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The free energy method and the Wright-Fisher
model with 2 alleles

by

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1 **THE FREE ENERGY METHOD AND THE WRIGHT-FISHER**
2 **MODEL WITH 2 ALLELES**

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ABSTRACT. We introduce a new systematic approach to the Wright-Fisher model of population genetics based on the free energy functional. In the present paper, the method is illustrated for the simplest case only, that of 2 alleles.

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13 *energy functional, entropy, entropy production, stationary distribution, reversible*
14 *distribution*

15 1. INTRODUCTION

16 The Wright-Fisher model is the basic model of mathematical population genetics.
17 It is concerned with the time course of the distribution of different alleles that can
18 occupy the same genetic locus in a population under the effects of random genetic
19 drift, mutation, and selection. In this paper, in order to make the – somewhat
20 difficult – mathematical content most transparent, we consider the case where there
21 are only two alleles present in the population. Let us denote these alleles by A^0 and
22 A^1 . The population consists of N individuals which are periodically replaced by
23 their offspring, the individuals of the next generation. The number N is kept fixed,
24 but apart from this global constraint, the number of offspring that any individual
25 can produce is variable. Here, we consider the case of diploid individuals, although
26 the slightly simpler case of haploid individuals is not essentially different in this
27 mathematical model. Thus, at the locus in question, each individual carries two
28 alleles which could be identical or different. In order to create the next generation,
29 each potential offspring randomly seeks two parents (they could be identical, but

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1 when N is large, the chance for that to occur becomes negligible).¹ Each individual
 2 can be chosen as parent several times. Each parent then donates one of its alleles.
 3 Mathematically, this just means that the allele pool of the next generation is created
 4 by random sampling with replacement from the allele pool of the current generation.
 5 In the absence of selective differences, all individuals have the same chance of getting
 6 chosen as a parent. And when no mutations are possible, the offspring faithfully
 7 inherits its alleles from its parents. In that case, the only stochastic effect is
 8 genetic drift. Then, almost surely, after some number of generation steps, one of
 9 the alleles gets extinct, simply because it happens that none of its carriers is chosen
 10 as parent in some generation, and then it will remain absent from the population
 11 forever. Thus, since there were only two alleles to begin with, one of them will
 12 become extinct and the other will survive as the sole allele in the population. This
 13 naturally leads to question like the relative chances of the alleles to be the survivor or
 14 the expected extinction time. The answers are not too difficult. When $0 < p < 1$ is
 15 the relative frequency of allele A^1 in the original population, and hence $0 < 1-p < 1$
 16 is that of A^0 , then the chance of A^1 to survive is p , and the expected extinction
 17 time is the entropy $-p \log p - (1-p) \log(1-p)$. This is classical, but in fact, we
 18 have developed a new constructive approach based on concepts from information
 19 geometry. Anyway, for the mathematical analysis it is most expedient! to pass
 20 to the limit $N \rightarrow \infty$ of an infinite population size and in turn to rescale the time
 21 between generations as $1/N$. The advantage is that the limit can be described by
 22 a partial differential equation, the Fokker-Planck or forward Kolmogorov equation.
 23 Let x be the relative frequency of A^1 , and $u(x, t)$ be the probability density that
 24 that frequency at time t is x . Then the evolution equation is

$$(1.1) \quad \partial_t u(x, t) = \frac{1}{2} \frac{\partial^2}{\partial x^2} (x(1-x)u(x, t)).$$

25 A mathematical difficulty arises from the fact that this equation becomes singular at
 26 the boundary, because the coefficient $x(1-x)$ vanishes when x is 0 or 1. Of course,
 27 this precisely corresponds to the extinction of one of the alleles, A^1 for $x = 0$
 28 and A^0 for $x = 1$. In particular, since one of the alleles will eventually become
 29 extinct almost surely, the process will run into a boundary singularity where $u(x, t)$
 30 becomes a delta distribution supported at $x = 0$ or $x = 1$.

