著者による論文解説
Author's Introduction to the Paper (English follows Japanese)

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配偶子有性生殖(gametic sexual reproduction)と異型配偶子生殖(anisogamy)の起源イベント

Yasui, Y., Hasegawa, E. The origination events of gametic sexual reproduction and anisogamy. *Journal of Ethology* 40, 273–284 (2022). https://doi.org/10.1007/s10164-022-00760-3

「性の 2 倍のコスト」

大部分の真核生物は減数分裂で作った配偶子が 2 つ接合して新個体が生じる配偶子有性生殖 gametic sexual reproduction を行います。しかしこの方式では、親のゲノム（2 倍体の場合２ｎ）のうち半分（ｎ）だけが子供に伝達されるため、減数分裂なしでクローンの子（２ｎ）を産む無性生殖（産雌性単為生殖セリトキーthelytoky）に比べて、遺伝子伝達効率は半分になります。この非効率を「減数分裂のコスト cost of meiosis」あるいは「ゲノム希釈コスト genome dilution cost」と呼びます。配偶子有性生殖が起源した段階では、配偶子はほぼ同じ大きさのもの同士が接合していた（同型配偶子生殖アイソガミーisogamy）と考えられますが、今日多くの多細胞生物は卵と呼ばれる大きな配偶子を精子と呼ばれる小さな配偶子が受精する異型配偶子生殖（アニソガミーanisogamy）を行います。卵を作る性が雌、精子を作る性が雄と定義されるため、アイソガミーからアニソガミーへの移行は雌と雄の進化に他なりません。アニソガミーの生物は通常、集団の半数は「資源は消費するがみずから子を産まない」雄であるために、雌ばかりからなるセリトキーの集団に対して増加率が世代あたり半分になります。この人口動態上の不利を「雄を作るコスト male production cost」と呼びます。

「減数分裂のコスト」と「雄を作るコスト」を総称して「性の 2 倍のコスト twofold cost of sex」と呼び、それにもかかわらず性が進化し大多数の生物に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。

性の利益

コストに対抗できる利益を有性生殖がもたらすなら、性の維持は理解できます。有性生殖の利益は様々な視点から提唱されてきました。有害突然変異の蓄積を防ぐ（マラーのラチェット説）、別個体に生じた突然変異を組み合わせて新たな適応を生み出す（フィッシャー・マラー効果）、病原体との軍拡競走に対応する（「赤の女王」説）などが代表的なものです。しかし利益があることとそれが 2 倍のコストに対抗するに十分かどうかは別問題です（第 2、第 3 論文のテーマ）。

