プレスリリース Press Release (English follows Japanese)

進化生物学最大の謎に挑んだ「性の進化三部作」が完成

“The Evolution of Sex Trilogy,” tackles the greatest mystery in evolutionary biology, is now complete

第 3 論文　The third paper of trilogy

Yasui, Y. The twofold cost of sex reconsidered: Meiotic mechanisms protect anisogamous populations from invasion by thelytoky. *J Evol Biol* **39**, (2026)

安井 行雄「性の 2 倍のコスト再考：減数分裂メカニズムがアニソガミー個体群をセリトキーの侵略から守っている」

ほとんどの多細胞生物は栄養豊富な卵を作る雌と小型で運動性の高い精子を作る雄に性別が分かれていて、卵を精子が受精する形（アニソガミーanisogamy）で繁殖します。アニソガミーの生物は通常雌と雄が同数生まれる（性比 1:1）ため、集団の半数はみずから子を産まない雄となり、母親が雌ばかりを産む単為生殖（セリトキーthelytoky）に比べて増殖率は半分となります。つまりアニソガミーの集団の中にセリトキー突然変異が生じれば、数世代で集団を置き換えることになる。アニソガミーが負っているこの 2 倍の増殖率の差を「雄を作る 2 倍のコスト twofold cost of male production」と呼び、そのコストにもかかわらず多くの種で雄が維持されている理由は進化生物学最大の謎とされています。

「性の進化三部作」の第 1 論文 Yasui and Hasegawa (2022)はまず配偶子有性生殖そのものの起源について、特に最初の配偶子はどうやって接合相手を見つけたのか（自分しかいなかったはず）を説明する seesaw effect 仮説と、最初は同じサイズの配偶子が接合していたものが卵と精子に二極化した過程（すなわち雌と雄の起源）について inflated isogamy 仮説を提唱しました。

第 2 論文 Yasui (2026a)とこの度の第 3 論文 Yasui (2026b)は、アニソガミーがなぜセリトキーに取って代わられないのかを「雄がもたらす隠れた利益」と「減数分裂の機械的制約」という全く異なる視点から論じたものです。「2 倍のコスト」など基礎用語については前回プレスリリースを参照してください。

見逃されてきた普遍的メカニズム「減数分裂の中期休止」

有性生殖をする以上、卵は自分勝手に発生を開始するわけにはいかず、精子の侵入を待つ必要があります。実際に後生動物に普遍的なメカニズムとして「減数分裂の中期休止

Meiotic metaphase arrest」（以下 MM 休止）が知られています（図 1）。脊椎動物、無脊椎動物など分類群によって異なりますが、減数分裂は第 1 分裂または第 2 分裂の中期（赤道面に染色体が並び紡錘体が形成されるステージ）で停止します。ヒトの場合、女児が母親の胎内にいたときにその将来卵巣になる組織の中ですでに減数第 1 分裂は終了して、第 1 回目の休止に入り、なんと 10 数年間そのまま待機しています。思春期を迎えると減数第 2 分裂が開始され、その中期で再び休止します。休止を解除し卵形成を再開するためには精子がもたらす Ca^{2+}イオンなどの刺激が必要です。このメカニズムにより、受精卵は一時的に 2 つの卵核（2n）と 1 つの精子核（n）を持つ 3 倍体となり、その後、卵核の 1 つが極体（n）として捨てられ、もう 1 つの卵核（n）と精子核（n）が融合して 2 倍体となり、その後胚発生が始まるというプロセスをたどります。したがって、減数分裂によってまず 1 倍体の卵が作られ、その卵が精子と受精して 2 倍体になるという教科書的な理解は多くの種では誤りなのです（ウニではそうなっているらしいが）。つまり、卵は単独では形成途中であり、精子が入ることによって初めて完成するのです。

それまでアニソガミーを続けてきた動物が、セリトキーに移行しようとしたとき、精子による受精なしで発生可能な胚を作る必要があります。Yasui (2026b)の「減数分裂制約仮説」は減数分裂からセリトキーへの移行には 3 つの障壁があると主張しています。