31 The situation becomes more interesting in a sense if we allow for mutations.
 32 That is, in the transmission from parent to offspring, an allele can mutate from
 33 A^0 to A^1 with some positive probability, and likewise from A^1 to A^0 with some,
 34 possibly different, probability. (1.1) is then replaced by

$$(1.2) \quad \partial_t u(x, t) = \frac{1}{2} \frac{\partial^2}{\partial x^2} (x(1-x)u(x, t)) - \frac{\partial}{\partial x} \left(\left(\frac{\theta_1}{2} - \frac{\theta_1 + \theta_0}{2} x \right) u(x, t) \right)$$

35 where θ_0 and θ_1 are the rescaled mutation rates from A^1 to A^0 and from A^0 to A^1 ,
 36 resp. Thus, there is an additional first order term on the right hand side in (1.2).
 37 Mathematically, this is called a drift term.²

¹Of course, this does not sound very biological, but this procedure simply serves to bring out the mathematical aspects most clearly, by ignoring aspects like mate choice etc that are not relevant for the formal properties of the basic model.

²We should point out an essential incompatibility between the mathematical and the biological terminology here. Mathematically, in a Fokker-Planck type equation, the leading part which contains second derivatives w.r.t. the spatial variables is called the diffusion part, and an additional

1 In that case, the effect of random genetic drift can be compensated by the effect of
 2 mutation which may restore the number of the less frequent allele and thereby per-
 3 haps prevent its extinction. In more formal terms, one may ask about the existence
 4 of a stationary distribution where the two effects are in balance. Here, stationary
 5 means that the left hand side of the corresponding Fokker-Planck equation (which
 6 in addition to (1.1) contains a term on the right hand side that represents the effect
 7 of mutation) vanishes. And when such a stationary distribution exists, which it
 8 indeed does in the case of positive mutation rates, one may ask about the rate of
 9 convergence towards such a limiting distribution.

10 One may then wonder what happens when there also selective effects. Here,
 11 selection simply means that the chances of an allele to be drawn as a parent allele
 12 depends on its type. The fitter type has a higher probability. When the fitness of
 13 genotype A_1A_1, A_1A_0, A_0A_0 is $1, 1 + \frac{sh}{2N}, 1 + \frac{s}{2N}$, respectively, (1.2) is replaced by

$$(1.3) \quad \partial_t u(x, t) = \frac{1}{2} \frac{\partial^2}{\partial x^2} \left(x(1-x)u(x, t) \right) - \frac{\partial}{\partial x} \left(\left(\frac{\theta_1}{2} - \frac{\theta_1 + \theta_0}{2} x + \right. \right. \\ \left. \left. + x(1-x)(h-1+x-2hx)s \right) u(x, t) \right).$$

14 The main purpose of this paper is to answer such questions with a powerful novel
 15 method, that of the free energy functional. This method was first introduced in
 16 connection with Fokker-Planck equations in [10]. A connection between statistical
 17 mechanics methods and population genetics was first applied in [9]. Here, we use
 18 these methods and ideas to bring them to bear on the classical model of population
 19 genetics, the Wright-Fisher model.

20 For background on the Wright-Fisher model, we refer to [6]. The general math-
 21 ematical perspective is developed in [8]. The current paper can also be seen as a
 22 sequel to [13] where we have presented an introduction to the mathematical struc-
 23 ture of the Wright-Fisher model for the case of 2 alleles, that is, for the case also
 24 treated here.

25 In more technical terms, in this paper, we shall systematically construct free
 26 energy functionals for the Fokker-Planck or Kolmogorov forward equation derived
 27 from the Wright-Fisher model with 2 alleles with mutation and selection, that is,
 28 (1.1) and its generalizations (1.2), (1.3). It will turn out that the positivity of
 29 the mutation rates is a necessary and sufficient condition for the Wright-Fisher
 30 diffusion process to have a unique stationary reversible probability measure. When
 31 this condition is satisfied, we show that the free energy plays the role of a Lyapunov
 32 functional along the flow of densities. The difference between the current and
 33 the final free energy is given by the relative entropy between the corresponding
 34 measures. The time derivative of this difference is the negative entropy production.
 35 When the two mutation rates (rescaled by the population size) are at least 1/2,
 36 one can reach a quantitative version; as we shall show in [14], in that case the
 37 flow of probability measures (densities) exponentially converges to the stationary
 38 reversible one under various notions of distance (total variation, entropy, L^1 , etc.).

first term, which may or may not be present, is called a drift term. In the biological model, random genetic drift, which is the most important component of the Wright-Fisher model, causes the diffusion, and not the drift term in the Fokker-Planck equation.

