), *R* is the luminosity factor (which is a function of the climatic change scenario simulated), *a* is the albedo, and σ is the Stefan Boltzmann constant ($\sigma = 5.67 \times 10^{-8}$). The temperature of a square is then given by the average of itself and all its directly adjacent squares. The global temperature is then recorded as the average temperature over all squares in the grid. The model was written in C,

Table 1   The basic simulation parameters used unless otherwise stated in the text

Fixed parameter	Symbol	Value
Insolation	S	1366
Luminosity factor	R	Variable depending on climate change scenario
Luminosity	L	0.8–1.2
Stefan Boltzmann constant	σ	5.67×10^{-8}
The latitude dependence of luminosity	Y	0.8–1.2
Bare ground albedo	a	0.5
Horizontal grid coordinate	x	1–50
Vertical grid coordinate	y	1–50
Daisy albedo	A	0–1
Maximum age of DAEsy	t_{max}	50
Temperature time step	t	1–70,000
Migration rate	m	3
Recombination rate	r	0.5
Dominance coefficient	h	0.2 unless stated otherwise
Mutation rate	μ	0.05
Temperature mutation deviation		0.1
Colour mutation deviation		0.05

using the parameters presented in Table 1. Further details about the evolutionary forces, DAE, the phenotype, reproduction and fitness is given in the Supplementary Materials and DAEsy-World Manual (https://github.com/ThatPerson/Gaia).

CODE AVAILABILITY

Simulations of our DAEsy-World model can be run under the following link (https://github.com/ThatPerson/Gaia).

SUPPLEMENTARY MATERIALS

The supplementary materials can be found online with this article at https://doi.org/10.15302/J-QB-021-0258.

AUTHOR CONTRIBUTIONS

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COMPLIANCE WITH ETHICS GUIDELINES

The authors Ben P. Tatman, Thomas Mock, Taoyang Wu and Cock van Oosterhout declare that they have no conflict of interests.

All procedures performed in studies were in accordance with the ethical standards of the institution or practice at which the studies were conducted.

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