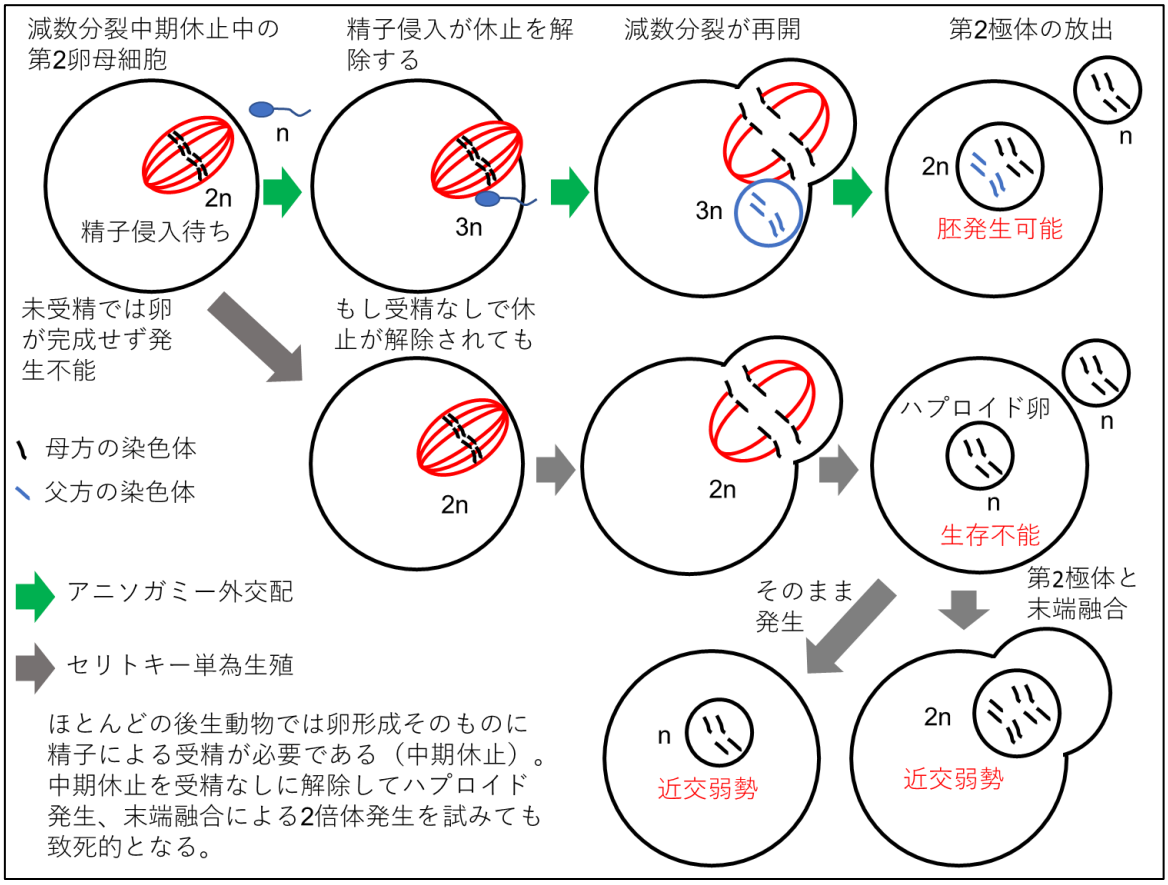


図 1　減数分裂中期休止とその後のあり得る経過（正常な受精と単為発生）

1） MM 休止を受精なしで解除することが極めて困難であるという実証データがマウス、オタマボヤ、アフリカツメガエル、ゼブラフィッシュなど多くのモデル生物で得られている。そもそも MM 休止中の卵は未完成であり発生することができない。
2） もし何らかの方法で精子なしで MM 休止が解除されても、雌ゲノムだけを持つハプロイド卵細胞が生じる結果となる。ほとんどの野生生物はゲノム中に致死相当量の劣性有害遺伝子をヘテロ接合で蓄積しており、もしハプロイドの卵がそのまま胚発生を始めたら有害遺伝子の発現により即死する。
3） もしハプロイド卵細胞が減数分裂のもう一つの産物である第 2 極体と融合する「末端融合型オートミクシス」を行って二倍体を回復してもほとんどの遺伝子座はホモ接合となるため、やはり有害遺伝子が発現する。

興味深いのは卵細胞と第 2 極体が多くの座位でクローナルであるのは、減数分裂の標準的なプロセスに原因があるということです。第 1 卵母細胞においてある遺伝子座が 01 のヘテロ接合であったとき（図 2 a ）、相同染色体はそれぞれコピーされ 0011 の 4 量体になります(b)。染色体はその後第 2 卵母細胞(図 2e)と第 1 極体(図 2f)に振り分けられますが、このとき同一染色体の 2 コピー（00 と 11）が一緒にどちらかの細胞に入るので、4 量体の時点(図 2c)で交差組換えを起こした座位以外は全て第 2 卵母細胞のなかでホモ接合となり、第 2 卵母細胞がそのまま分裂したハプロイドの卵子(図 2h)と第 2 極体(図 2i)はほとんどの座位でクローンになります。この 2 つが再融合するのが末端融合型オートミクシス(図 2j)なので 00 の近交弱勢を引き起こす結果となります。もし第 1 減数分裂が 01 の第 2 卵母細胞と 01 の第 1 極体（それぞれ姉妹染色体 1 組）に分割されるパターンであれば、末端融合は 01 となりヘテロ接合度は母親と同じ、劣性致死遺伝子はマスクされたままだったでしょう。このことは今日見られる減数分裂のプロセス自体が有性生殖を無性生殖の侵入に対して耐性を持たせるように進化した結果であることを示唆します（単為生殖をしようとしたら死ぬようになっている）。