1 The stationary distribution is an important quantity in conservative Markov
 2 processes, in particular in diffusion processes derived from population genetics.
 3 However, it is not so easy to get its explicit form in general. A more tractable but
 4 much stronger condition is reversibility. This means that at stationarity the process
 5 has the same distribution as its time reversal. When stationary distributions can
 6 be found explicitly, they usually can be shown to be reversible. We refer the reader
 7 to [6] p.107 for an interesting role of reversibility in population genetics concerning
 8 the prospective and retrospective aspects of the processes. See also, for example,
 9 [11], [12], [15] for various applications of reversibility in population genetics models.

10 In this paper, by using the free energy functional method, we show that the
 11 positivity of the mutation rates is the necessary and sufficient condition for the
 12 Wright-Fisher model with 2 alleles with mutation and selection to have a unique
 13 stationary reversible distribution.

14 This fits into a wider framework. The evolution of many physical or biological
 15 systems is characterized by two kinds of driving mechanisms: diffusion and drift.
 16 The competition between these two types of dynamics may lead the system to a
 17 thermodynamical equilibrium. Recently, the rate of convergence to equilibrium
 18 has been studied in detail for a class of such Fokker Planck type equations (see,
 19 for example, [1], [3] for spatially homogeneous systems, [4], [7], [5] for spatially
 20 inhomogeneous systems). Here, we shall use such techniques to investigate the
 21 convergence to the stationary reversible distribution in the Wright-Fisher diffusion
 22 model with 2 alleles and positive mutation rates.

23 2. THE KOLMOGOROV (FOKKER-PLANCK) EQUATION

24 We consider a diploid Wright Fisher population of N individuals with 2 alleles
 25 A^0 and A^1 . Assume that there are mutations from A^1 to A^0 with rate $\frac{\theta_0}{4N}$ and from
 26 A^0 to A^1 with rate $\frac{\theta_1}{4N}$ (the time unit is $2N$ generations). Then the expectation
 27 values for the change of the frequency X_t of allele A^1 at generation $2Nt$ satisfy

$$(2.1) \quad \begin{aligned} \mathbb{E}(\delta X_t | X_t) &= \left(\frac{\theta_1}{2} - \frac{\theta_1 + \theta_0}{2} X_t \right) (\delta t) + o(\delta t), \\ \mathbb{E}((\delta X_t)^2 | X_t) &= X_t(1 - X_t)(\delta t) + o(\delta t), \\ \mathbb{E}((\delta X_t)^\alpha | X_t) &= o(\delta t), \quad \text{for } \alpha \geq 3. \end{aligned}$$

28 The Kolmogorov forward equation for the family of density functions $\{u(\cdot, t)\}_{t \geq 0}$
 29 in the probability measure space $([0, 1], dx)$ thus becomes (see [6], for instance)

$$(2.2) \quad \partial_t u(x, t) = \frac{1}{2} \frac{\partial^2}{\partial x^2} \left(x(1-x)u(x, t) \right) - \frac{\partial}{\partial x} \left(b(x)u(x, t) \right)$$

30 with drift coefficient

$$b(x) = \frac{\theta_1}{2} - \frac{\theta_1 + \theta_0}{2} x.$$

31 **Remark 2.1.** We note that in our case $A(x)$ does not satisfy a uniform ellipticity
 32 condition as in [2]. In fact, when x goes to the boundary $\partial[0, 1]$, $A(x)$ goes to 0.

33 We first observe an integration by parts formula.

Lemma 2.2.

$$(2.3) \quad \int_0^1 f(x) \partial_x (A(x)g(x)) dx = - \int_0^1 A(x)g(x) \partial_x f(x) dx$$

1 for all $f, g \in C^1([0, 1])$.

2 *Proof.* This is easy to see because $A(x) = \frac{1}{2}x(1-x) = 0$ as $x = 0, 1$. \square

3 To construct a free energy functional for this equation, we shall rewrite it in the
4 following form

$$(2.4) \quad \begin{aligned} \partial_t u(x, t) &= \frac{\partial}{\partial x} \left(\frac{x(1-x)}{2} \frac{\partial}{\partial x} u(x, t) \right) + \frac{\partial}{\partial x} \left(\left(\frac{1-2x}{2} - b(x) \right) u(x, t) \right) \\ &= \frac{\partial}{\partial x} \left(\frac{x(1-x)}{2} \frac{\partial}{\partial x} u(x, t) \right) + \frac{\partial}{\partial x} \left(\frac{x(1-x)}{2} u(x, t) \left(\frac{1-\theta_1}{x} - \frac{1-\theta_0}{1-x} \right) \right) \\ &= \partial_x \left(A(x) \partial_x u(x, t) \right) + \partial_x \left(A(x) u(x, t) \partial_x \psi(x) \right) \\ &= \partial_x \left(A(x) u(x, t) \partial_x (\log u(x, t) + \psi(x)) \right), \end{aligned}$$

