VOLUME 94, NO. 2 *THE QUARTERLY REVIEW OF BIOLOGY* JUNE 2019

MATHEMATICAL MODELS OF FERTILIZATION—AN ECO-EVOLUTIONARY PERSPECTIVE

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KEYWORDS
fertilization functions, egg, sperm, gamete, fertilization models, sperm limitation

ABSTRACT

Mathematical models of fertilization have been developed for many taxa, for both external and internal fertilizers. They estimate the proportion or number of fertilized gametes based on gamete concentrations and parameters relating to the biology of the model organism, as well as serve multiple purposes: a predictive purpose, with applications in, for example, artificial insemination; they clarify causal components of fertilization success such as concentration, size, collision rates and swimming speed of gametes, and polyspermy block times; and they function as components of models in evolutionary ecology, which often require understanding of fitness consequences of resource allocation between gametes and other traits. We pay particular attention to this last category, which has received less attention than other uses. Many evolutionary models assume the simplest relationship between fertilization success and gamete numbers: all eggs are fertilized. In nature, however, it is not uncommon for eggs to be sperm limited, and fertilization success must decrease as sperm density approaches zero. Fertilization functions become important in the range between these two extremes. We focus on models in evolutionary ecology, but aim for a resource that is useful regardless of topic or taxon by reviewing models developed for different purposes in a common mathematical framework.

The Quarterly Review of Biology, June 2019, Vol. 94, No. 2

0033-5770/2019/9402-0003$15.00

Introduction

FERTILIZATION is a fundamental process and crucial component of fitness for all sexually reproducing organisms, and the only way for obligately sexual organisms to reproduce and to pass on their genetic information to the next generation. Many aspects of this process have been modeled using mathematical models (henceforth called *fertilization functions*—see Appendix 1), which describe the proportion or number of fertilized gametes as a function of total gamete numbers. These functions have potential applications in several fields. They have significantly added to our understanding of the ecology of marine broadcast spawners (Vogel et al. 1982; Styan 1998; Millar and Anderson 2003) where empirical and theoretical developments have reinforced each other (Styan and Butler 2000; Franke et al. 2002; Levitan et al. 2007; Okamoto 2016; Levitan 2018). An obvious application, with potential economic impact, is artificial insemination of livestock, where a good understanding of fertilization is necessary for optimal use of sperm when the aim is to fertilize as many females as possible using a limited supply of high-quality sperm. In other words, the aim is to use enough sperm per insemination, but no more than necessary (Salisbury and Van-Demark 1961; Foote and Kaproth 1997; Den Daas et al. 1998). Our goal is to provide a resource that is of value regardless of topic, but we will pay particular attention to an application that has received less attention than the two mentioned above: the use of fertilization functions as components of mathematical models in evolutionary ecology. Many models, including the majority of sperm competition models (Parker 1998; Parker and Pizzari 2010), assume the simplest possible relationship between the proportion of fertilized eggs and the total number of sperm: that is, that there are always sufficient sperm to fertilize all eggs. This is often well justified in the biological scenarios that these models investigate, and we do not criticize this approach—instead, we aim to complement it. We show that comprehensive mathematical machinery exists that can be integrated into such models with relative ease whenever the biological question of interest necessitates this. And such cases clearly exist: it is intuitively clear that if the number of sperm is zero, then the number of fertilized eggs must also be zero. What happens in between, when sperm is present but not necessarily sufficient to fertilize all eggs? This intermediate scenario, not uncommon in nature, is often known as sperm limitation (or, more generally, gamete limitation), and it is considered to be a particularly potent selective force in marine external fertilizers (Levitan and Petersen 1995; Yund 2000; Levitan 2010), which was likely the mode of reproduction of our ancestors (Levitan 2010). Although several published models do account for sperm limitation in some form (Cox and Sethian 1985; Ball and Parker 1997; Mesterton-Gibbons 1999; Levitan 2000; Bode and Marshall 2007; Iyer and Roughgarden 2008; Lehtonen and Kokko 2011; Henshaw et al. 2014), many (but not all) of these models have derived the fertilization process anew from the ground up, without reference to existing models of fertilization. The use of fertilization functions already available in the literature may streamline development of such models, while making it easier to account for various features of fertilization, such as polyspermy (Styan 1998; Millar and Anderson 2003; Bode and Marshall 2007) or isogamy (Togashi et al. 2007; Lehtonen 2015).

The aim of this review is to combine existing fertilization functions, currently scattered throughout different (often quite specialized) research topics, into a clear and easily accessible source. Fertilization functions may have been initially published using a variety of notations and conventions; here we will present them in a common mathematical framework that facilitates comparison and selection of fertilization functions, as well as their integration into further evolutionary models. We will examine features that are common to most fertilization functions regardless of taxon, while pointing out their unique features. In doing so, we also discuss extensions of existing models, and suggest future directions for research on mathematical models of fertilization.

Scope, Purpose, Structure, and Notation of Fertilization Functions

Fertilization functions can be applied to a great taxonomic range of sexually reproducing organisms, from marine broadcast spawners (Rothschild and Swann 1951; Vogel et al. 1982; Styan 1998; Millar and Anderson 2003) to cattle (van Duijn 1964, 1965; Schwartz et al. 1981; Fearon and Wegener 2000), humans (at least on a qualitative and illustrative level; Amann 1989), and even to isogamous organisms that reproduce sexually via syngamy, but do not have separate male and female gametes (Togashi et al. 2007; Lehtonen 2015). Although some models have been tailored to a specific study organism or taxon, most fertilization functions have several features in common. Case-specific details may be vital when studying the ecology of particular species or taxa, but broader, species-independent features of fertilization can become more important in evolutionary models that aim to address questions that apply to a broad range of organisms. The fact that such near-universal properties of fertilization functions exist in the first place is not surprising, given that regardless of case-specific details, all fertilization functions aim to describe the same fundamental process: the coming together of gametes for successful fertilization as a function of gamete numbers or concentrations. The fertilization functions we discuss in this article generally refer to total fertilizations as a function of total gamete numbers: they describe the overall outcome of a fertilization event, but not how that outcome is divided between, say, competing males. We also initially leave aside phenotypic variation between gametes (within a sex or mating type), effects of the fertilization environment, and how these factors may interact. In other words, we intentionally retain fertilization functions (denoted by F or p—see below) as separate, modular components from, for example, sperm competition, cryptic female choice, gamete-mediate mate choice, and other factors that affect division of the total fertilization outcome. We then discuss how these factors can be combined into a single model.

Fertilization functions are most commonly presented as the proportion of eggs fertilized. This can alternatively be interpreted as the probability that a randomly chosen egg is fertilized. Therefore, a typical fertilization function takes on values in the range [0,1]. In commonly studied scenarios with clearly diverged male and female gametes, this is a very practical approach; in a typical study species, the relative size difference between eggs and sperm is enormous (Parker 1982), and it is intuitive to think of the proportion of fertilized eggs varying as a function of sperm density. In other words, the fertilization function is considered from an egg's perspective, in line with how we typically envision an egg being fertilized by a spermatozoon, rather than vice versa. However, things are not as clear-cut once we broaden our taxonomic focus to isogamous or near-isogamous species, which are common and can be found in all eukaryotic supergroups (Lehtonen et al. 2016a). In such cases, where gametes are morphologically similar, there is no obvious preferred perspective, and it becomes ambiguous to speak of proportions or probabilities of fertilization.

In this article we therefore adopt two notations for fertilization functions. We use the letter p for the proportion of fertilized gametes (or, equivalently, probability of fertilization). In the standard, anisogamous case we denote the number of eggs with x and the number of sperm with y. In situations where there are no morphologically diverged gametes (isogamy), these letters arbitrarily denote the two mating types (Lehtonen et al. 2016a; see Appendix 1). x and y can also be used as subscripts (as in p_x or p_y) to clarify whether we mean the fertilization probability of an x or y gamete. A gamete collision rate parameter is denoted with the letter a. This parameter is sometimes called "'aptitude' for union" (Scudo 1967:286), "bimolecular reaction constant" (Vogel et al. 1982:195), or simply fertilization efficiency parameter. In a more general context, which may cover, for example, rates of encounters between predator and prey or between females and males, the term "encounter-rate kernel" is often used (Kiørboe 2008:8). This parameter may play slightly different roles in different fertilization functions, and some models include more than one parameter. In this article, the notation $p_x(x, y)$ refers to the probability of fertilization of an egg, when there are x eggs and y sperm. This notation suggests the common practice of treating a as a parameter, but this does not need to be the case—in some situations, we may be interested in the fertilization probability of a fixed number of gametes as a function of the collision rate. Furthermore, a can be composed of several components, such as the collision area and relative velocity of gametes (Vogel et al. 1982; Togashi et al. 2007). We will later encounter more complicated fertilization functions that have additional variables or parameters such as gamete mortality rates, survival times, and polyspermy block times. x and y may be termed gamete numbers, concentrations, or densities in different models. Concentration is the number of gametes per volume, and there is therefore no fundamental difference between these two conventions, but it is important to be aware of this terminological difference. It may also be necessary to scale the constant a when total numbers are used instead of concentrations (Togashi et al. 2007).

Although a probability-based notation is often very clear and simple, it is useful to introduce an alternative notation that makes comparisons of fertilization functions between different gametic systems (i.e., isogamy, anisogamy, oogamy—see Appendix 1) more convenient. We use F to denote the total number of fertilizations, so that $F(x, y)$ refers to the total number of successful fertilizations (per unit volume of suspension, when working with gamete concentrations), when there are x and y gametes of the two types. The reason that this notation is in some sense more general is that it is unambiguous, regardless of whether we are dealing with isogamy, anisogamy, or oogamy. When the outcome is overall number of successful fertilizations, no decision needs to be made about which perspective is chosen (i.e., probability of fertilization for an x-type gamete or for an y-type gamete). In fact, the total number of fertilizations must necessarily be the same for the two sexes (or mating types) if gametes cannot fuse with their own type. This seemingly simple fact has far-reaching evolutionary consequences and is often termed the Fisher condition (Houston and McNamara 2005). It is not uncommon to accidentally construct a model that violates this condition, either at the level of gametes or adult organisms (see Lehtonen and Kokko 2011; Jennions and Fromhage 2017, where the former explicitly discusses the gamete perspective). Using the F-notation makes it easier to avoid such mistakes when using fertilization functions, because the common currency that links the fitnesses of the two sexes is explicitly visible. One tradeoff in using this notation is that although it is perspective-independent (the same number F applies to the x- and y-perspectives), it is not volume-independent: the total number of fertilizations may depend on the volume of suspension being observed, while probability of fertilization does not (assuming a homogenous fertilization environment). It is simple to transition between these two notations: if there are x eggs, and F successful fertilizations, then the proportion of fertilized eggs must simply be $\frac{F}{x}$, so that $p_x(x, y) = \frac{F(x,y)}{x}$ and $F(x, y) = xp_x(x, y)$. By a similar argument we have $p_y(x, y) = \frac{F(x,y)}{y}$ and $F(x, y) = yp_y(x, y)$. In this article we use both notations, depending on which allows for a simpler and clearer argument.