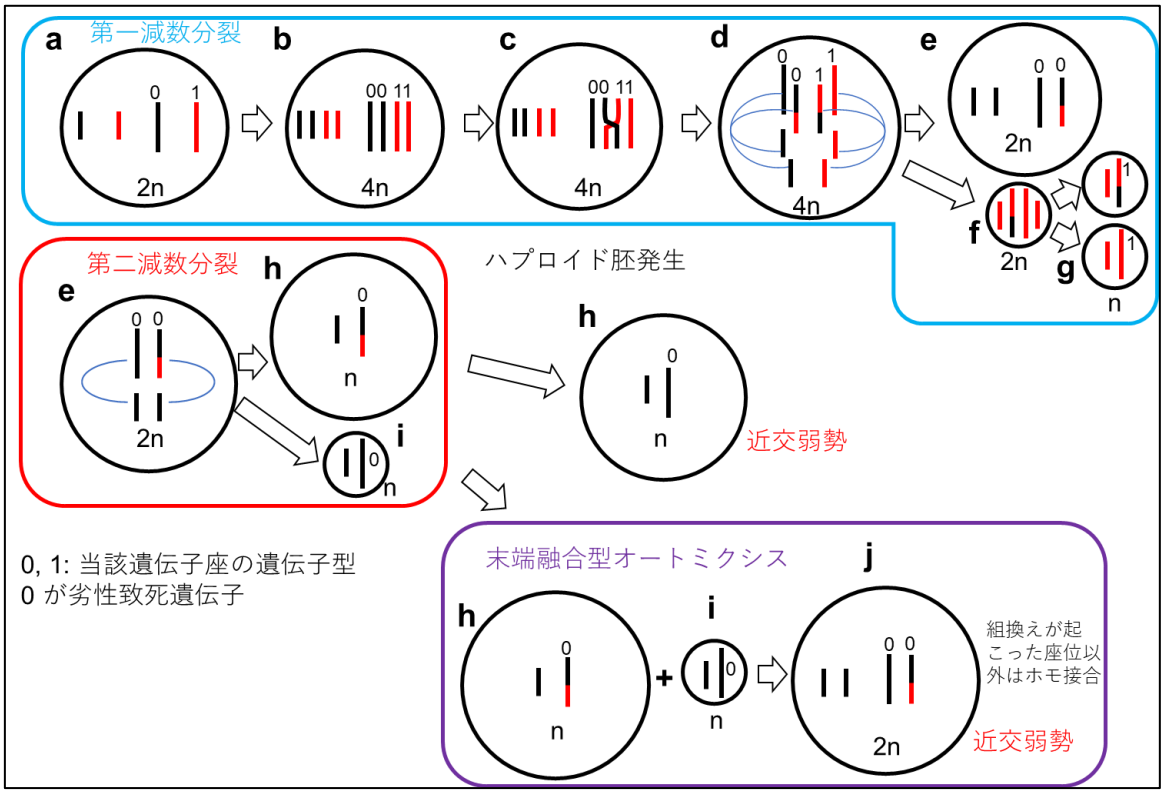


図 2　標準的な減数分裂の経過と単為生殖に移行した場合の結末：第 2 卵母細胞は同じ染色体の 2 コピーを含む

安井教授はさらに集団遺伝学数理モデルを作り、ゲノム中の機能遺伝子数 L と劣性致死突然変異の起こる確率 p から、ハプロイド卵が 1）そのまま胚発生する場合、2）第 2 極体と末端融合して胚発生する場合、および 3）非血縁雄の精子と受精して胚発生する正常なアニソガミーの場合、で胚の生存率を推定し比較しました。モデルの予測通りに、ゲノムサイズが大きく突然変異率が高いほど、有性生殖から無性生殖に切り替えたときの死亡率が高いことが示されました（図 3）。きわめて興味深いことに、ショウジョウバエ、マウス、ヒトにおける L と p の推定値はアニソガミーとセリトキーの適応度が等しくなる境界線上に位置していることがわかりました。この事実は、「有性生殖なら生きられるが単為生殖をしたら死ぬ」という崖っぷちまでこれらの動物が進化してゲノムサイズがそこでとどまっていることを示唆します。今後もっと多くの生物でこの関係が明らかになればゲノムの進化における性の役割をより深く明らかにできるかもしれません。