ゲノムサイズと性の有無

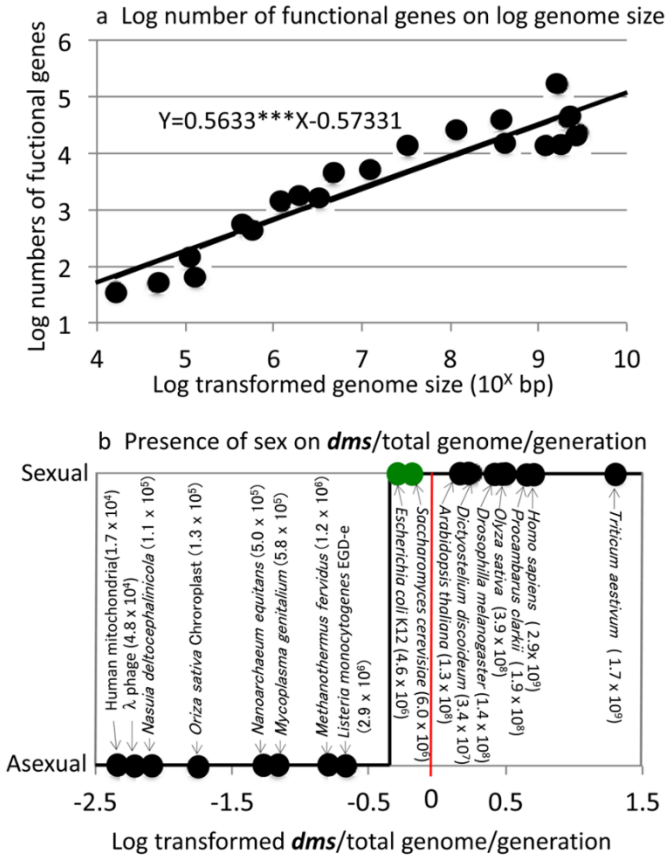

図 1. ゲノムサイズと機能遺伝子数の関係（**a**）および世代あたりゲノム当たり生じる有害遺伝子数と義務的有性生殖の有無の関係（**b**）。突然変異率は全生物で塩基対あたり 1 世代（または 1 複製）につきおよそ $10^{-8\sim-9}$ のオーダー。つまりマラーのラチェットが回転する(毎世代 1 突然変異が起こる)には $10^{8\sim9}$ 塩基対以上の機能配列の総長(コンドラショフ臨界：赤線)が必要。コンドラショフ臨界を境に義務的 obligate な性が生じ、真核生物と配偶子生殖も始まる(臨界近辺の酵母と大腸菌は条件的 facultative な性を持つ)。

図 1 はヒトミトコンドリアからパンコムギまで 21 生物において、ゲノムサイズと機能遺伝子数は正に相関し、遺伝子数の多い生物ほど有害突然変異を起こしやすく、ある臨界（コンドラショフ臨界）を超えると毎世代有害遺伝子が生じるためマラーのラチェットが必然的に回転する。それと同時に無性から義務的有性への切り替えが起こっていることを示しています。これは性の第一機能は有害遺伝子除去であり「赤の女王」は二次的機能であることを示唆しています（細菌もファージに寄生されるのに義務的な性を持たないものがいるからです）。

配偶子有性生殖の起源・アニソガミーの起源

このように性の利益については理論的・実証的に多数の研究がありますが、配偶子生殖がどのように起源し、それがアニソガミー（雌雄二極化）へと進化したかについてはまだよくわかっていません。約 10 億年前の海の中で起こったと思われる出来事について化石記録が残っているわけではなく、論理的な説得力によって仮説の妥当性が決まります。

香川大学農学部の安井行雄教授（進化生物学・昆虫学）は北海道大学農学部の長谷川英祐准教授と共に 2022 年、2 つの斬新な仮説を発表し長年の難問に一石を投じました。

第 1 仮説　配偶子生殖の起源「シーソー効果 seesaw effect」

最初の有性個体が減数分裂をしたとき、同じ有性突然変異が同時に他個体にも生じ、しかも接合できるほど至近距離にいたとは考えられません。また減数分裂をしたとたん「ゲノム希釈コ

スト」は直ちに生じます。どうやって 2 倍不利なはずの最初の有性個体は生き延びて、無性集団中で頻度を増やし定着することができたのか。

著者らはまず祖先型として単細胞で 2 倍体の真核生物を想定しました[注 1]（図 2）。無性二分裂増殖で世代を繰り返し、複雑化してゲノムサイズが増大するような進化の結果、コンドラショフ臨界を超える総遺伝子長になり、マラーのラチェットが回転して 2 ゲノム全体に損傷した（有害な）遺伝子が蓄積しています。このとき損傷した遺伝子の総数 *dms* が致死臨界 *dmt* を超えると死ぬ[注 2]（閾値反応）と考えます。例えば *dmt* = 100 としたとき、*dms* が 100 までは正常ですが 101 になると死ぬ。しかし突然変異は 2 ゲノムに独立に生じるため *dms* = 100 であってもゲノム 1 とゲノム 2 に 50 ずつ均等に分配されていることは稀で、ランダムな偏りがあると考えられます。例えば 60 と 40 に分かれているとして、60 を「汚い」ゲノム D とし、40 を「きれいな」ゲノム C と呼びます。

生殖モード（mode of reproduction）を決める遺伝子座は、無性生殖を支配する野生型対立遺伝子 N に対して、有性突然変異 S は減数分裂と接合を支配し、N に対して顕性（優性）[注 3]であると考えます。

注1　ここで想定している出来事は約 10 億年前の海の中で起こったことで、祖先型が 2 倍体であったという証拠（化石記録など）はありません。しかし減数分裂をする以上、その生物は 2 倍体（偶数倍体）である必要があります。

注2　すなわち突然変異蓄積による死 mutation meltdown は量的形質であるという想定です。この段階では、遺伝子座間の機能分化はまだ十分でなく、特定の遺伝子座が強い働きを持つよりも、多数の座位が相補的に働いている。したがって個々の遺伝子座での顕性潜性もありません。マラーのラチェットやコンドラショフ効果もそういう想定をしています。

注3　S が潜性（劣性）の場合ももちろんありますが、その場合 NS が無害中立で集団中に遺伝的浮動で広がり、S がもう一度生じるのを待つ必要があります。当然長い時間がかかる。簡略化のためここでは S を顕性と置いています。