FERTILIZATION FUNCTIONS: FROM SIMPLE TO COMPLEX

(OVER)SIMPLIFIED FERTILIZATION FUNCTIONS

In evolutionary models, the use of a fertilization function is often implicit: many models assume that all eggs are fertilized, and although this might not be explicitly written out, it can be thought to be underpinned by a fertilization function that states, in mathematical form, that all gametes of the less numerous type are fertilized. For the purposes of this article, it is useful to express even these very simple cases using the same syntax as we do with more complicated functions. This makes it easier to see exactly where such assumptions are made in an application in evolutionary modeling, and how they could be relaxed by replacing the fertilization function with a more general one. Although it may seem like oversimplifying the point, doing so reveals unifying structures among models, and makes it easier to recognize where a fertilization function could be "plugged into" an existing model, to convert it to a more general one that explicitly accounts for the fertilization process. In this spirit, our simplest function arises from the assumption that in an anisogamous gametic system, all eggs are fertilized (Figure 1A).

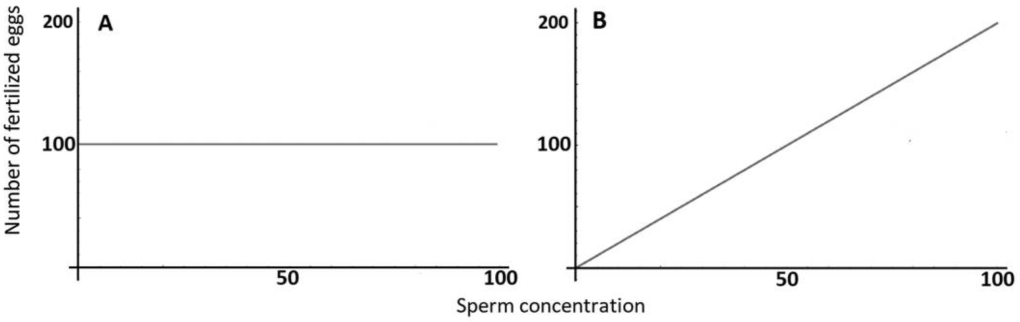

Figure 1. Simple Fertilization Functions

Number of fertilized eggs F versus sperm concentration y (μl^{-1}) for Equation 1 (panel A; F_0 in Table 1) and Equation 3 (panel B; F_1 in Table 1). The initial number of eggs x in the equations is set at 100. In panel B, the rate parameter a is arbitrarily assigned a value of 0.02. See the online edition for a color version of this figure.

$$F(x, y) = x, \text{ or } p_x(x, y) = 1 \tag{1}$$

where F is the successful number of fertilizations, y the number of sperm, and x the number of eggs in a given fertilization event.

This is obviously not useful as a predictive model, and it does not give us much insight into causal factors in the fertilization process. Yet it does have value for clarifying the structure of evolutionary models. Take, for example, a classic, simple sperm competition model based on the "raffle principle" (Parker 1998:9, converted to the notation used in this article). Parker considers group spawning fish, where N males compete for a set of x eggs. Now, if there is one mutant male in the group who releases y_m sperm while the (N–1) "residents" release y_r sperm, the expected fitness gain of the mutant male from this spawning event is $w(y_m, y_r, x) = (\frac{y_m}{y_m + (N-1)y_r})x$. The first component is due to the raffle principle: each male's fertilization success is assumed to be proportional to his relative contribution to the sperm pool that competes for the x eggs. The point of revisiting this simple model here is that, by virtue of Equation (1), the fitness equation can be rewritten as

$$\begin{aligned} w(y_m, y_r, x) &= \left(\frac{y_m}{y_m + (N-1)y_r}\right)x \\ &= \left(\frac{y_m}{y}\right)F(x, y) \end{aligned} \tag{2}$$

where y without a subscript now refers to the total sperm number in the spawning group, i.e., $y = y_m + (N-1)y_r$. Equation (2) makes it explicit that this model (perhaps the simplest sperm competition model) can be thought to already contain a simple fertilization function. As we explore other fertilization functions, we can envision replacing $F(x, y)$ in Equation (2) with each of these functions, to account for different aspects of the biology of the fertilization process. In a similar way, one can take many other (potentially more complex) models from behavioral and evolutionary ecology that make the assumption of all eggs being fertilized, identify the place of the fertilization function in the model, replace the function with a suitable alternative and, thus, convert the model into one that accounts for the risk of incomplete fertilization. We will revisit this topic in more detail later. Note that Equation (2) also underlines the approach of this article, where we think of fertilization functions as mathematical functions that estimate the *total* number of fertilizations $F(x, y)$, while sperm competition is modeled as a separate, multiplicative component ($\frac{y_m}{y}$). The point of the preceding equations is not to say that existing sperm competition models never account for sperm limitation (some do, reviewed in Parker and Pizzari 2010). Instead, our aim is to provide tools and templates that facilitate future work on models of sperm competition and other topics, with access to functions accounting for various biological aspects of fertilization from simple phenomenological models to more complicated ones incorporating factors such as polyspermy or isogamy.

Nevertheless, Equation (1) clearly does not account for sperm limitation. Perhaps the simplest approach to correct this (but a problematic one, as we will soon see) is to assume that the number of fertilized eggs increases linearly with the number of sperm, leading to Equation (3), where the number of realized fertilizations, or zygotes, is proportional to the product of number of sperm and eggs:

$$F(x, y) = axy, \text{ or } p_x(x, y) = ay \qquad (3)$$

where a is a collision rate parameter. This function has been used in models of the evolution of anisogamy that emphasize the selection for maximizing gamete contact rates (Kalmus 1932; Iyer and Roughgarden 2008; Roughgarden and Iyer 2011). Although Equation (3) may be a reasonable approximation under extremely low gamete densities, visualizing it (Figure 1B) immediately reveals a fundamental problem with it under more general conditions. The problem is that the number of fertilizations increases indefinitely with an increasing amount of sperm (assuming $x > 0$, $a > 0$):

$$\lim_{y \to \infty}(F(x, y)) = \infty. \qquad (4)$$

Given that the number of fertilizations can never exceed the number of the less numerous gamete type (usually eggs), this is obviously biologically impossible. It can be shown that many of the more realistic fertilization functions are approximately equal to the mathematical form of Equation (3) under very gamete limited conditions (Lehtonen 2015), but given its very limited applicability, it seems prudent to avoid using this function when better options are available.

In addition to these simple (but often biologically unrealistic) fertilization functions, a number of more realistic functions have been derived to account for properties we expect the fertilization process to have (Table 1). The remainder of this review will be mainly concerned with these more realistic fertilization functions. In this paper we focus on fertilization functions that can be presented explicitly in closed form, but will briefly discuss functions that cannot be presented in closed form in the section titled Properties of the Fertilization Environment in External and Internal Fertilizers.

SATURATION CURVES

Equations (1) and (3) are both clearly very limited models of fertilization. They suffer from opposite problems: the value of Equation (1) does not change with changing sperm concentration, whereas the value of Equation (3) never stops changing. The value given by Equation (1) is constant across all sperm concentrations, which is clearly not realistic when considering a wide range of concentrations. Equation (3) fixes this issue by making fertilization probability dependent on sperm concentration, but it introduces the problem of never-ending increase. As a minimum requirement, a realistic fertilization function must fix these problems: it must initially increase with sperm concentration, but it cannot increase indefinitely. To resolve the problem of a function unrealistically increasing past the biological maximum number of fertilizations, the majority of fertilization functions are saturating functions of sperm concentration. That is, as the number of sperm increases, the number of fertilizations increases at a gradually decreasing rate, approaching the maximum number of possible fertilizations (or the number of eggs). A variety of different derivations can lead to a similar qualitative shape.

A simple version of a saturation curve (Fearon and Wegener 2000) can be seen in equation F_2 (Table 1, visualized in Figure 2), which attempts to rectify the main problem of equation F_1 (Table 1) exceeding the number of eggs by introducing a maximum value to the equation equal to the number of eggs available.

Many fertilization functions, including equations F_3, F_4, F_5, and F_6 (Table 1, visualized in Figure 3), have an outcome that is qualitatively similar in some respects, but with a more gradually saturating curve. Equation F_3 (Figure 3A) is based on a model of

TABLE 1

Compilation of fertilization functions covering a wide range of biological scenarios

Equation	Rationale	References; examples of applications
$F_0(x, y) = x$	All eggs are fertilized.	Implicitly used in many models in evolutionary ecology.
$F_1(x, y) = axy$	Assumes that the number of realized fertilizations, or zygotes, is proportional to the product of the numbers of the two gamete types.	Kalmus (1932) and Iyer and Roughgarden (2008) in models of the evolution of anisogamy.
$F_2(x, y) = x \times \min\{1, ay\}$	Similar to F_1, with maximum number of fertilizations restricted to the number of eggs.	Explicitly used by Fearon and Wegener (2000) in a study of cattle fertility, who based their equation on sketches by Salisbury and VanDemark (1961) for cattle fertility and Amann (1989) for human fertility.
$F_3(x, y) = x \frac{y}{a^{-1} + y}$	Based on a model of enzyme kinetics. Not derived from known biological justifications in a fertilization context.	Enzyme kinetic model derived by Michaelis and Menten (1913). Used to model fertilization in reef fish (Warner et al. 1995), in sperm competition models (Mesterton-Gibbons 1999), and studies of cattle fertility (Fearon and Wegener 2000).
$F_4(x, y) = x(1 - e^{-ay})$	Can be derived by assuming that egg-sperm encounters follow a Poisson distribution (Schwartz et al. 1981) or using differential equations based on principles of bimolecular kinetics (Vogel et al. 1982).	Rothschild and Swann (1951) and Vogel et al. (1982) on sea urchin fertilization success. Schwartz et al. (1981) and Fearon and Wegener (2000) in the context of artificial insemination of livestock.
$F_5(x, y) = x \times \max\left\{0, \left(1 - \frac{1}{(ay)^{\gamma}}\right)\right\}$ Here γ is a parameter relating to sperm mortality, as well as other factors that affect mortality outside of sperm numbers (see van Duijn 1964, 1965; Fearon and Wegener 2000).	Derived for the purposes of artificial insemination. Based on the assumption that the number of viable spermatozoa decays exponentially with time since insemination, and the probability that a viable egg will become fertilized is constant until the number of viable spermatozoa falls below a critical value, when it drops to zero.	Derived in van Duijn (1964, 1965). Later used by Fearon and Wegener (2000).

continued

TABLE 1
Continued

Equation	Rationale	References; examples of applications
$F_6(x, y) = xe^{-\frac{1}{ay}}$	No known biological justification provided.	Found to fit empirical data on bovine artificial insemination better than other exponential forms by Pace et al. (1981). See also Fearon and Wegener (2000).
$F_7(x, y) = \begin{cases} xy\frac{1-e^{at(y-x)}}{x-ye^{at(y-x)}} = xy\frac{e^{atx}-e^{aty}}{xe^{atx}-ye^{aty}} & x \neq y \\ \frac{atx^2}{1+atx} & x = y \end{cases}$ Here, x and y refer to mating types if the two sexes have not diverged. t can refer to experimental time, or life span of the shorter-lived gamete type if time is not restricted. a can be decomposed into gamete collision cross section and relative gamete velocity. a must be scaled by volume unless gamete concentrations are used for x and y (Togashi et al. 2007), but for many modeling purposes at can be replaced with a single parameter describing fertilization efficiency. The two forms in the top row are equivalent. The latter has the benefit of clearly displaying the symmetry of the mathematics, while the former may have computational benefits when x and y are very large but similar in size.	Does not assume anisogamy; gamete types are treated symmetrically. Based on the assumption that gametes have fixed life spans, or that there is a fixed experimental time. See also the section on generalizations.	Derived in Togashi et al. (2007). Used as a component in a model of anisogamy evolution (Lehtonen and Parker 2019).
$F_8(x, y) = x(1 - e^{-z(t)})$ Here $z(t) = F_e \frac{y}{x}(1 - e^{-axt})$, F_e is the fertilization efficiency of a particular egg and sperm suspension (this notation follows Styan 1998) and t is time (often approximated by sperm half life if the process is allowed to run for a length of time that exceeds gamete survival). In this context, the gamete collision rate (or "bimolecular reaction constant") a is a product of the mean spermatozoon speed and the cross section area of an egg.	Can be thought to describe so-called nonpathological or physiological polyspermy (see Jaffe and Gould 1985; Snook et al. 2011): multiple spermatozoa may stick to one egg, diminishing sperm concentration, and any egg with one or more potentially fertilizing sperm-egg interaction is successfully fertilized.	Derived by Vogel et al. (1982). Later applied in several studies of fertilization in broadcast spawners (Levitan 2000).