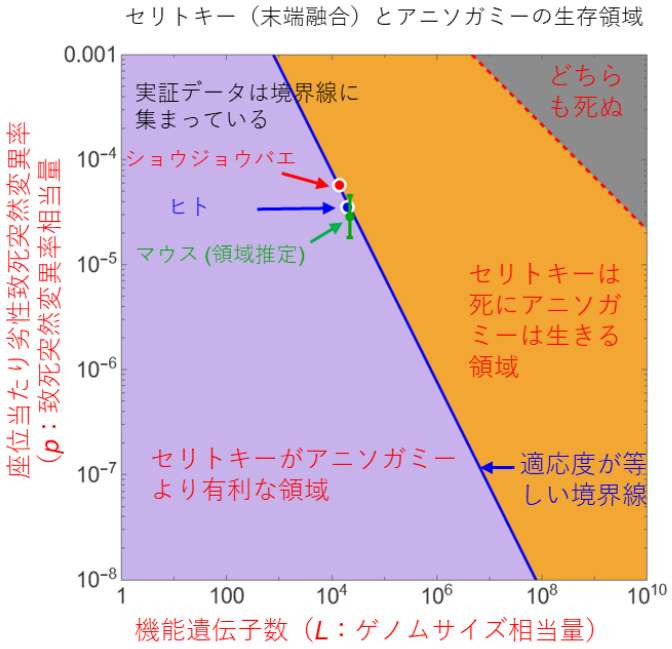


図 3　数理モデルの理論的予測：$Lp < 1$（紫色の領域）ではハプロイド卵はセリトキーを選んだとき 2 倍のコストを負うアニソガミーより有利であるが、$Lp = 1$ の青線（致死遺伝子が 1 つ発現する）上で、セリトキーは半数が死にアニソガミー（雌雄 1：1）と適応度（生き残る娘数）が同等になる。この境界線上に 3 種の実測値が乗っている。$Lp > 1$（オレンジの領域）ではセリトキーは死にアニソガミーは生き残る。灰色の領域では非血縁の雄の精子とでも同じ座位に致死遺伝子を持つ組み合わせが生じ、アニソガミーも死ぬ。1 つでも致死遺伝子が発現すれば死ぬのでゲノムサイズには上限がある。

一方で、この仮説は減数分裂を経ない形式の単為生殖メカニズムは進化可能であることを示唆しています。タンポポのような多くの植物やアブラムシ、ミジンコのような一部の無脊椎動物でアポミクシス（apomixis：体細胞分裂でクローン胚を作る生殖様式）が知られています。子供は親のクローンになるため有害遺伝子の蓄積度合いは親と同じであり単為生殖をしても直ちに死ぬということはありません。しかしアポミクシスを実現するには体細胞に分化全能性 totipotency を回復させねばならずこれが新たな障壁となります。植物は基本的に体細胞が全能性を維持していて栄養生殖（組織片からの再生、挿し木など）が可能ですが多細胞動物では分化した体細胞はエピジェネティック修飾を受けており全能性回復は厳しく制限されています。その結果、多くの多細胞動物はこれらの機械的制約から逃れられず、2 倍のコストがかからず有利なはずの単為生殖に移行することができないのです。

Think different

MM 休止という現象は 1970 年代から知られており、分子生物学、発生生物学的な詳細な研究が行われてきました。しかし研究者たちはその生物学的意義については「卵がハプロイドのまま胚発生を始めるのを防ぐため」としか認識せず、「性の 2 倍のコスト」問題と結び付ける議論はありませんでした。パラダイムを転換するには発生生物学や細胞生物学と理論進化生物学の両方をカバーできる広い視野が必要なのです。また「2 倍のコスト」に対抗する有性生殖の利点として定番理論となっている「赤の女王」や「マラーのラチェット」説は世代遅れで戻ってくる遺伝的利益に基づいているため、毎世代 2 倍に増えるセリトキーの侵入を防ぐには、もっと速い即時的プロセスが必要です。

「性の進化三部作」は、第 1 論文で最初の有性生殖はいかに成立したか（起源）、第 2 論文と第 3 論文で 2 倍のコストがかかる雄がなぜ維持されているかを説明しました。「雄の進化的維持」という同一のテーマを扱いながら、第 2 論文では雄からもたらされる隠れた利益がアニソガミーを有利にし（適応論）、第 3 論文では減数分裂のメカニズムが機械的制約となりセリトキー移行を不利にする（制約論）という全く異なるアプローチで、その世代で即時働くプロセスを提唱しました。雄からの利益が期待できるのは昆虫や脊椎動物など個体間の社会的相互作用や資源防衛行動が発達した生物に限られるので、第 2 論文の適用範囲には限界がありました（例えば植物はそのような行動をしない）。しかし第 3 論文は減数分裂を行う全ての生物が対象となるので事実上雌と雄を持つ全ての種をカバーできます。

「性の 2 倍のコスト」問題の解決

減数分裂を行う大多数の生物は、雄生産をやめて無性生殖へ移行しようとすると、胚が致死となる制約があるため、たとえ「2 倍のコスト」を負っていても雄を維持することが可能です。雄による間接的な資源供給が「2 倍の利益」を生み出せば「2 倍のコスト」は完済されます。それでも無性生殖は減数分裂を伴わない形（アポミクシスなど）で進化可能ですが多細胞動物では分化した体細胞の全能性回復が困難なため別の制約を受けます。見過ごされがちですが、基本的に体細胞が分化全能性を維持しアポミクシスや栄養生殖が可能な多くの植物や条件的単為生殖が可能な一部の動物（アブラムシ、ミジンコなど）ではアニソガミーと無性生殖を両立できるので、彼らのアニソガミーが無性生殖を上回る効率を示す必要はありません。彼らは急速な個体群成長が必要なときは無性生殖を、有害遺伝子の除去や病原体対策が必要なときは有性生殖を、使い分けているのです。それゆえ植物やミジンコで「性の 2 倍のコスト」を問題視するのは的外れだと言えるでしょう。アポミ