5 where

$$A(x) = \frac{x(1-x)}{2},$$

6 and

$$(2.5) \quad \psi(x) = (1-\theta_1) \log x + (1-\theta_0) \log(1-x).$$

7 We shall also write (2.4) as

$$(2.6) \quad \partial_t u = Lu$$

8 with

$$(2.7) \quad Lu := \partial_x (A(x) \partial_x u) + \partial_x (A(x) u \partial_x \psi(x)),$$

9 We shall also need to consider the adjoint L^* of L which is given by

$$(2.8) \quad L^*v = \partial_x (A(x) \partial_x v) - \partial_x \psi A(x) \partial_x v.$$

10 When in addition to mutation, there are also selection effects, things do not
11 change much. Let the fitness of an individual of type A^1A^1, A^1A^0, A^0A^0 be $1, 1 +$
12 $\frac{sh}{2N}, 1 + \frac{s}{2N}$, resp. Then the frequency X_t of allele A^1 at generation $2Nt$ satisfies

$$(2.9) \quad \begin{aligned} \mathbb{E}(\delta X_t | X_t) &= \left(\frac{\theta_1}{2} - \frac{\theta_1 + \theta_0}{2} X_t + s X_t (1 - X_t) (1 - h + (1 - 2h) X_t) \right) (\delta t) + o(\delta t), \\ \mathbb{E}((\delta X_t)^2 | X_t) &= X_t (1 - X_t) (\delta t) + o(\delta t), \\ \mathbb{E}((\delta X_t)^\alpha | X_t) &= o(\delta t), \quad \text{for } \alpha \geq 3. \end{aligned}$$

13 For the family of density functions $\{u(\cdot, t)\}_{t \geq 0}$ on the probability measure space
14 $([0, 1], dx)$, the Kolmogorov forward equation then is

$$(2.10) \quad \partial_t u(x, t) = \frac{1}{2} \frac{\partial^2}{\partial x^2} \left(x(1-x)u(x, t) \right) - \frac{\partial}{\partial x} \left(b(x)u(x, t) \right)$$

1 with drift coefficient

$$b(x) = \frac{\theta_1}{2} - \frac{\theta_1 + \theta_0}{2}x + sx(1-x)(1-h + (1-2h)x).$$

2 We thus see that, compared to the case without selection effects, selection only
3 leads to addition term that do not become singular at the boundary. Therefore,
4 the case with selection can be handled essentially in the same manner as the case
5 without. Consequently, we shall not spell out all the details.

6 As before, we rewrite (2.10) as

$$(2.11) \quad \begin{aligned} \partial_t u(x, t) &= \frac{\partial}{\partial x} \left(\frac{x(1-x)}{2} \frac{\partial}{\partial x} u(x, t) \right) + \frac{\partial}{\partial x} \left(\left(\frac{1-2x}{2} - b(x) \right) u(x, t) \right) \\ &= \frac{\partial}{\partial x} \left(\frac{x(1-x)}{2} \frac{\partial}{\partial x} u(x, t) \right) + \frac{\partial}{\partial x} \left(\frac{x(1-x)}{2} u(x, t) \left(\frac{1-\theta_1}{x} - \frac{1-\theta_0}{1-x} - \right. \right. \\ &\quad \left. \left. 2s(1-h + (1-2h)x) \right) \right) \\ &= \partial_x (A(x) \partial_x u(x, t)) + \partial_x (A(x) u(x, t) \partial_x \psi(x)) \\ &= \partial_x \left(A(x) u(x, t) \partial_x (\log u(x, t) + \psi(x)) \right), \end{aligned}$$

7 where now

$$\psi(x) = (1-\theta_1) \log x + (1-\theta_0) \log(1-x) - 2s((1-h)x + \frac{1}{2}(1-2h)x^2).$$