$F_9(x, y) = x\{1 - e^{-z(t)} - (1 - e^{-z(t)} - z(t)e^{-z(t)})(1 - e^{-b})\}$ Here $z(t)$ and F_e are as above, and $b = F_e \frac{y}{x}(1 - e^{-axt_b})$ where t_b is the polyspermy block time: time after first fertilization before a polyspermy block occurs. t can be approximated by sperm half-life as above.	Lethal polyspermy: extended from F_8 to account for lethal effects of multiple fertilizations that occur in many species.	Derived by Styan (1998). Applied in many studies of fertilization in broadcast spawners (Levitan et al. 2007).
$F_{10}(x, y) = x\begin{cases} z(t)e^{-z(t)} & t \leq t_b \\ [z(t) - z(t - t_b)]e^{-z(t)} - [e^{-z(t_b)} - e^{-z(t)}]e^{axt_b} & t > t_b \end{cases}$ Here $z(t)$ and t_b are as above.	Lethal polyspermy: corrects potential problems in the derivation of F_9.	Derived by Millar and Anderson (2003). Applied in a study of fertilization success in New Zealand geoducks (Gribben et al. 2014).
$F_{11}(x, y) = \beta x_i(\Sigma_j y_j c_{ij})[e^{-(\Sigma_j y_j c_{ij})}]$ Yields the number of fertilized eggs of type i. Here i refers to an egg expressing recognition protein of type i, and j to sperm expressing protein of type j. c_{ij} is the affinity between eggs and sperm carrying given protein types. β is a constant that rescales the function so that the maximum value equals 100% fertilization.	A phenomenological model accounting for lethal polyspermy combined with intrapopulation variation in gamete recognition proteins.	Used in a model of recognition protein diversification (Tomaiuolo and Levitan 2010). Similar functions, accounting for polyspermy, but without variation in recognition proteins, have been used by Bode and Marshall (2007) and Tomaiuolo et al. (2007).

In a given fertilization event, F is the number of successful fertilizations (or zygotes), y is the initial number or concentration of sperm, x is the initial number of eggs, and a is a gamete collision rate parameter or, more generally, a fertilization efficiency parameter that can in some cases be thought to account for factors such as gamete mortality, gamete aging, and gamete swimming speed. Under isogamy, x and y refer to the two mating types instead of eggs and sperm. Other model components are explained under the function where they appear. All functions could be further multiplied by an additional parameter denoting the maximum proportion of eggs that can be fertilized (see Fearon and Wegener 2000). This parameter would simply be a multiplier in front of each function, and we omit it from all equations throughout this manuscript for clarity.

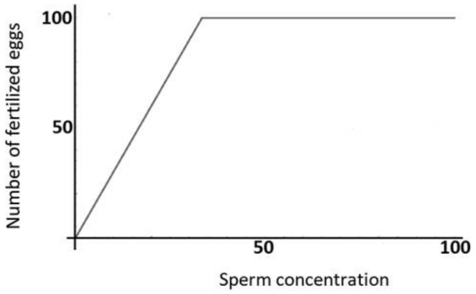

FIGURE 2. A SIMPLE SATURATING FERTILIZATION FUNCTION

Number of fertilized eggs F versus sperm concentration y (μl^{-1}) for equation F_2 (Table 1). The initial number of eggs x in the equations is set at 100, and the rate parameter a is assigned a value of 0.1. See the online edition for a color version of this figure.

enzyme kinetics commonly used in biochemistry (Michaelis and Menten 1913). It has been applied as a fertilization function (Mesterton-Gibbons 1999; Fearon and Wegener 2000), but we do not know of explicit biological justifications for this. Similarly, equation F_6 (Figure 3D) seems to be based mainly on a good fit with data in artificial insemination (Pace et al. 1981) with no clear biological rationale. Both of these equations therefore appear to be phenomenological, where the relationship between the variables seeks to best describe the data without considering underlying biological processes (Hilborn and Mangel 1997). Contrarily, equation F_4 (Figure 3B) can be derived under the biological assumption that the egg-sperm encounters follow a Poisson distribution (Schwartz et al. 1981 for artificial insemination) or using differential equations (Vogel et al. 1982 for sea urchins). These models are mechanistic, where the relationship is instead derived from biological processes that are thought to have given rise to the data (Hilborn and Mangel 1997).

Despite the different methods used to arrive at the equations above, as well as the apparent differences when reading the equations (Table 1), it is evident when repre-

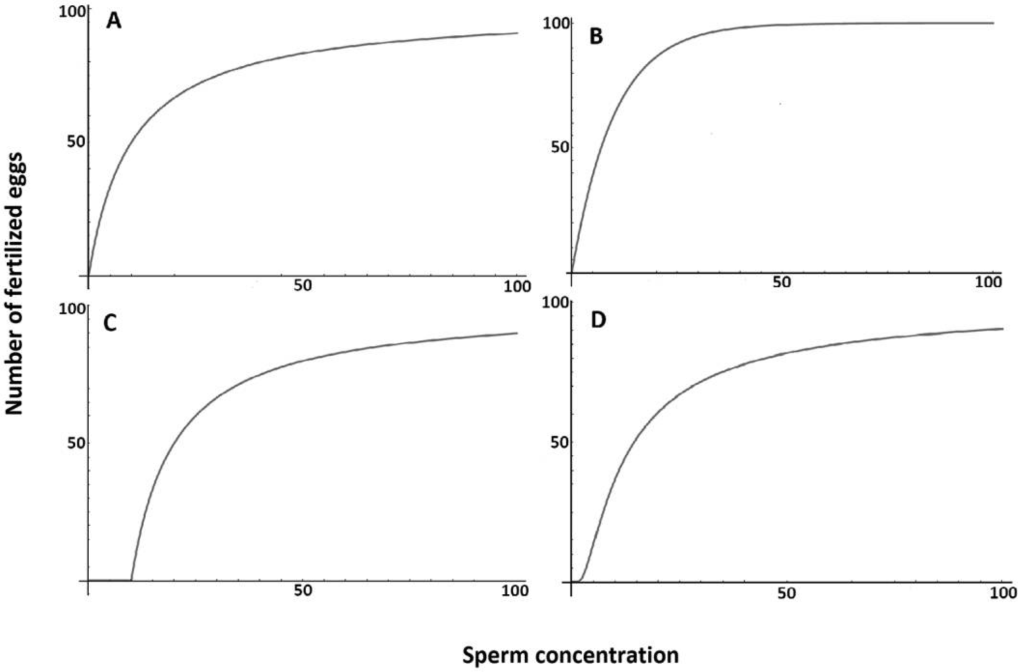

FIGURE 3. SATURATING FERTILIZATION FUNCTIONS

Number of fertilized eggs F versus sperm concentration y (μl^{-1}) for equations F_3 (panel A), F_4 (panel B), F_5 (panel C), and F_6 (panel D) from Table 1. The initial number of eggs x in the equations is set at 100, and the rate parameter a is arbitrarily assigned a value of 0.1. In panel C, $\gamma = 1$. See the online edition for a color version of this figure.

sented visually (Figure 3) that the functions all produce qualitatively similar saturation curves, at least over part of their range. However, it is important to note that equations F_5 (Figure 3C) and F_6 (Figure 3D; Table 1) both have initial phases where the fertilization success does not increase with sperm density until a minimum value is reached (F_5), or increases more slowly at first (F_6). In other words, both equations have an initial "accelerating" (convex) phase with equation F_5 accelerating in a stepwise fashion, while the other saturating curves are decelerating (concave) the entire way. The two "accelerating" functions therefore suggest that fertilization is either impossible or less efficient until a critical density of sperm is achieved. Whether such an assumption is realistic is debatable, and the answer may be taxon-specific. Schwartz et al. (1981) question the derivation of equation F_5 originally proposed by van Duijn (1964, 1965) for artificial insemination of livestock, stating that the assumptions about aspects of sperm kinetics introduced by the formula were complicated and not well understood. The equation is a good fit to the data presented by van Duijn, as well as that presented by Schwartz et al. (1981), but in both cases there are no data for very low sperm concentrations and low fertilization probability, which is where the threshold or acceleration effect would be observable. Similarly, equation F_6 seems to have been first explicitly proposed by Pace et al. (1981) who found that it fit their data better than other exponential forms, while offering no biological justification.

The case of a threshold of sperm concentration seems inconclusive. Van Duijn (1965) and Pace et al. (1981) both found that the "threshold versions" fit their empirical data best. On the other hand, fertilization is possible when sperm concentration in the immediate vicinity of eggs is low, such as in marine invertebrates (Franke et al. 2002) as well as mammals (Hunter 1996). The only potential biological reason for such a threshold or accelerating effect that we are aware of is polyspermy in birds: contrary to most taxa, it has been shown that the fertility of chicken and turkey initially increase with the number of sperm that penetrate the perivitelline layer of the egg (Bramwell et al. 1995; Wishart 1997). In other words, polyspermy (if defined as multiple sperm penetrating the perivitelline layer) can be beneficial in birds. However, females seem to compensate for low sperm concentrations by enhancing sperm progression to the ovum (Hemmings and Birkhead 2015), potentially canceling the threshold effect in the overall relationship between inseminated sperm concentration and fertility. We are not aware of such accelerating functions having been proposed for describing fertilization in external fertilizers. However, it is important to be aware that fertilization functions or fertilization data are quite commonly presented on a logarithmic scale, which may give the impression that the sperm concentration-fertilization relationship is initially accelerating even for those functions that are in fact decelerating all the way (Styan 1998; Levitan 2004, 2005; Okamoto 2016). The initial seemingly convex phase in these cases arises only because of how the logarithm transforms the data. The existence of an initial accelerating phase may be of relatively little importance for the purposes of artificial insemination, where the main interest lies in the part of the curve that maximizes fertility. However, in the context of marine external fertilizers there has been much interest in fertilization under low sperm concentrations (Levitan 1993; Levitan and Petersen 1995; Yund 2000; Franke et al. 2002; Okamoto 2016), where a hypothetical initial accelerating phase would be important. Similarly, such details are relevant in models in evolutionary ecology, where the shape of the function may have important consequences for the evolutionary origin of the two sexes (Kalmus 1932; Iyer and Roughgarden 2008; Lehtonen and Parker 2014; Parker and Lehtonen 2014) and for sex-specific selection on further asymmetries once males and females have evolved (Lehtonen et al. 2016b; Parker et al. 2018). The only two models in Table 1 with an initial convex phase are F_5 and F_6. The biological assumptions of the former have been questioned (Schwartz et al. 1981), while no biological justification was given for the latter by Pace et al. (1981). Furthermore, the empirical data used to test these functions appears to not cover low enough fertility to test for such an accelerating phase. For these reasons, we are somewhat skeptical of such functions.