クシス等で完全に無性になった生物（この論考に立つと果たして実在するか疑わしいが）は一時的に繁栄しても性の長期的利益（マラーのラチェット、赤の女王）を失うため適応放散が制限され絶滅に向かい、短期間しか系統樹上に存在できない。これで大部分の多細胞生物に雄と雌が存在し、一部に雌だけの種がいるという自然界の現状が説明できる。この三部作を通して進化生物学最大の謎である「性の 2 倍のコスト」問題は理論的にはほぼ解決を見たと言えるでしょう。現時点でもかなりの実証的証拠がありますが、今後の研究の進展が期待されます。

English

Yasui, Y. The twofold cost of sex reconsidered: Meiotic mechanisms protect anisogamous populations from invasion by thelytoky. *J Evol Biol* **39**, (2026)

Most multicellular organisms are divided into two sexes—females, which produce nutrient-rich eggs, and males, which produce small, highly motile sperm—and reproduce through a process in which sperm fertilize the eggs (anisogamy). Since organisms that reproduce via anisogamy typically produce an equal number of males and females (a sex ratio of 1:1), half of the population consists of males that do not produce offspring themselves; consequently, the reproduction rate is half that of thelytoky, a form of asexual reproduction in which mothers produce only females. In other words, if a thelytoky mutation occurs within an anisogamous population, it will replace the entire population within a few generations. This twofold difference in growth rate associated with anisogamy is referred to as the “twofold cost of male production,” and the reason males are maintained in so many species despite this cost is considered one of the greatest mysteries in evolutionary biology.

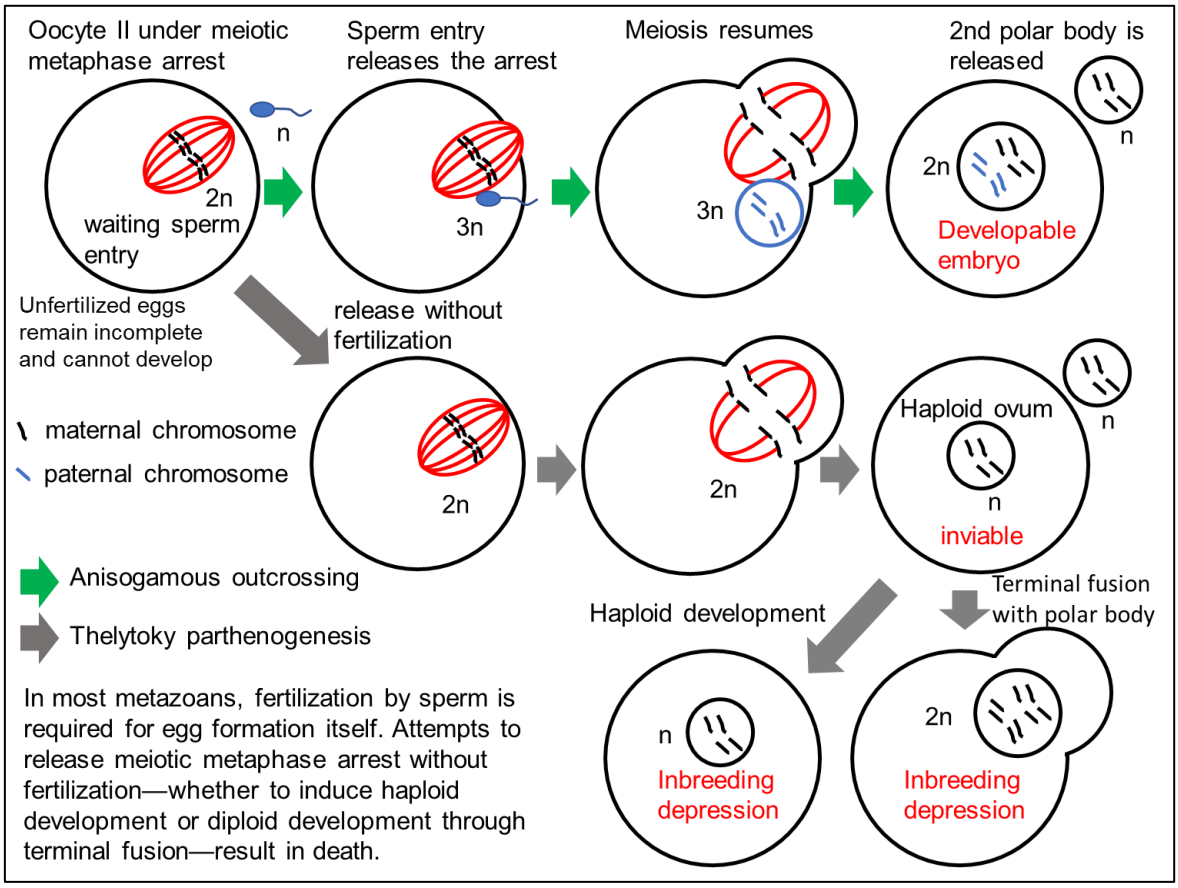
The first paper in the “Trilogy on the Evolution of Sex,” Yasui and Hasegawa (2022) first addressed the origin of gametic sexual reproduction itself, proposing the seesaw effect hypothesis—which explains how the first gamete found a partner for fusion (since there was presumably no one else)—and the inflated isogamy hypothesis, which describes the process by which gametes of the same size initially fused but later polarized into eggs and sperm (i.e., the origin of females and males).