8

3. ENTROPY AND FREE ENERGY

9 **Definition 3.1.** For a nonnegative function $f(x)$ defined on $[0, 1]$ with $\int_{[0,1]} f dx = 1$
10 (i.e., f is a density), we define its (negative) entropy functional by

$$(3.1) \quad S(f) = \int_{[0,1]} f \log f dx.$$

11 **Definition 3.2.** For a family of densities $\{u(\cdot, t)\}_{t \geq 0}$ on $[0, 1]$ satisfying an evolution
12 equation of the form (2.2), we define the potential energy functional by

$$(3.2) \quad \Psi(u(\cdot, t)) := \int_{[0,1]} u(x, t) \psi(x) dx.$$

13 and the free energy functional by

$$(3.3) \quad \begin{aligned} F(u(\cdot, t)) &:= \int_{[0,1]} u(x, t) \left(\log u(x, t) + \psi(x) \right) dx \\ &= S(u(\cdot, t)) + \Psi(u(\cdot, t)). \end{aligned}$$

1 **Remark 3.3.** The connection between Fokker-Planck equations and free energy
 2 functionals was first established in [10]. In particular, in [10], it was demonstrated
 3 that a Fokker-Planck equation with gradient drift term may be interpreted as a
 4 gradient flux, or a steepest descent, of a free energy functional with respect to a
 5 certain (Wasserstein) metric.

6 **Definition 3.4.** Let f_1, f_2 be densities on $[0, 1]$. The relative entropy (Kullback–
 7 Leibler divergence) of f_1 with respect to f_2 is

$$D_{\text{KL}}(f_1 \| f_2) := \begin{cases} \int_{[0,1]} f_1(x) \log \frac{f_1(x)}{f_2(x)} dx, & \text{if } \text{supp}(f_1) \subset \text{supp}(f_2) \\ \infty, & \text{otherwise} \end{cases}$$

8 The following observation will be important.

Lemma 3.5.

$$Z(\theta_1, \theta_0) := \text{Beta}(\theta_1, \theta_0) := \int_0^1 e^{-\psi(x)} dx = \int_0^1 x^{\theta_1-1} (1-x)^{\theta_0-1} dx$$

9 or, when there is also selection present,

$$Z(\theta_1, \theta_0, s, h) := \int_0^1 e^{-\psi(x)} dx = \int_0^1 x^{\theta_1-1} (1-x)^{\theta_0-1} e^{2s((1-h)x + \frac{1}{2}(1-2h)x^2)} dx$$

10 is finite if and only if both θ_1 and θ_0 are positive.

11 Here, the notation Z indicates that this expression is a partition function in the
 12 sense of statistical mechanics, whereas the notation Beta simply expresses the fact
 13 that we are dealing with a Beta-function.

14 **Definition 3.6.** A probability measure μ on $[0, 1]$ is called *stationary (invariant)*
 15 with respect to the Wright-Fisher diffusion ((2.2) or (2.10)) if

$$(3.4) \quad \int_{[0,1]} L^* f(x) \mu(dx) = 0, \quad \forall f \in C_0^\infty([0, 1]).$$

16 It is called *reversible* if

$$(3.5) \quad \int_{[0,1]} g(x) L^* f(x) \mu(dx) = \int_{[0,1]} f(x) L^* g(x) \mu(dx), \quad \forall f, g \in C_0^\infty([0, 1]).$$

17 **Theorem 3.7.** In a diploid Wright–Fisher model of N individuals of 2 alleles
 18 A_0, A_1 . Assume that there are mutations from A^1 to A^0 with rate $\frac{\theta_0}{4N}$ and from A^0
 19 to A^1 with rate $\frac{\theta_1}{4N}$. Then the necessary and sufficiency condition to have a unique
 20 stationary distribution is

$$(3.6) \quad \theta_0 > 0, \theta_1 > 0.$$

21 The stationary distribution then is of the form

$$(3.7) \quad \mu_\infty^m(dx) = u_\infty^m(x) dx = \frac{x^{\theta_1-1} (1-x)^{\theta_0-1}}{\text{Beta}(\theta_1, \theta_0)} dx$$

22 in the absence of selection. In the presence of selection, this becomes

$$(3.8) \quad \mu_\infty^{ms}(dx) = u_\infty^{ms}(x) dx = \frac{x^{\theta_1-1} (1-x)^{\theta_0-1} e^{2s((1-h)x + \frac{1}{2}(1-2h)x^2)}}{Z(\theta_1, \theta_0, s, h)} dx.$$