FURTHER BIOLOGICAL AND PHYSICAL FACTORS IN FERTILIZATION FUNCTIONS

GAMETE AGE, MORTALITY, AND MOTILITY

The fertilization capacity of gametes decreases, and the proportion of abnormal embryos resulting from fertilizations increases with gamete age (Salisbury and Hart 1970; Reinhardt 2007). Although both sperm and eggs senesce (Salisbury and Hart 1970), on the timescale of a single fertilization event sperm aging is dominant and, hence, most fertilization functions only account for sperm aging. Many models account for gamete aging explicitly (van Duijn 1964, 1965; Vogel et al. 1982; Lehtonen 2015; Okamoto 2016), although the mathematical details may differ significantly between models. For example, in function F_7 (Table 1; Togashi et al. 2007; Lehtonen 2015), t can denote fixed gamete life span or a fixed experimental time, which results in an overall fertilization efficiency parameter that can be decomposed into multiplicative components: gamete encounter rate and gamete life span. Alternative functions presented by Lehtonen (2015), and a model accounting for polyspermy by Okamoto (2016) implement a constant mortality rate on gametes, which corresponds to exponentially distributed gamete life spans if gametes were allowed to die of old age. Functions F_8–F_{10} in Table 1 all contain a time parameter t, which is in practice often approximated with sperm half-life (Vogel et al. 1982; Styan 1998; Millar and Anderson 2003). Even in phenomenological functions, such as F_3, it may be useful to qualitatively envision that the parameter a is influenced by gamete aging.

Most fertilization functions treat sperm aging so that spermatozoon behavior does not change until they effectively "die" and are removed from the pool of available sperm. In reality, it is likely that the aging process is more gradual, with the fertilization ability of a single spermatozoon decreasing over time, and a discrete death event may not even be discernible. In fact, a decrease in sperm motility may be the main expression of sperm aging (see Reinhardt 2007 and references therein). This suggests that a mortality rate of spermatozoa, or other ways of modeling gamete "death" may not be the most realistic way to model gamete aging. A more realistic alternative may be to make the gamete collision rate a function of time, so that $a = \alpha(t)$, and gamete aging effects can be included in the function $\alpha(t)$. We will return to this topic later and show that many existing models can be readily converted to this line of thinking. It is also worth noting that simply observing a decrease in the fertilization ratio of eggs with increased sperm age does not, by itself, enable us to differentiate between the effects of, say, sperm dying and sperm slowing down.

UPPER LIMIT TO FERTILITY

Evidence suggests that less than 100% of eggs are fertilized even under optimum conditions in internal fertilizers (Salisbury and VanDemark 1961; Schwartz et al. 1981) as well as external fertilizers (Hodgson et al. 2007). To maintain focus on the biological features of interest that differ between the functions, and to avoid superfluous parameters, we have omitted this component of the fertilization functions in Table 1 (as do many of the articles from which the functions were sourced). This intentional omission can be easily amended by multiplying each function with an additional parameter that controls maximum fertility (see Schwartz et al. 1981; Hodgson et al. 2007).

FRACTION OF EGG SURFACE THAT IS FERTILIZABLE, OR FERTILIZATION EFFICIENCY

Although the eggs of many species are not picky in that any point on the surface of the egg is fertilizable, in some species sperm can enter the egg only at certain locations on the surface (Jaffe and Gould 1985). The Don Ottavio model (F_8) as originally presented by Vogel et al. (1982), as well as that of Millar and Anderson (2003) accounts for this by using two collision constants, one corresponding to the total cross section of the egg, the other to the fertilizable area. However, in Table 1 we have instead followed the notation of Styan (1998) who argues that, in practice, it is difficult to separate the fertilizable fraction of the egg from other effects, such as characteristics of the quality of sperm, or incompatibility between certain combinations of egg and sperm. Instead of two collision constants, Styan uses a single parameter F_e that determines the fraction of sperm-egg contacts that are potentially fertilizing, thus incorporating all of the above effects. This is the notation that we follow in F_8–F_{10} (Table 1), which are all based on the framework laid out in Vogel et al. (1982).

ISOGAMY

Most fertilization functions have been derived with oogamous organisms in mind. They start (justifiably) from a clearly asymmetrical starting point, treating the gametes of females and males differently. These types of functions may mislead if applied to organisms where gamete dimorphism is low or absent. A model that is compatible with isogamy (i.e., a gametic system where gametes are of similar size; Lehtonen et al. 2016a) must instead be able to treat the two gamete types symmetrically, with no preexisting assumptions about differences between eggs and sperm. Applications of such isogamete-compatible fertilization functions could relate to understanding the ancestral divergence in gamete sizes (see recent reviews by Lessells et al. 2009; Togashi and Cox 2011; Lehtonen and Parker 2014) or to contemporary species in which gametes are identical or very similar in size (which are more common than one might think; Lehtonen et al. 2016a). Equation F_7 (Table 1; Togashi et al. 2007; Lehtonen 2015) is symmetrical for both gamete types mathematically and visually (Figure 4A). Togashi et al. (2007) derive a similar equation for species without mating types (not shown in Table 1), and Lehtonen (2015) derives three other equations that are compatible with isogamy with mating types (not shown in Table 1), based on different assumptions about gamete mortality. Additionally, Iwasa and Sasaki (1987) derived fertilization kinetics for isogamous organisms with multiple mating types as components of a model on the evolution of the number of sexes. We do not show the equations of Iwasa and Sasaki (1987) in Table 1 but note that they may be useful in models of isogamous systems with more than two mating types.

To our knowledge, there is currently no direct empirical evidence for these fertilization functions under isogamous or near-isogamous conditions (although they coincide with other, previously derived fertilization functions as the ratio of gamete numbers increases; Figure 4B in this article; Figure 1 in Lehtonen 2015). Their main benefit for now is to provide a mathematical basis that remains logically consistent across the continuum from isogamy to anisogamy and oogamy, which is essential in theoretical investigations of the evolution of anisogamy (Togashi et al. 2007; Lehtonen and Kokko 2011; Lehtonen and

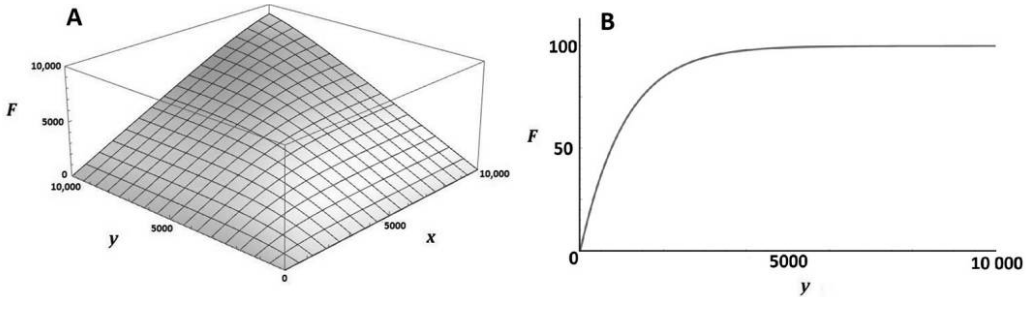

Figure 4. A Fertilization Function that Does Not Assume Anisogamy

(Panel A) Number of fertilizations F versus number of gametes type x and type y for equation F_7 from Table 1. The two gamete types (x, y) are interchangeable and symmetrical, compatible with isogamy. (Panel B) A cross section of the three-dimensional plot so that y is fixed at 200, representing an anisogamous situation across most of the range. $a = 0.001$, $t = 1$. See the online edition for a color version of this figure.

Parker 2014; Parker and Lehtonen 2014). Whereas anisogamous fertilization functions have been applied to explicit empirical fertilization data for both internal fertilization (Schwartz et al. 1981; Fearon and Wegener 2000) and external fertilization (Warner et al. 1995; Styan and Butler 2000; Gribben et al. 2014; Okamoto 2016), the same has not yet been done for isogamous functions, and it remains unconfirmed whether these functions capture the key biological processes that influence fertilization in isogamous organisms. For example, it is not clear how polyspermy (see below) would function along the continuum from isogamy to anisogamy and oogamy, and currently no model accounts for isogamy and polyspermy at the same time. However, it has been shown that in the isogamous *Chlamydomonas reinhardtii* "polygamy" (an isogamous version of polyspermy) is very rare (Johnson 2010; Liu et al. 2010), which suggests that a model that does not account for lethal polyspermy (e.g., models in Togashi et al. 2007; Lehtonen 2015) may be reasonably realistic for these purposes.

POLYSPERMY

None of the fertilization functions previously mentioned in this article take into account polyspermy, where more than one sperm may enter the egg cytoplasm (Rothschild 1954; Jaffe and Gould 1985; Snook et al. 2011). Polyspermy unions are lethal for the resulting zygote in many species (Rothschild 1954), although there is much variation by taxon (Snook et al. 2011). For example, birds may benefit from multiple sperm penetrating the perivitelline layer of the egg, and in chicken and turkey the optimum number of penetrating spermatozoa seems to be six (Bramwell et al. 1995; Wishart 1997). Polyspermy is an intricate, sometimes controversial, and widely studied topic (see Byrd and Collins 1975; Jaffe 1976; Nuccitelli and Grey 1984; Jaffe and Gould 1985; Brawley 1987, 1992; Wong and Wessel 2004; Snook et al. 2011; Hemmings and Birkhead 2015 for just a few examples), and beyond the scope of this review in its biological details. Nevertheless, in terms of fertilization functions polyspermy can be a crucial factor to take into consideration, at least in many marine invertebrates. Although the Don Ottavio model of Vogel et al. (1982; F_8 in Table 1) is not described as a polyspermy model, it could be interpreted as one that models nonpathological or physiological polyspermy (see Jaffe and Gould 1985; Snook et al. 2011): multiple spermatozoa may stick to one egg in the model, and any egg with one or more potentially fertilizing sperm-egg interactions is successfully fertilized. The diminishing effect these multiple gamete collisions have on sperm concentration is explicitly accounted for.

Styan (1998) argues that the model of Vogel et al. (1982) implicitly assumes that eggs have a polyspermy block that is instantaneous with no possibility for other sperm to fertilize an egg once an initial sperm already has. In reality, there would be a time period between the initial fertilization and the activation of a polyspermy block, in which time additional lethal fertilizations can potentially occur (Jaffe 1976; Jaffe and Gould 1985). Styan (1998) expands on the fertilization model of Vogel et al. (1982), in what seems to be the first model accounting for lethal polyspermy (equation F_9 in Table 1), including an explicit parameter for polyspermy block time (t_b), which can vary significantly across taxa (Lambert and Lambert 1981; Styan 1998). Only those eggs that receive no further fertilizations before activation of the polyspermy block are successfully fertilized in this model. Figure 5 illustrates the effect of variation in the polyspermy block time on fertilization success using Styan's (1998) fertilization function.