The second paper, Yasui (2026a), and this third paper, Yasui (2026b), examine why anisogamy has not been replaced by thelytoky from two entirely different perspectives: “hidden benefits provided by males” and “mechanical constraints of meiosis.” For basic terminology such as “twofold cost,” please refer to the previous press release.

“Meiotic Metaphase Arrest”: A Universal Mechanism That Has Been Overlooked

To perform sexual reproduction, an egg cannot simply begin development on its own; it must wait for a sperm to enter. In fact, “meiotic metaphase arrest” (MM arrest) is known as a mechanism universal to metazoans. Although it varies by taxonomic group—such as vertebrates and invertebrates—meiosis arrests during metaphase of either the first or second division (the stage where chromosomes align at the equatorial plane and the spindle forms). In humans, when a female fetus is in the mother’s womb, meiosis I has already been completed within the tissue that will become the daughter’s ovaries; the cells then enter the first arrest and remain in this state for over a decade. Upon reaching puberty, meiosis II begins and arrests again during metaphase. Stimulation, such as Ca^{2+} ions delivered by sperm, is required to release this arrest and resume oogenesis. Through this mechanism, the fertilized egg temporarily becomes a triploid cell containing two egg nuclei (2n) and one sperm nucleus (n). Subsequently, one of the egg nuclei is discarded as a polar body (n), while the other egg nucleus (n) fuses with the sperm nucleus (n) to form a diploid cell, after which embryonic development begins. Therefore, the textbook understanding—that meiosis first produces a haploid egg, which then becomes diploid upon fertilization by a sperm—is incorrect for many species (though this appears to be the case in sea urchins). In other words, the egg is not formed on its own; it is only completed when a sperm enters it.

When an animal that has practiced anisogamy in the last generation attempts to transition to thelytoky, it must produce embryos that can develop without being fertilized by sperm. According to Yasui (2026b)'s "Meiosis Constraint Hypothesis," there are three barriers to the transition from meiosis to thelytoky.



1) Empirical data from mice, larvacean, *Xenopus*, zebrafish, and other species indicate that it is extremely difficult to release MM arrest without fertilization. In fact, eggs in MM arrest are incomplete and cannot develop.

2) Even if MM arrest were somehow released without sperm, the result would be the formation of haploid egg cells containing only the female genome. Most wild organisms have accumulated a lethal amount of recessive deleterious genes in a heterozygous state within their genomes; if a haploid egg were to begin embryonic development as is, it would die immediately due to the expression of these deleterious genes.

3) Even if terminal fusion automixis—in which a haploid egg cell fuses with the second polar body, another product of meiosis, to restore diploidy—were to occur, most loci would remain homozygous, and the deleterious genes would still be expressed.

Interestingly, the fact that oocytes and the second polar body are clonal at many loci is due to the conventional process of meiosis. When a particular locus in the primary oocyte is heterozygous for 01 (Fig. 2a), the homologous chromosomes are each duplicated, resulting in a tetrad of 0011 (Fig. 2b). The chromosomes are subsequently distributed to the second oocyte (Fig. 2e) and the first polar body (Fig. 2f). Since two copies of the same chromosome (00 and 11) enter one of these cells together, all loci—except those where crossover occurred at the tetrad stage (Fig. 2c)—become

homozygous within the second oocyte, and the haploid egg (Fig. 2h) and the second polar body (Fig. 2i)—which result from the further division of the second oocyte—become clones at almost all loci. Since the refusion of these two cells constitutes terminal fusion automixis (Fig. 2j), this results in inbred depression at the 00 locus. If the first meiotic division had resulted in a pattern where the second oocyte (01) and the first polar body (01)—each containing a pair of sister chromosomes—were separated, the terminal fusion would have been 01, the heterozygosity would have been the same as the mother's, and the recessive lethal gene would have remained masked. This suggests that the process of meiosis as we see it today is the result of sexual reproduction evolving to be resistant to the intrusion of asexual reproduction (as if attempting parthenogenesis would result in death).