1 *Proof.* (1) (\Rightarrow) : (3.6) is equivalent to

$$(3.9) \quad \int_{[0,1]} e^{-\psi(x)} dx < \infty.$$

2 Consequently, $\mu_\infty(dx) = \frac{e^{-\psi(x)}}{Z} dx$ is well-defined. We now execute the
3 following steps

4 Step 1: $\mu_\infty(dx) = \frac{e^{-\psi(x)}}{Z} dx$ is reversible with respect to L^* :

$$(3.10) \quad \begin{aligned} \int_{[0,1]} f L^* g d\mu_\infty &= \int_{[0,1]} f \left(\partial_x (A(x) \partial_x g) \right) u_\infty(x) dx - \int_{[0,1]} f \left(\partial_x \psi A(x) \partial_x g \right) u_\infty(x) dx \\ &= - \int_{[0,1]} A(x) \partial_x g \partial_x \left(f \frac{e^{-\psi(x)}}{Z} \right) dx - \int_{[0,1]} \left(\partial_x \psi A(x) \partial_x g \right) f u_\infty(x) dx \\ &\quad \text{(due to (2.3))} \\ &= - \int_{[0,1]} A(x) \partial_x g \left(\partial_x f - f \partial_x \psi(x) \right) \frac{e^{-\psi(x)}}{Z} dx - \int_{[0,1]} \left(\partial_x \psi A(x) \partial_x g \right) f u_\infty(x) dx \\ &= - \int_{[0,1]} A(x) \partial_x g \partial_x f \frac{e^{-\psi(x)}}{Z} dx \\ &= - \int_{[0,1]} A(x) \partial_x g \partial_x f d\mu_\infty(x). \end{aligned}$$

6 which is symmetric between f and g .

7 Step 2: $\mu_\infty(dx) = \frac{e^{-\psi(x)}}{Z} dx$ is stationary with respect to L^* :

8 By applying Step 1 with an arbitrary f and $g = 1$ and using $L^*1 = 0$.

9 Step 3: $\mu_\infty(dx) = \frac{e^{-\psi(x)}}{Z} dx$ is the unique absolutely continuous stationary
10 density reversible with respect to L^* :

11 Assume that ν is absolutely continuous, stationary and reversible with
12 respect to L^* . Then $\nu(dx) = k(x) \mu_\infty(dx)$ for some positive function k
13 and of course we also have $\mu_\infty(dx) = k(x)^{-1} \nu(dx)$. Therefore

$$(3.11) \quad \begin{aligned} 0 &= \int_{[0,1]} L^* f d\nu \\ &= \int_{[0,1]} L^* f k d\mu_\infty \\ &= \int_{[0,1]} f L^* k d\mu_\infty, \quad \text{due to the symmetry of } \mu_\infty \end{aligned}$$

14 This implies that $L^*k = 0$. Similarly, because of the symmetry of ν ,
15 we also have $L^*(k^{-1}) = 0$. Thus

$$(3.12) \quad \begin{aligned} 0 &= L^*(1) - k L^*(k^{-1}) - k^{-1} L^*k \\ &= A(x) \partial_x k \partial_x k^{-1} \\ &= - \frac{A(x) \partial_x k \partial_x k}{k^2} \end{aligned}$$

1 which implies that k is constant. Because ν and μ_∞ are probability
 2 measures, k should be 1. This means that $\nu = \mu_\infty$.
 3 (2) (\Leftarrow): Assume that $\nu(dx) = v(x)dx$ is an absolute continuous stationary
 4 probability measure that is reversible with respect to L^* . This implies that
 5 $Lv = 0$, where

$$Lv = \partial_x(A(x)\partial_x v) + \partial_x(A(x)vZ(x))$$

6 for some vector Z depending on $b(x)$ and $A(x)$. Solving it we have

$$\partial_x \log v = -Z(x).$$

7 Thus, Z is of the form $\partial_x \psi$ for some ψ . Thus, $v = Ce^{-\psi}$. Because of
 8 $\int_{[0,1]} v dx = 1$ we obtain $C = \frac{1}{Z} < \infty$, which means that $\{u(\cdot, t)_{t \geq 0}\}$ satisfies
 9 (3.9) which is equivalent to (3.6). This completes the proof. \square