At least three further models accounting for lethal polyspermy have been published since Styan's (1998) work. Millar and Anderson (2003) derived an alternative model (equation F_{10} in Table 1), again using the model of Vogel et al. (1982) as a starting point. Although qualitatively similar, the derivation of Millar and Anderson (2003) is more rigorous, avoids the use of some of the approximations used in Styan's (1998) derivation, and suggests that the earlier model may underestimate the fraction of polyspermic fertilizations. Some evolutionary models (Bode and Marshall 2007; Tomaiuolo et al. 2007) have used a simple, phenomenological fertiliza-

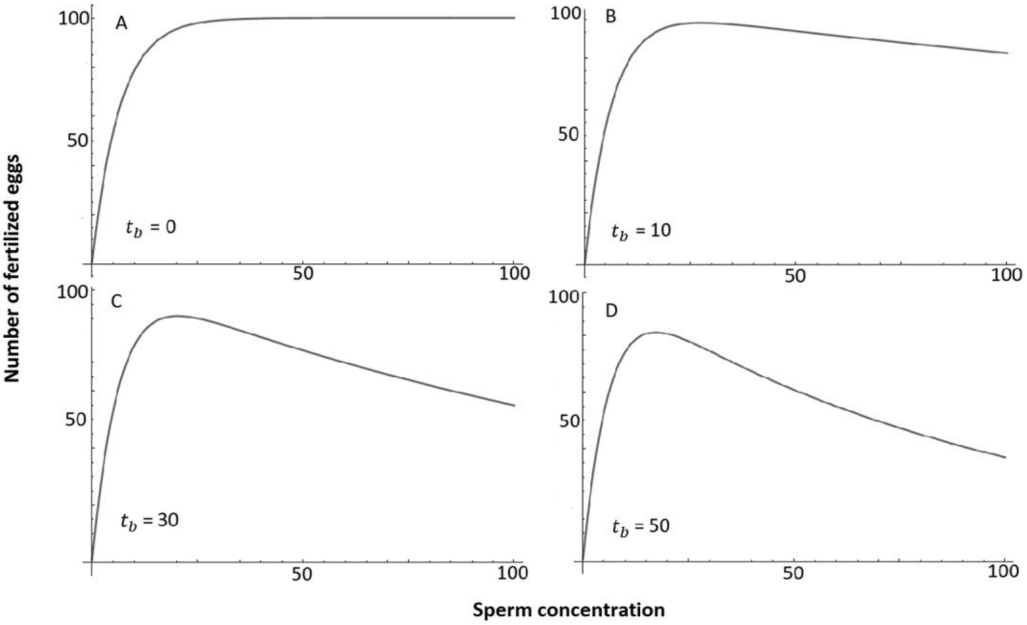

FIGURE 5. POLYSPERMY

Number of fertilizations versus sperm concentration y (μl^{-1}) for equation F_9 (Table 1). The parameters F_e and a arbitrarily assigned a value of 0.01, with the sperm half-life (τ) set to 800. The polyspermy block time (tb) is assigned a value of 0 for panel A (resulting in a version not accounting for lethal polyspermy), 10 for panel B, 30 for panel C, and 50 for panel D. A longer delay in polyspermy block activation increases the risk of polyspermy. See the online edition for a color version of this figure.

tion function (similar to the probability density function of the gamma distribution; Weisstein 2002) that qualitatively accounts for lethal polyspermy. However, a mathematically very similar function can be derived from simple biological principles, as we show in the section titled Generality, Taxonomic Scope, and the Value of Simplicity. Recently, in conjunction with an empirical study, Okamoto (2016) produced an alternative, compartmentalized differential equation model that accounts for polyspermy, and also explicitly models gamete mortality. This model cannot be expressed in closed form and requires integration at the last step to obtain the number of successful fertilizations. These last two functions are not shown in Table 1.

GAMETE POLYMORPHISMS WITHIN SEXES

Although the most obvious phenotypic differences between gametes occur between the male and female sexes, intrapopulation variation also exists within sexes. In terms of fertilization functions, the most palpable kind of within-sex variability is perhaps that in gamete size, longevity, speed, and other features that may have an immediate impact upon the central variables and parameters of fertilization functions, such as gamete numbers or collision rates. This is an issue that may be encountered, for example, in "loaded raffle" sperm competition models. In a loaded raffle, sperm may not be equal in their fertilization capacity or competitiveness, for example, due to differences in motility (Parker and Pizzari 2010). A fertilization function that is founded on the assumption that sperm are equal may not be suitable for use in such models. Some models of loaded raffle sperm competition between two males have incorporated sperm limitation using a modified version of the phenomenological function F_3, where the total sperm number y has been replaced with a weighted sum of sperm numbers from the two males: $y = y_1 + ry_2$, where r is a loading factor that determines the "unfairness" of the raffle by adjusting the inequality in fertilization capacity of sperm of the two males.

A related but perhaps less immediately obvious kind of variability is nonrandom fusion of gametes, variation in compatibility between pairs of gametes, and so-called "gamete-mediated mate choice," which can facilitate sexual selection at the level of gametes (Kekäläinen and Evans 2018). Compatibility can be mediated via membrane-bound molecules, including carbohydrates and proteins (Kekäläinen and Evans 2018). The evolution of gamete recognition proteins has been examined in theoretical studies making use of fertilization functions. Gamete recognition proteins are expressed on the surface of both gamete types (Wong and Wessel 2010; Kosman and Levitan 2014). Evidence for rapid adaptive evolution and intrapopulation variation in gamete recognition proteins exists for many taxa, and several hypotheses have been put forward to explain these patterns (see Tomaiuolo and Levitan 2010; Vacquier and Swanson 2011 and references therein). At least one such study has made use of a fertilization function that accounts for different affinities between combinations of gamete recognition proteins in eggs and sperm, together with lethal polyspermy (Tomaiuolo and Levitan 2010). This function (equation F_{11} in Table 1) is a phenomenological one, and similar in its underlying mathematical form to the polyspermy functions used by Bode and Marshall (2007) and Tomaiuolo et al. (2007). Tomaiuolo and Levitan (2010) used their model to show that the evolution of gamete recognition proteins in external fertilizers may be linked to the strength of sperm competition and the extent of polyspermy. For example, sperm limited conditions are expected to select for high fertilization rates and reduced variation in recognition proteins so that the number of compatible gamete encounters is maximized. The opposite extreme of high sperm concentration, strong direct competition between sperm from several males for a single egg, and polyspermy is expected to result in variation in recognition proteins maintained by frequency-dependent selection, with matched sets of compatible sperm-egg proteins (Tomaiuolo and Levitan 2010; Levitan 2018).

From a theoretical standpoint, there is a close affinity between loaded raffle sperm competition, variation in gamete compatibility, and gamete mediated mate choice. All of these biological factors imply that the effect of gamete numbers on fertilization success is no longer mediated by a simple sum of gamete numbers. One approach is to replace the total number of sperm (y) with a weighted sum of different types of sperm (as was done in Mesterton-Gibbons 1999; Ball and Parker 2000; Tomaiuolo and Levitan 2010). Although this is likely a good approximation in simple cases, the range of biological conditions for which it is valid is uncertain. It would be valuable to derive fertilization functions accounting for variability mechanistically, starting from clear biological assumptions in future research (see the section titled Future Directions).

PROPERTIES OF THE FERTILIZATION ENVIRONMENT IN EXTERNAL AND INTERNAL FERTILIZERS

So far in this article we have not been very explicit about the fertilization environment. The fertilization environment can of course refer to many factors, biotic and abiotic, which may have considerable effects on the overall fertilization outcome. Many of the fertilization functions that we focus on in this article (Table 1) assume that the fertilization environment is in some sense homogeneous, or that deviations from homogeneity can be dealt with by using average values for gamete density. This often permits mathematically tractable closed form solutions, and although it allows us to cover a great deal of interesting and relevant biological ground in a palatable form, it inevitably excludes some more complex models and variation that may appear in nature. It is also well known that when there is significant variation in, say, gamete concentrations within a gamete population, simply using the average concentration over the population to compute fertilization success may lead to misleading results (see Denny 2017 for a recent discussion). The spatial distribution of the spawning population, and the mixing, stirring, and flow properties of the fertilization environment are examples of factors that have been examined in more complicated models (Denny and Shibata 1989; Babcock et al. 1994; Claereboudt 1999; Lauzon-Guay and Scheibling 2007; Crimaldi 2012; Thomas et al. 2013), and also covered in a recent review of the physics of broadcast spawning (Crimaldi and Zimmer 2014). These models account for specific features of the fertilization environment in more detail but, as a drawback, become much more complicated and difficult to apply as modular components of evolutionary models, one of the main aims of this review (see the section titled A Brief Guide to Using Fertilization Functions in Evolutionary and Ecological Models).

Factors such as mixing and spatial distribution of spawning individuals do not only affect the overall fertilization outcome, but also the extent of competitive versus noncompetitive fertilizations, sperm limitation, and polyspermy (Levitan 2018) that, in turn, can influence selection on gamete affinity and on variation in gamete compatibility types (Tomaiuolo and Levitan 2010; Levitan 2018; see the section on gamete polymorphisms above). Internal fertilization also comes with its own "environmental" factors with potentially significant consequences. Here we are referring to the internal environment of the female reproductive tract, and the relevant factors may be very different from those affecting external fertilizers. In some internally fertilizing species only a small fraction of sperm ever reach the ovum, to the extent that the reproductive tracts of birds and mammals have been described as "hostile" to sperm (Birkhead et al. 1993). This also raises the possibility of cryptic female choice of sperm (Eberhard 1996), which is a major component of postcopulatory sexual selection, alongside sperm competition (Parker and Pizzari 2010). Cryptic female choice implies unequal fertilization probabilities for sperm from different males, which can give rise to loaded raffle sperm competition (Parker and Pizzari 2010; see the above section). Hence, with both external and internal fertilization, properties and implications of the fertilization environment are linked to polymorphisms in gamete phenotypes.

Generality, Taxonomic Scope, and the Value of Simplicity

the value of simple functions

A brief look at Table 1 makes clear that there is great variation in the complexity of fertilization functions, from F_0 to $F_{11.}$ This may raise the question of whether there is any value to the simpler functions, such as F_0 to F_4. We argue that there is value to these simpler forms, for at least three reasons. First, examining the range of functions from simple to complex, while attempting to understand the biological meaning of each alteration can be a very valuable learning tool. It may also point the way to factors that may be missing from our current understanding, both in terms of mathematical modeling, and in terms of empirical testing. Second, modeling in evolutionary ecology often aims to understand patterns that span very broad taxonomic ranges. In such models it is desirable to avoid dependence on specifics of any individual species or taxon: a modeler might seek something that applies approximately to a wide range of taxa, rather than something that applies in more detail to a single taxon. Complex models of fertilization tailored to specific systems may not be very useful in such cases. Third, from a practical standpoint in the context of evolutionary modeling, it is easier to work with simpler functions that may allow for explicit, analytical solutions that are not necessarily accessible with complex ones. A hybrid approach is often useful, where one starts with simple models, possibly with analytical solutions. The robustness of such solutions can then be tested with complex functions, using numerical methods if necessary.