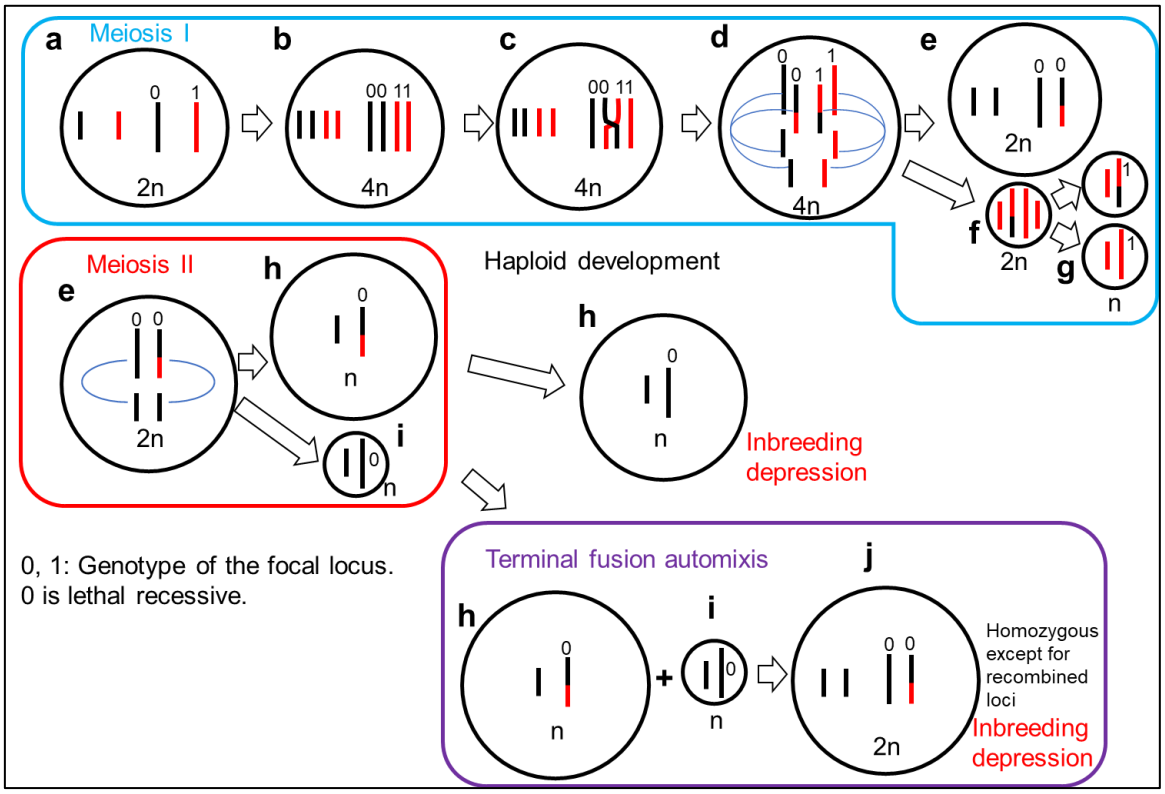


Figure 2: The course of conventional meiosis and the outcome when it transitions to parthenogenesis: The secondary oocyte contains two copies of the same chromosome at each locus

Professor Yasui further developed a mathematical population genetics model to determine, based on the number of functional genes *L* in the genome and the probability *p* of a recessive lethal mutation occurring, whether a haploid egg 1) proceeds with embryonic development as is; 2) fuses with the second polar body to proceed with embryonic development; and 3) undergoes normal anisogamy by fertilization with sperm from an unrelated male—and compared the resulting embryo survival rates. As

predicted by the model, the results showed that the larger the genome size and the higher the mutation rate, the higher the mortality rate when switching from sexual to asexual reproduction (Fig. 3). Most intriguingly, we found that the estimated values of *L* and *p* for fruit flies, mice, and humans lie on the boundary where the fitness of anisogamy and thelytoky are equal. This finding suggests that these animals have evolved to the very cliff's edge—where they can survive through sexual reproduction but die if they resort to asexual reproduction—and have remained there. If this relationship can be clarified in more species in the future, it may shed deeper light on the role of sex in genomic evolution.