11 Thus, when the mutation rates are positive, the unique minimizer of the free
 12 energy functional is the Gibbs density

$$(3.13) \quad u_\infty^m(x) := \frac{e^{-\psi(x)}}{Z(\theta_1, \theta_0)} = \frac{x^{\theta_1-1}(1-x)^{\theta_0-1}}{\text{Beta}(\theta_1, \theta_0)},$$

13 and it solves the stationary density equation

$$(3.14) \quad 0 = \partial_x \left(A(x)u_\infty(x)\partial_x(\log u_\infty(x) + \psi(x)) \right).$$

14 We also observe

Lemma 3.8. *The minimum of the free energy F (3.3) is*

$$F_\infty = \int_0^1 f_\infty(x)(\log f_\infty(x) + \psi(x))dx = -\log Z(\theta_1, \theta_0) = -\log \text{Beta}(\theta_1, \theta_0),$$

15 or, if selection is present,

$$F_\infty = \int_0^1 f_\infty(x)(\log f_\infty(x) + \psi(x))dx = -\log Z(\theta_1, \theta_0, s, h).$$

16 4. THE EVOLUTION OF THE FREE ENERGY

17 We shall assume (3.6), that is, positive mutation rates, in order to have a unique
 18 stationary reversible density by Theorem 3.7, and want to show that our flow of
 19 density functions exponentially converges to this Gibbs density function and the
 20 free energy functional plays the role of the Lyapunov functional. We consider the
 21 evolution of the free energy along the flow of densities $\{u(\cdot, t)\}_{t \geq 0}$

$$(4.1) \quad F(u(\cdot, t)) := \int_0^1 \psi(x)u(x, t)dx + \int_0^1 u(x, t) \log u(x, t)dx.$$

22 We shall prove that the free energy functional is a Lyapunov functional.

23 **Lemma 4.1.** *$F(u(\cdot, t))$ decreases along the flow of densities.*

1 *Proof.* Using the divergence form of the flow, we have

$$\begin{aligned}
(4.2) \quad \frac{\partial}{\partial t} F(u(\cdot, t)) &= \int_0^1 \psi(x) \frac{\partial}{\partial t} u(x, t) dx + \int_0^1 \log u(x, t) \frac{\partial}{\partial t} u(x, t) dx + \underbrace{\int_0^1 \frac{\partial}{\partial t} u(x, t) dx}_{=0} \\
&= \int_0^1 \psi(x) \partial_x (A(x) \partial_x u(x, t)) dx + \psi(x) \partial_x (A(x) u(x, t) \partial_x \psi(x)) dx \\
&\quad + \int_0^1 \log u(x, t) \partial_x (A(x) \partial_x u(x, t)) dx + \log u(x, t) \partial_x (A(x) u(x, t) \partial_x \psi(x)) dx \\
&= - \int_0^1 \partial_x \psi(x) (A(x) \partial_x u(x, t)) dx - \partial_x \psi(x) (A(x) u(x, t) \partial_x \psi(x)) dx \\
&\quad - \int_0^1 \partial_x \log u(x, t) (A(x) \partial_x u(x, t)) dx - \partial_x \log u(x, t) (A(x) u(x, t) \partial_x \psi(x)) dx \\
&\quad \text{(due to (2.3))} \\
&= - \int_0^1 \partial_x \psi(x) (A(x) \partial_x u(x, t)) dx - \partial_x \psi(x) (A(x) u(x, t) \partial_x \psi(x)) dx \\
&\quad - \int_0^1 \frac{\partial_x u(x, t) (A(x) \partial_x u(x, t))}{u(x, t)} dx - \partial_x u(x, t) A(x) \partial_x \psi(x) dx \\
&= - \int_0^1 I(x, t) dx
\end{aligned}$$

2 where

$$\begin{aligned}
(4.3) \quad I(x, t) &= u(x, t) \partial_x \psi(x) (A(x) \partial_x \psi(x)) + \frac{1}{u(x, t)} \partial_x u(x, t) (A(x) \partial_x u(x, t)) \\
&\quad + 2 \partial_x \psi(x) (A(x) \partial_x u(x, t)) \\
&= u \langle \partial_x \psi, \partial_x \psi \rangle_{A(x)} + \frac{1}{u} \langle \partial_x u, \partial_x u \rangle_{A(x)} + 2 \langle \partial_x \psi, \partial_x u \rangle_{A(x)} \\
&\geq 0.
\end{aligned}$$

3 This completes the proof. \square

4 By Theorem 3.7,

$$\mu_\infty(dx) = u_\infty(x) dx = \frac{e^{-\psi(x)}}{Z} dx$$

5 is reversible with respect to L^* .