For example, Mesterton-Gibbons (1999) examined the effect of incomplete fertilization risk on a previously published model of sperm competition that assumed all eggs are fertilized (Parker 1990). Mesterton-Gibbons used the function F_3 (Table 1) in his analysis. Although this function is a phenomenological one with apparently no clear biological justification, it is visually similar to those found with other models (Figure 3), and fits empirical data quite well at least in cattle (Fearon and Wegener 2000). Combined with its mathematical simplicity, these factors suggest that F_3 is a reasonable starting point in gaining a qualitative understanding of how sperm limitation may alter results of existing models. Bode and Marshall (2007) similarly used a simplified, phenomenological fertilization function accounting for polyspermy in an investigation of the effect of sperm limitation and polyspermy on sperm competition models in broadcast spawners. Again, the choice to use a simple function made it possible to solve the models analytically, which may be more valuable in gaining initial insight into the question at a qualitative level. If doubt remains about the robustness of the results, the fertilization functions in the models of Mesterton-Gibbons (1999) and Bode and Marshall (2007) could be replaced by other, more biologically grounded alternatives from Table 1, and robustness could be confirmed numerically if necessary. A recent article examining the evolutionary influence of gamete size on sex-specific competitive traits (Lehtonen et al. 2016b) used this type of approach: a result on sex-specific selection was first derived analytically for a class of relatively simple fertilization functions (e.g., F_3 and F_4 in Table 1), and this was then generalized to more complex functions (F_7 and F_9) using numerical methods. The simpler functions therefore pointed the way toward a result that may have been difficult to see directly from a more complicated one.

INTERNAL VERSUS EXTERNAL FERTILIZATION AND SIMPLE EXAMPLE DERIVATIONS

Another interesting and important question that arises from the range of superficially different functions is whether internal and external fertilization can be described by similar mathematical forms. Biologically speaking, there are several fundamental differences between external fertilization and internal fertilization. In general, internal fertilization has more protection from the outside environment and predators as well as a more clearly delineated route to the opposite gamete. However, more energy is generally required to bring males and females into intimate contact, and internal development of offspring places a limit as to how many can be produced in a given reproductive event (Heath 1977). External fertilizers have potential for a larger number of offspring in a single reproductive event, and they also save energy making use of natural mediums for the gametes to drift. Sexual selection operates differently in many respects in internal and external fertilizers (Levitan 2010; Parker 2014), and sperm competition and male gonad investment tend to be lower in internal fertilizers than in external fertilizers (Parker 2016; Parker et al. 2018). Gamete structure, as well as the relationship between gamete structure and swimming speed, may differ between the two types of fertilizers (Popham 1974; Simpson et al. 2014). The list could go on, but the point is that with the differences pointed out above, one might assume the functions required to describe the fertilization process for the two types of fertilizers would be quite different. Again, this depends on the level of detail that is needed. For example, equation F_4 (Table 1) appears to have been independently derived for both internal and external fertilization. Rothschild and Swann (1951) and Vogel et al. (1982) derived equation F_4 in studies of sea urchin fertilization (with slightly different derivations), while Schwartz et al. (1981) converged on the same equation in a study of artificial insemination of livestock. This is partly due to the probabilistic nature of the process being modeled, as can be seen with a brief and heuristic example derivation, modified from Schwartz et al. (1981) who originally considered internal fertilizers.

Consider x eggs and y sperm randomly mixing—in the case of many internal fertilizers, we might simply have $x = 1$. Now assume that any given spermatozoon fertilizes any given egg with a very small probability q. Let us further assume that any egg that is "fertilized" by one or more sperm will develop normally. In other words, we assume that polyspermy causes no adverse effects in the first place, or that the polyspermy block is so fast that harmful effects of additional fertilizations are prevented. The probability that any given egg is fertilized n times is binomially distributed with mean $\lambda = qy$, and because q is assumed to be very small, a Poisson distribution with the same mean gives a good approximation (Rice 2004). This in turn implies that the probability that a given egg is fertilized exactly n times is $\frac{\lambda^n e^{-\lambda}}{n!}$. In particular, the probability that an egg is fertilized exactly 0 times is $\frac{\lambda^0 e^{-\lambda}}{0!} = e^{-\lambda}$. Under our assumptions, the probability of a successful fertilization is the complement of this, which yields $p_x = 1 - e^{-\lambda} = 1 - e^{-qy} = 1 - e^{-ay}$, where we have finally equated the probability q with the fertilization parameter a. Alternatively, this can be written using the F-notation: $F = xp_x = x(1 - e^{-ay})$, which is F_4 in Table 1.

This should not be taken as a rigorous derivation, and we have not been explicit about all of the assumptions it entails, but an important message here is that there is nothing in the derivation that is obviously specific to internal or external fertilization. Although the above equation will not suffice for all purposes (e.g., polyspermy: Styan 1998; Millar and Anderson 2003; isogamy: Togashi et al. 2007; Lehtonen 2015), it does demonstrate that there is no fundamental reason why similar mathematics could not describe both internal and external fertilization when the process is examined at a fairly general level. Note also that if we let the exponent ay increase indefinitely, then $e^{-ay} \approx 0$ and $F = x(1 - e^{-ay}) \approx x$. At the other extreme, for very small values of ay we have $e^{-ay} \approx 1 - ay$ (first order Taylor polynomial for the exponential function; Weisstein 2002) and hence $x(1 - e^{-ay}) \approx axy$. In other words, the function we have heuristically derived above describes a range of conditions from complete lack of sperm limitation to very sperm limited, and at the two extremes it is approximately equal to F_0 and F_1 (Table 1).

Similar logic can be used to derive a simple model accounting for polyspermy. Above we modeled a Poisson process with mean $\lambda = qy$. Now consider lethal polyspermy: if there is no polyspermy block, then only those eggs that come into contact with exactly one spermatozoon are viable. Under the Poisson approximation, the probability of exactly one fertilization is $\frac{\lambda^1 e^{-\lambda}}{1!} = \lambda e^{-\lambda} = aye^{-ay}$, using the same notation as above (Rice 2004). This gives a biological rationale for the general form of the polyspermy fertilization functions used in some recent evolutionary models (although not exactly identical; see Bode and Marshall 2007; Tomaiuolo et al. 2007; Tomaiuolo and Levitan 2010). Although this derivation accounts for lethal polyspermy, it is noteworthy that it does not include a polyspermy block.

BEYOND BROADCAST SPAWNERS AND ARTIFICIAL INSEMINATION

Although most fertilization functions originate from work on artificial insemination or marine external fertilizers, the simple derivations above show that on some level, similar principles should apply across a broad range of taxa, covering very different reproductive systems. Flowering plants offer a good example. Despite the great differences between the life cycles and reproductive biology of flowering plants, livestock, and marine broadcast spawners, the same functions have been used in all three cases. An influential short paper on limits to seed production in plants (Haig and Westoby 1988) used a simple graphical model of the relationship between pollen attraction effort and effectively pollinated ovules, very similar to the saturating functions in Figure 3. Later research has explicitly used functions F_3 (Ashman et al. 2004; Burd 2008; Rosenheim et al. 2014) and F_4 (Kohn and Waser 1985; Waser and Price 1991; Porcher and Lande 2005) to model the relationship between pollen attraction and fertility, or the direct relationship between pollen load and fertility. Clearly there is much potential for synergy between these diverse fields in the context of modeling fertilization. For example, a recent article (Petersen and Burd 2017) points out similarities in the evolution of heterospory (bimodal size distributions with small male spores and large female spores) in land plants and the evolution of anisogamy (in the fertilization dynamics context of Lehtonen and Kokko 2011), and suggests that a model tailored to plant life cycles could elucidate plant evolution.

Do the same fertilization functions have applications in human biology? On some level, the answer is certainly yes. Qualitatively, at least, fertilization functions can provide insight and understanding in humans as they can in other organisms. Data on pregnancy rate versus sperm concentration in humans (Bonde et al. 1998) suggests a saturating response qualitatively similar to the functions in Figure 3. Amann (1989) uses a graphical fertilization function, adapted from the artificial insemination literature (Salisbury and VanDemark 1961) to illustrate concepts related to human fertility; however, the general topic of Amann's (1989) paper is the difficulty and complexity of predicting human fertility based on sperm characteristics. An extensive survey of the medical literature is beyond the scope of this article, but a brief review suggests that there has not been much use of explicit fertilization functions of the kind discussed in this article in research on human fertility. Declining sperm count in humans over time is a pressing issue (Levine et al. 2017) but, at the same time, the relationship between semen quality and fecundity is complicated, with several potentially important predictors beyond sperm concentration (Guzick et al. 2001; Cooper et al. 2010; Virtanen et al. 2017). It may therefore be the case that simple functions relating sperm numbers or concentration to pregnancy rate do not have the kind of predictive power that would be useful in determining fertility in a medical context.

A Brief Guide to Using Fertilization Functions in Evolutionary and Ecological Models

general guidelines

As we have seen, fertilization functions have improved our understanding of the fertilization process in organisms ranging from marine broadcast spawners to artificially inseminated livestock. Perhaps less obvious and potentially underused is their wide applicability in models of adaptive evolution in evolutionary and behavioral ecology, where fertilization functions can provide a mathematical link between evolutionary change and its consequent effects on overall fertilization success. This can be considered a type of eco-evolutionary or ecogenetic link (Kokko and López-Sepulcre 2007) that acts on a short timescale. Such models often deal with tradeoffs and their expected evolutionary consequences, commonly using optimization methods (Parker and Maynard Smith 1990), integrating aspects of game theory and adaptive dynamics when necessary (Maynard Smith 1982; Parker and Maynard Smith 1990; Dieckmann and Law 1996; McGill and Brown 2007; Lehtonen 2018). Fertilization functions enter the scene when the model concerns a tradeoff that affects allocation to gametes under potentially sperm limited or polyspermic conditions, e.g., when seeking evolutionarily stable investment into gonads versus allocation into survival (Parker et al. 2018).

The importance of fertilization functions as a component of fitness under natural conditions is particularly clear with external fertilizers, where the dilution of gametes into an external medium means that there is a higher risk of gamete limitation (Levitan and Petersen 1995; Levitan 1998a, 2010; Yund 2000). In other words, even though sperm usually vastly outnumber eggs, fertilization of all eggs is far from guaranteed. The same may be true in some species when sperm concentration is too high, where lethal polyspermy may alter the expected evolutionary outcome and generate sexual conflict (Bode and Marshall 2007; Levitan 2010). Sperm limitation or polyspermy that impacts total fertilization success can act simultaneously with sperm competition, which impacts the division of fertilizations between competing individuals (Bode and Marshall 2007; Lehtonen and Kokko 2011; Levitan 2018; Parker et al. 2018). This in turn implies that any change in allocation to gamete production may have a considerable impact on fertilization success, in a fashion that may be difficult to see intuitively. As a related point, although research in sexual selection has been largely focused on internal fertilizers, it has long been argued that external fertilizers can provide deep insight into sexual selection and into some of the most fundamental ancestral transitions in reproductive biology (Levitan 1998b, 2010; Parker 2014; Beekman et al. 2016), such as the evolution of anisogamy (Parker et al. 1972; Lessells et al. 2009; Togashi and Cox 2011; Lehtonen and Parker 2014), fertilization mode (Bishop and Pemberton 2006; Henshaw et al. 2014), and sexual dimorphism (Parker 2014; Parker et al. 2018).

Interestingly, early models of the transition from isogamy to anisogamy were in their essence gamete limitation models (Kalmus 1932; Scudo 1967) and, thus, included a model of fertilization success. These early models were, however, later recognized to be based on group selection, while a model based on gamete competition demonstrated that anisogamy can evolve entirely via individual-level selection (Parker et al. 1972). Widely known as the PBS model (named after its three authors), it remains the most widely accepted explanation for the origin of male and female gametes to this day. However, it seems apparent that gamete competition, gamete limitation, and polyspermy can all be significant selective pressures, particularly in external fertilizers and, in this vein, there has been a recent tendency to combine both gamete competition and gamete limitation in mathematical models of the reproductive biology of external fertilizers (Bode and Marshall 2007; Lehtonen and Kokko 2011; Henshaw et al. 2014; Parker et al. 2018). One consequence of these models is that the driving forces behind the earliest models of anisogamy evolution (Kalmus 1932; Scudo 1967) and those behind later models (Parker et al. 1972) are not in conflict, and instead act in the same direction and can reinforce and complement each other (Lehtonen and Kokko 2011; reviewed in Lehtonen and Parker 2014).