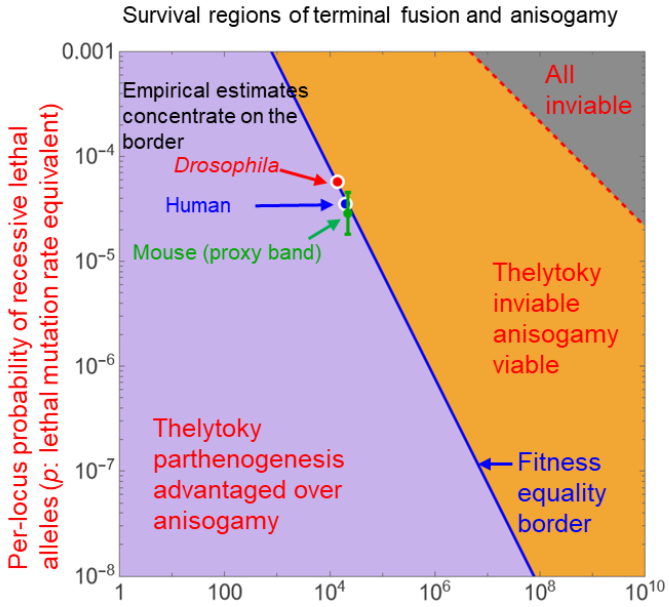


Figure 3: Theoretical predictions of the mathematical model: In the region where $Lp < 1$ (purple region), haploid eggs are at an advantage over anisogamy—which incurs the twofold cost—when selecting thelytoky; however, on the blue line at $Lp = 1$ (where one lethal gene is expressed), thelytoky results in half the offspring dying, and fitness (number of surviving daughters) becomes equivalent to that of anisogamy (male:female ratio of 1:1). The observed data for three species lie on this boundary line. Where $Lp > 1$ (the orange region), thelytoky perish whilst anisogamy survives. In the grey region, combinations arise where even sperm from unrelated males carry a lethal gene at the same locus, causing anisogamy to perish as well. As the organism dies if even a single lethal gene is expressed, there is an upper limit to genome size.

On the other hand, this hypothesis suggests that a form of parthenogenesis that does not involve meiosis could have evolved. Apomixis (a reproductive mode in which clonal embryos are produced through somatic cell division) is known to occur in many plants,

such as dandelions, as well as in some invertebrates, such as aphids and water fleas. Since the offspring are clones of their parent, the accumulation of harmful genes is the same as that of the parent, so they do not die immediately after asexual reproduction. However, to achieve apomixis, somatic cells must regain totipotency, which presents a new barrier. In plants, somatic cells generally retain totipotency, making vegetative reproduction (such as regeneration from tissue fragments or cuttings) possible; however, in multicellular animals, differentiated somatic cells undergo epigenetic modifications, and the restoration of totipotency is severely restricted. Consequently, many multicellular animals cannot escape these mechanical constraints and thus cannot switch to asexual reproduction, which should be advantageous because it does not entail twofold costs.

Think different

The phenomenon called MM arrest has been known since the 1970s, and detailed research has been conducted in the fields of molecular biology and developmental biology. However, researchers have only recognized its biological significance as "preventing eggs from initiating embryonic development while remaining haploid," and there has been no discussion linking it to the issue of the "twofold cost of sex." To achieve a paradigm shift, a broad perspective is required that encompasses both developmental biology and cell biology, as well as theoretical evolutionary biology. Furthermore, the "Red Queen" and "Müller's ratchet" hypotheses—standard theories regarding the advantages of sexual reproduction in countering the "twofold cost"—are based on genetic benefits that are realized with a generations-long delay; therefore, preventing the invasion of thelytoky, which doubles with each generation, requires a faster, immediate process.

The "Trilogy on the Evolution of Sex" explained, in the first paper, how the first sexual reproduction arose (its origin), and in the second and third papers, why males—which incur twofold costs—are maintained. While addressing the same theme of "the maintenance of males," the second paper adopts a completely different approach—focusing on the hidden benefits provided by males that immediately make anisogamy advantageous (the adaptive theory)—whereas the third paper examines how the mechanism of meiosis acts as a mechanical constraint that immediately makes the transition to thelytoky disadvantageous (the constraint theory). Since the provision of resources from males to females can only be expected in organisms such as insects and vertebrates, which have developed social interactions between individuals and resource-defense behaviors, the scope of the second paper was limited (for example, plants do not exhibit such behaviors). However, as the third paper covers all organisms that undergo meiosis, it virtually encompasses all species with both male and female sexes.

Solving the “Twofold Cost of Sex” Problem

The vast majority of organisms that undergo meiosis are able to maintain males even if this entails a twofold cost, as there is a constraint whereby embryos become lethal if the organism ceases male production and attempts to switch to asexual reproduction. If the indirect supply of resources provided by males yields a twofold benefit, the twofold cost is fully offset. Nevertheless, asexual reproduction can evolve in forms that do not involve meiosis (such as apomixis); however, in multicellular animals, this faces a different constraint due to the difficulty of restoring totipotency in differentiated somatic cells. Although it is often overlooked, in many plants—where somatic cells generally retain totipotency, enabling apomixis and vegetative reproduction—and in some animals capable of conditional parthenogenesis (such as aphids and water fleas), anisogamy and asexual reproduction can coexist; consequently, there is no need for their anisogamy to be more efficient than asexual reproduction. They utilise asexual reproduction when rapid population growth is required, and sexual reproduction when the elimination of deleterious genes or defence against pathogens is necessary. Therefore, concerning the “twofold cost of sex” in plants and water fleas is fundamentally misguided. Organisms that have become entirely asexual through apomixis or similar processes (though, based on the arguments presented here, it is doubtful whether such organisms actually exist) may flourish temporarily; however, as they lose the long-term benefits of sex (the Muller’s ratchet and the Red Queen effect), their adaptive radiation is restricted, leading them towards extinction, and they can only exist on the phylogenetic tree for a short period. This explains the current state of the natural world, in which the majority of multicellular organisms possess both males and females, whilst a small number of species consist solely of females. Through this trilogy, it can be said that the twofold cost of sex—the greatest enigma in evolutionary biology—has been largely resolved from a theoretical perspective. While there are already substantial amounts of empirical evidence, we look forward to further progress in future research.