6 We can now compute the decay rate of the free energy functional towards its
7 asymptotic limit along the evolution of the probability density function u . For
8 simplicity, we shall write $F(t)$ in place of $F(u(\cdot, t))$.

9 **Theorem 4.2.** *The difference of the present free energy and the final free energy is*
10 *equal to the relative entropy (Kullback-Leibler divergence) between the corresponding*
11 *densities and also equal to the (negative) entropy of their ratio with respect to the*
12 *stationary probability measure:*

$$F(t, \boldsymbol{\theta}) - F_\infty(\boldsymbol{\theta}) = D_{\text{KL}}(u \| u_\infty) = S_{\mu_\infty}(h) \geq 0.$$

1 *Proof.* We have

$$\begin{aligned}
 (4.4) \quad F(t, \boldsymbol{\theta}) &= \int_{[0,1]} u(\log u + \psi) dx \\
 &= \int_{[0,1]} u(\log u_\infty + \psi) dx + \int_{[0,1]} u(\log u - \log u_\infty) dx \\
 &= \int_{[0,1]} u(-\log Z) dx + \int_{[0,1]} u \log \frac{u}{u_\infty} dx \\
 &= -\log Z + \int_{[0,1]} u \log \frac{u}{u_\infty} dx \\
 &= -\log Z + \int_{[0,1]} h \log h d\mu_\infty
 \end{aligned}$$

2 and

$$F_\infty(\boldsymbol{\theta}) = F(u_\infty) = \int_{[0,1]} u_\infty(\log u_\infty + \psi) = -\log Z.$$

3 This implies the proof. \square

4 **Theorem 4.3.** *The rate of change of the free energy functional (3.3) is equal*
 5 *to the negative of the entropy production (equivalently, the negative of the Fisher*
 6 *information):*

$$\frac{d}{dt} S_{\mu_\infty}(h) = \partial_t F(t, \boldsymbol{\theta}) = -J_{\mu_\infty}(h) := - \int_{[0,1]} \frac{A(x) \partial_x h \partial_x h}{h} d\mu_\infty.$$

7 *Proof.* We have

$$\begin{aligned}
 (4.5) \quad \partial_t F(t, \boldsymbol{\theta}) &= \int_{[0,1]} \partial_t u(\log u + \psi) dx + \int_{[0,1]} u \partial_t (\log u + \psi) dx \\
 &= \int_{[0,1]} \partial_x (Au \partial_x (\log u + \psi)) (\log u + \psi) dx + \int_{[0,1]} \partial_t u dx \\
 &\quad (\text{because } \partial_t \psi = 0) \\
 &= - \int_{[0,1]} (Au \partial_x (\log u + \psi)) \partial_x (\log u + \psi) dx + \partial_t \left(\int_{[0,1]} u dx \right) \\
 &\quad (\text{due to (2.3)}) \\
 &= - \int_{[0,1]} Au \partial_x (\log h) \partial_x (\log h) dx \\
 &= - \int_{[0,1]} \frac{A \partial_x h \partial_x h}{h} u_\infty dx.
 \end{aligned}$$

8 Since $F(u_\infty)$ is independent of t , this yields the proof. \square

1 When the mutation rates have a suitable lower bound, we can reach more precise
2 conclusions. This will be carried out in [14]. For instance, we have

3 **Theorem 4.4.** *For the Wright–Fisher model with 2 alleles with mutation rates*
4 *$\theta_0, \theta_1 > \frac{1}{2}$, the stationary distribution $f_\infty dx$ satisfies the LSI(ρ_1, ∞) with*

$$\rho_1 = \left(\frac{\sqrt{\theta_1 - \frac{1}{2}} + \sqrt{\theta_0 - \frac{1}{2}}}{2} \right)^2.$$

5 **Corollary 4.5.** *Under the above assumptions, the rate of convergence of the relative*
6 *entropy $D_{\text{KL}}(u||u_\infty)$ is*

$$D_{\text{KL}}(u(t)||u_\infty) \leq e^{-2\rho t} D_{\text{KL}}(u(0)||u_\infty).$$

7

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