Some models in evolutionary and behavioral ecology have incorporated a custom model of fertilization, which may have been built into the overall model either implicitly or explicitly (Scudo 1967; Ball and Parker 1996, 1997; Bode and Marshall 2007; Lehtonen and Kokko 2011). There is nothing wrong with this approach. However, one of the points we wish to make is that some of these models could be simplified and unified, and links between models could be clearer if existing fertilization functions were used to model the fertilization process. This allows for a "modular" construction of models (Lehtonen 2015), which may reveal a clearer structure behind complicated models, and allows for straightforward incorporation of many different biological assumptions (Table 1) using one underlying model framework with a placeholder for a fertilization function.

To illustrate this, we now return to Parker's (1998:9) simple fair raffle model of sperm competition, which we rewrote earlier as

$$\begin{aligned} w(y_m, y_r, x) &= \left(\frac{y_m}{y_m + (N-1)y_r}\right)x \\ &= \left(\frac{y_m}{y}\right)F(x, y) \end{aligned} \tag{5}$$

where y_m is the mutant male's sperm number, while the $(N-1)$ "residents" release y_r sperm. The total sperm number released in the group is $y = y_m + (N-1)y_r$. Now, having covered a range of fertilization functions, we can readily see ways to explore specific cases of this underlying, modular model. Recall that the original model (Parker 1998:9) can be interpreted to make use of F_0, the simplest fertilization function that assumes that all eggs are fertilized. But we are free to use any function from Table 1. For example, we could account for the effect of sperm limitation using the simple negative exponential model F_4 (Rothschild and Swann 1952; Schwartz et al. 1981; Vogel et al. 1982):

$$\begin{aligned} w(y_m, y_r, x) &= \left(\frac{y_m}{y}\right)F_4(x, y) \\ &= \left(\frac{y_m}{y}\right)x(1 - e^{-ay}). \end{aligned} \tag{6}$$

The structure of the model remains exactly the same, only the fertilization function changes along with its biological consequences. The model now describes how sperm competition and sperm limitation together determine the mutant individual's fitness. The sperm competition and sperm limitation components are both impacted by the mutant trait value y_m, so the model tells us how y_m influences fitness via the sperm competition and sperm limitation components (note that y_m also appears in the denominator, as well as in the exponent, because we have used the short notation $y = y_m + (N-1)y_r$). This permits us to estimate selection on the trait. The evolutionary implications of such a model can be explored using similar overall methods regardless of which function we choose to use, although the resulting equations differ in their appearance and complexity and will not be analytically solvable in all cases. In exactly the same way we could also incorporate the possibility of lethal polyspermy into the model by using F_9 or F_{10} instead of F_4. There would be no fundamental difference to Equation (6), except for the replacement of the fertilization function. If, instead of fish (as in the original model), the aim is to model isogamous or near-isogamous organisms, we can use F_7 (Togashi et al. 2007; note also the special case x = y in Table 1):

$$\begin{aligned} w(y_m, y_r, x) &= \left(\frac{y_m}{y}\right) F_7(x, y) \\ &= \left(\frac{y_m}{y}\right) xy \frac{e^{aty} - e^{atx}}{ye^{aty} - xe^{atx}}. \end{aligned} \tag{7}$$

Although the model remains structurally similar, an interesting difference appears in this case: the fertilization function component of the model is now symmetrical for *x* and *y*, and we could write an equation for the *x*-type that would simply look like a mirror image of Equation (7). This means that the biological symmetry of an isogamous or near-isogamous system is reflected in the symmetrical structure of the mathematics, and it makes it possible to use mathematical models (e.g., evolutionary game theory) to investigate how the fundamental asymmetry of anisogamy might arise from a symmetrical starting point. Equation (7) is already very close to the structure of a model for the evolution of anisogamy that incorporates both gamete competition and gamete limitation. Where gamete competition and gamete limitation select for increased sperm numbers, adding a third component that models zygote survival as a function of size would create the disruptive selection for increased egg size that is thought to have caused the ancestral divergence of the two sexes (Parker et al. 1972). See Lehtonen (2015) and Parker and Lehtonen (2014) for further details on this kind of model structure, and how function F_7 can be applied to such questions.

STRUCTURED POPULATIONS, KIN SELECTION, AND GROUP SELECTION

The importance of population structure and interactions with kin is widely recognized in evolutionary modeling (Hamilton 1964; Frank 1998; Rousset 2004; Marshall 2015). In a structured population (say, with limited offspring dispersal from spawning groups), rare mutants have an increased probability of interacting with other mutants, and this can have important consequences for selection on these rare mutants, and on the evolutionary outcome. For example, competition between related males is theoretically predicted to diminish sperm expenditure (Parker 2000) and has been suggested to shift the relative importance of selective forces from sperm competition to sperm limitation and polyspermy (Lehtonen 2016). It is important to be aware that the population structure we discuss here is very different from the type of spatial structure in the section titled Properties of the Fertilization Environment in External and Internal Fertilizers, where we briefly discussed spatial population characteristics of spawning subpopulations that may influence the local fertilization process. The population structure we discuss here is the kind that can generate differences in genetic compositions between groups, which can influence how selection operates. Although we will not go deep into this topic, we note that modern methods make it relatively straightforward to incorporate the effects of simple population structure and kin interactions of this kind. In particular, the direct fitness method (Taylor and Frank 1996; Frank 1998) provides a very powerful toolkit for analyzing the effect of population structure and kin interactions. This method also allows for the incorporation of class structure. Consider a scenario where *k* females and *n* males aggregate in spawning groups. We may envision a scenario where females within a group are related to each other, or males within a group are related to each other, or that both apply simultaneously, and that females and males are also related to each other. If male and female offspring dispersal rates differ, the relatedness coefficients within and between classes may also differ, and the evolutionary outcome of interactions via sperm competition and sperm limitation in such cases is far from obvious. The direct fitness method (Taylor and Frank 1996) provides tools for analyzing such cases. It allows for multiple classes of individuals, with potentially different reproductive values (Fisher 1930; Taylor 1990) and different relatedness coefficients. Such models are broadly called kin selection models, although the technical methodology is quite different from that initially developed by Hamilton (1964). In simple cases it is also possible to convert a direct fitness kin selection model into group selection formalism, in the sense proposed by Price (1972), simply by rearranging the mathematical components of a kin selection model in a specific way (Lehtonen 2016). Although the evolutionary predictions do not differ, presenting these two alternative viewpoints to natural selection may make the results accessible to a broader audience with different methodological preferences. Second, kin and group selection models can be thought to present different causal decompositions of selection (Okasha 2016). For example, in a simple model incorporating sperm competition and sperm limitation (very similar to Equations 5–7 above), kin selection offers technical convenience, but the group selection viewpoint produces a cleaner split between the selective effects of sperm competition and sperm limitation, fitting the ecological aspects of the question better in this sense (see Lehtonen 2016 for a worked example).

GENERALIZATIONS FOR DECREASING GAMETE MOTILITY

It has been suggested that the main effect of sperm aging is a decrease in motility (Reinhardt 2007). A change in motility would, in turn, alter the collision rate parameter a (Vogel et al. 1982; Togashi et al. 2007). This implies that instead of strict gamete death, it may be more realistic to make gamete collision rate dependent on gamete age. In other words, instead of a constant a we would have a function $\alpha(t)$ that determines the collision rate for gametes of age t. The form of $\alpha(t)$ encapsulates the effects of gamete aging, and we should expect $\alpha(t)$ to be a decreasing (but always nonnegative) function of t. It is possible to modify many existing fertilization functions in this way, and their overall mathematical form is relatively unaffected by the change. We demonstrate this modification with a rederivation of a simple negative exponential function (F_4 in Table 1), while accounting explicitly for time. The derivation is based on that of Vogel et al. (1982). We first rederive the function in its original form, with a constant parameter a, and then modify it with time-dependent motility.

Vogel et al. (1982) derive their simplest fertilization function, which they term the Don Giovanni model, under the assumption that sperm concentration is so much higher than egg concentration that the effect of egg-sperm collisions and fertilizations on sperm concentration is negligible, and hence sperm concentration or number y is considered constant. Now, if we denote total egg number by x (which is also a constant) and the number of unfertilized eggs by x_u (not a constant), then the change in the number of unfertilized eggs is described by the differential equation

$$\frac{dx_u}{dt} = -ayx_u. \tag{8}$$

That is, each fertilization removes one unfertilized egg from the gamete pool, and the rate at which fertilizations take place is proportional to the number of sperm times the number of available (unfertilized) eggs (mass action; Otto and Day 2007). Under the assumptions described above, ay is a constant, which implies that Equation (8) is a standard differential equation for exponential decay with decay constant ay (Weisstein 2018). The number of unfertilized eggs therefore decays exponentially as follows:

$$x_u = x_{u0}e^{-ayt} = xe^{-ayt} \tag{9}$$

where the initial number of unfertilized eggs x_{u0} is simply equal to the total number of eggs, because all eggs start off as unfertilized. Now the number of fertilized eggs F is the total number of eggs minus the number of unfertilized eggs:

$$F = x - x_u = x - xe^{-ayt} = x(1 - e^{-ayt}), \tag{10}$$

which is of the same form as F_4 (Table 1), with time t explicitly shown. Note that essentially the same function has been derived elsewhere using different methods (Rothschild and Swann 1951; Schwartz et al. 1981;

see also the heuristic derivation earlier in this article).

Next, we show how this derivation can be modified to account for a time-dependent collision parameter. We begin with the same differential equation, but with the constant *a* replaced with a function $\alpha(t)$:

$$\frac{dx_u}{dt} = -\alpha(t)yx_u. \tag{11}$$

To solve this, we make the substitution $T = \int_0^t \alpha(\tau)\,d\tau$, implying $\frac{dT}{dt} = \alpha(t)$, or $dt = \frac{dT}{\alpha(t)}$. Substituting this expression for *dt* into Equation (11), we get

$$\frac{dx_u}{\left(\frac{dT}{\alpha(t)}\right)} = -\alpha(t)yx_u \tag{12}$$

or

$$\frac{dx_u}{dT} = -yx_u. \tag{13}$$

This is of exactly the same form as Equation (8) with $a = 1$, and with *t* replaced by *T*. But based on Equations (8–10) we already know the solution to this is

$$x_u = x_{u0}e^{-yT} = xe^{-yT} \tag{14}$$

and using the identity $T = \int_0^t \alpha(\tau)\,d\tau$ to return to the original notation, we have

$$x_u = xe^{-y\int_0^t \alpha(\tau)\,d\tau}. \tag{15}$$

So for the number of fertilized eggs we have

$$F = x\left(1 - e^{-y\int_0^t \alpha(\tau)\,d\tau}\right). \tag{16}$$

In other words, *at* in the exponent has been replaced by the integral $\int_0^t \alpha(\tau)\,d\tau$, which generalizes the solution to scenarios where the collision rate changes with gamete age. Equation (10) is still covered as a special case, as can be seen by setting $\alpha(\tau) = a$ and integrating: $\int_0^t a\,d\tau = at$. Although this particular problem could have been solved more directly without using the substitution method, the value of the method is that it works equally well in many other cases: an analogous line of reasoning using the same substitution can be used to generalize many other fertilization functions in the same way. For example, Vogel et al.'s (1982) main Don Ottavio model (nonpathological polyspermy in our terminology, F_8 in Table 1) and Togashi et al.'s (2007) model for isogamy with fixed gamete life spans or experimental time (F_7 in Table 1) can both be generalized in this way by replacing *at* with the integral $\int_0^t \alpha(\tau)\,d\tau$. With F_7 it should be noted that both gamete types may senesce at similar rates. The time-dependent collision rate would then depend on changing motility of both gamete types, thus decreasing their relative velocities. Applying this change to the equations describing lethal polyspermy appears more complicated, and we leave this question for future work.

This generalization is useful in at least two ways. First, because $\alpha(\tau)$ always enters the equation in the same way inside the integral $\int_0^t \alpha(\tau)\,d\tau$, in many modeling applications we can treat the entire integral as a parameter, without explicitly modeling the underlying time-dependent collision rate. This implicitly covers a wide range of scenarios, where the underlying collision rate can depend on time in potentially complicated ways. Second, the generalized equations can be used as a foundation for fertilization models that explicitly account for age dependence of the collision rate. $\alpha(\tau)$ and consequently the integral $\int_0^t \alpha(\tau)\,d\tau$ could potentially be estimated from empirical observations. Interestingly, Levitan (2010) has noted that sperm velocity seems to trade off with sperm longevity within and between species. This suggests that overall fertilization efficiency as determined by the integral could remain relatively similar, if species with higher initial values of $\alpha(\tau)$ also experience faster rates of decline in $\alpha(\tau)$ Whether this is actually the case would of course depend on the detailed shapes of $\alpha(\tau)$.

FUTURE DIRECTIONS

Much progress has been made in understanding the ecology of fertilization, both theoretically and empirically. Mathematical models of fertilization seem to have been particularly successful in describing the fertilization process in marine broadcast spawners (Rothschild and Swann 1951; Vogel et al. 1982; Styan 1998; Millar and Anderson 2003; Levitan 2010; Okamoto 2016), which may not be particularly surprising. Broadcast spawning is in some respects simple compared to internal fertilization. The fertilization environment consists of a relatively uniform physical environment, rather than complicated internal organismal structures that may be difficult to probe. As a consequence of this, it is also easier to count fertilized eggs soon after fertilization. Each fertilization event generally involves a much larger number of eggs and fertilizations than internal fertilization (where it is not uncommon for there to be either 0 or 1 fertilizations per insemination), which makes it simpler to collect the amount of data required for evaluating the fit of theory with data. However, in saying that the models have been successful, the implication is not that they predict fertilization with great accuracy under all conditions. Instead, they have been particularly useful in pushing forward our understanding of the fertilization process. There is no doubt that there are still useful unexplored directions for developing fertilization functions and related empirical fields. The main avenues to push the field forward depend on what the objectives of the modeler are. If the aim is to gain a more finely detailed understanding of external fertilization in natural conditions, it may be necessary to go beyond the relatively simple closed form solutions presented in Table 1, instead moving onto more complicated models at the interface of physics and ecology (Crimaldi and Zimmer 2014). If the goal is (as in this review) to integrate models of fertilization into models in evolutionary ecology, exploring new ground does not necessarily require very complicated models.

A recent article, combining empirical experiments with mathematical models (Okamoto 2016) suggested that a single collision rate parameter (a in our notation) may not be able to describe collision rates under different gamete concentrations. Instead, the empirical results were consistent with a collision rate that declines with egg density. This indicates that the bimolecular kinetics approach (Vogel et al. 1982) often used to model fertilization may require reconsideration, at least in external fertilizers. Note that such a gamete concentration-dependent collision rate would introduce quite a different mathematical problem than the time-dependent collision rate we have explored above, because it would make even the simplest differential Equation (8) nonlinear in x_u. The consequences of Okamoto's work (2016) remain largely unexplored.

An area that seems to have been relatively little studied empirically is the relationship between gamete densities and fertilization success in isogamous organisms. Isogamy is common in unicellular organisms (Lehtonen et al. 2016a), which tend to receive less research interest than their multicellular counterparts. For example, although aspects of the reproductive biology of some unicellular algae are now known in some detail (Suda et al. 2005; Johnson 2010; Liu et al. 2010), our knowledge of fertilization success in unicellular algae has always lagged behind that of multicellular algae (Brawley and Johnson 1992). The isogamy-compatible fertilization function (F_7 in Table 1; Togashi et al. 2007) and others developed in Lehtonen (2015) therefore remain largely empirically untested.

Most existing fertilization functions have limited capacity to handle within-sex (or within-mating type) variation in gamete properties, which can be a problem for modeling in evolutionary ecology. Evolutionary models must, by their very nature, assume heritable variation in the population being modeled. This does not cause problems if the cause of variation ultimately enters the fertilization function only via gamete numbers, which is usually the focus of fertilization functions. For example, we might model a population of broadcast spawners where a rare mutant produces slightly more or less gametes than the resident type. The fertilization function is then simply applied to the total number of gametes in a spawning group, including gametes of the mutant and residents (see Equations 5–7). Complications may arise if we consider mutations that alter the collision rate parameter a, or, e.g., gamete mortality, or if we are modeling a population that is otherwise polymorphic for these traits. Such difficulties can arise, for example, in "loaded raffle" sperm competition models where different sperm phenotypes may have different levels of competitiveness (Parker and Pizzari 2010), in cryptic female choice (Eberhard 1996), which can occur in internal as well as external fertilizers (Alonzo et al. 2016), or when there are differences in compatibility between different types of gametes for any reason (Kosman and Levitan 2014; Nadeau 2017; Kekäläinen and Evans 2018).

Although the total number of potentially fertilizing gametes (if they are identical) can often simply be added up, and the fertilization function can be applied to the total, it is not clear how and under what conditions this would work for the collision parameter a. Some published models (Mesterton-Gibbons 1999; Ball and Parker 2000, 2007; Tomaiuolo and Levitan 2010) have solved this problem by using simple fertilization functions where total sperm number has been replaced by a sum with different sperm types weighted by loading factors or fertilization affinities. The fertilization function used by Tomaiuolo and Levitan (2010; F_{11} in Table 1) allows for an unrestricted number of affinities simultaneously in the population. Although this function was used to model variation in gamete recognition proteins, the affinities between pairs of protein types (c_{ij}) in the model have a very similar effect to the parameter a. F_{11} or variants of it could therefore potentially be used as an approximate model for fertilization when there is any kind of variation in encounter and fertilization rates. It remains uncertain how this function would generalize to account for further complications such as sperm depletion, gamete mortality, gamete aging, polyspermy blocks, isogamy, and so on, and it would be useful to explore alternatives to F_{11} with explicit biological justification. As an alternative to explicit fertilization functions, it is possible to implicitly account for small variation in gamete mortality rates (as was done in Lehtonen and Kokko 2011), and variation in collision rate could likely be accounted for in a similar, implicit way. It is important to keep in mind that when variation of this kind is combined in a model with sperm competition, a mutant gamete type with a higher affinity or collision rate or with lower mortality gains a larger share of fertilizations than its resident counterpart. In other words, we must account for the effect of variation on both the overall fertilization outcome, and on how that outcome is divided between competitors (see Mesterton-Gibbons 1999; Ball and Parker 2000; Tomaiuolo and Levitan 2010; Lehtonen and Kokko 2011).

Recent empirical evidence is making it clear that nonrandom fusion of gametes is quite common (Nadeau 2017; Kekäläinen and Evans 2018). Given the interest to incorporate this nonrandomness into evolutionary models, we see the integration of variation in gamete phenotypes, preferably mechanistically grounded in clear biological assumptions, as one of the most important future directions in the development of fertilization functions.

CONCLUSIONS

Fertilization functions attempt to predict the proportion or number of successful fertilizations as a function of gamete numbers or concentration and additional parameters relevant to the biology of the model organism. They are used in a wide range of contexts, ranging from artificial insemination of livestock to empirical studies of broadcast spawners to theoretical models of adaptive evolution, and their methods of derivation as well as underlying biological assumptions can vary significantly. Although fertilization functions have been used in some models in evolutionary and behavioral ecology, they remain somewhat scattered in literature on diverse topics and may not be easy to find. Many models in behavioral and evolutionary ecology that assume that all eggs are fertilized could relatively easily be generalized to include the effects of gamete limitation or polyspermy using existing fertilization functions. A range of relatively simple functions have been developed, including functions with clearly unrealistic properties to more realistic saturating functions. Although simple saturating fertilization functions may not account for details of specific species or taxa, they have value particularly in evolutionary models that attempt to answer questions that relate to a broad range of taxa and, hence, cannot be based on species-specific assumptions. Simple models can also be used to argue that similar mathematical principles may apply, at least as an approximation, to internal and external fertilization. More complex functions accounting for lethal polyspermy have been developed for broadcast spawners. These functions describe how fertilization success increases with sperm concentration, until a maximum is reached, and thereafter decreases due to increasing risk of polyspermy. Fertilization functions accounting for isogamy are useful in theoretical and empirical research on isogamous organisms or on the ancestral origin of the two sexes, but contrary to many of the anisogamous functions, they have not yet been compared to explicit empirical fertilization data. Most models of fertilization model gamete aging in a way that assumes that gametes remain unchanged until their death. However, decreasing motility is likely the main effect of sperm aging in nature; we show that many fertilization functions can readily be generalized to account for decreasing sperm motility. We suggest directions for future research in fertilization functions, particularly highlighting the importance of incorporating variability in gametes and gamete compatibility in their derivation.

ACKNOWLEDGMENTS

The authors are grateful to Lisa Schwanz, Russell Bonduriansky, Daniel Falster, Geoff Parker, Don Levitan, and two anonymous reviewers for very helpful comments, suggestions, and discussions on this manuscript at various stages of development. Jussi Lehtonen was funded by a University of New South Wales Vice-Chancellor's Post-Doctoral Fellowship, and by an Australian Research Council Discovery Early Career Research Award (project number DE180100526) from the Australian Government.

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Associate Editor: Rafael L. Rodríguez
Handling Editor: James D. Thomson

APPENDIX 1
Glossary

Anisogamy: Gametic system where the gamete types are dimorphic in size: one type (e.g., eggs) is larger than the other (e.g., sperm).

Female: The adult phenotype that produces the larger gametes in an anisogamous system.

Fertilization function: A mathematical function that predicts the proportion or number of successfully fertilized gametes based on gamete numbers or concentrations and additional parameters relating to the biology of the model organism.

Isogamy: Gametic system where the gamete types are of similar size.

Male: The adult phenotype that produces the smaller gametes in an anisogamous system.

Mating types: Molecular mechanisms that regulate compatibility in sexually reproducing eukaryotes. Mating types enable disassortative fusion in isogamous systems.

Oogamy: A form of anisogamy where the female gamete is significantly larger than the male gamete. The female gamete is usually not nonmotile.

Polyspermy: More than one sperm enters the egg cytoplasm. Usually fatal, except in “physiological” or “nonpathological” polyspermy.

Sperm competition: Competitive process and selective force in postcopulatory sexual selection that occurs when the ejaculates of different males compete to fertilize a given set of ova.

Sperm limitation: Occurs when there is not enough sperm to fertilize all eggs.

Syngamy: The fusion of two gametes to form a zygote.