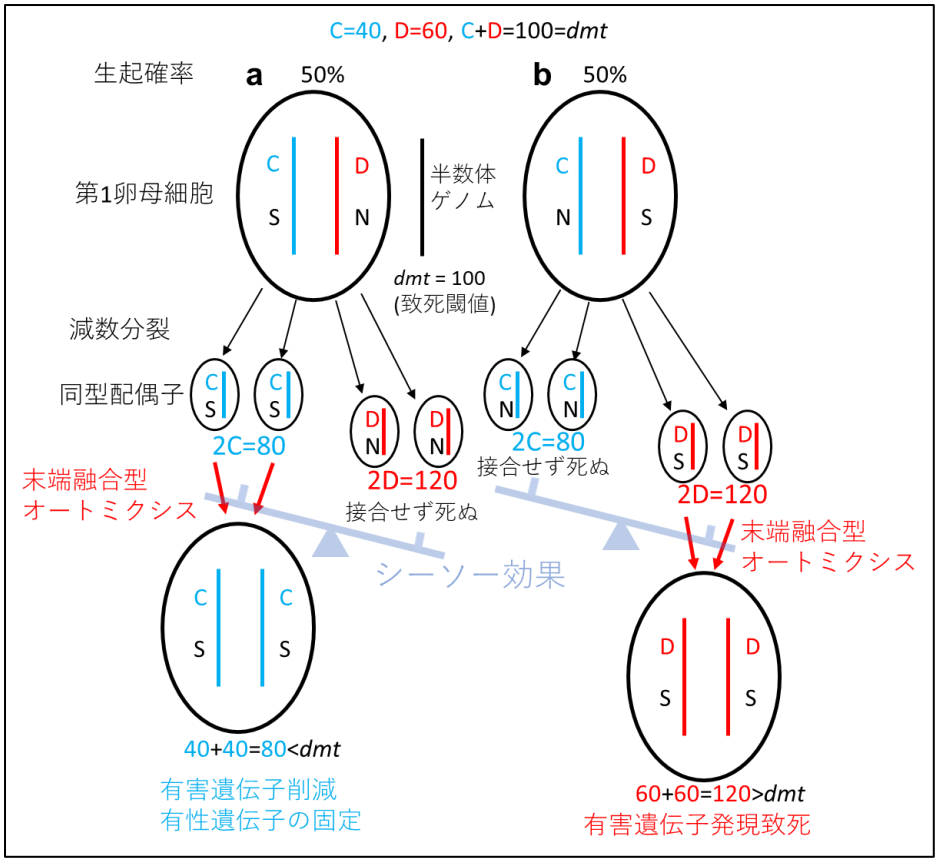

図 2　シーソー効果

有害遺伝子が 2 ゲノムに非対称に分布している状況で **a**「きれいな」ゲノム C に有性突然変異 S が生じれば CS 配偶子同士の接合（末端融合型オートミクシス自殖）が起こり、有害遺伝子総数の削減と有性対立遺伝子 S の固定が一度で同時に達成される。

有性突然変異 S が生じたとき、ゲノム C に入る確率と D に入る確率はそれぞれ 50%です。もし C に入ったとき、CS（きれいで有性）の配偶子が 2 つ、DN（汚く無性）の細胞が 2 つ作られます（図 2a）。最初の有性個体には配偶者はいませんが、この 2 つの CS 配偶子が接合することができます。すなわち最初の配偶子生殖は自殖（自家受精）だったのです。これは今日の単為生殖生物でも見られる末端融合型オートミクシス terminal fusion automixis というプロセスに相当します。自殖と言えば通常は有害なイメージ（潜性有害遺伝子がホモになる）が強いですが、ここでは *dms* = 40 + 40 = 80 となり、逆に有害遺伝子の削減（致死閾値 100 から 80 へ）をもたらしています。同時に作られる DN のハプロイド細胞は無性生殖型 N なので接合能力を持たず、2 倍体へ戻れないまま死にます。母親が持つ有害遺伝子を 2 つのゲノムに不均等に分割することで、一方の遺伝的荷重を重くする代わりに他方を軽くするこのプロセスをシーソー効果 seesaw effect と名付けました。重要なことは CS+CS の接合の際に S 遺伝子が生殖モード遺伝子座に固定することです。これによりこの個体に由来する子孫集団は有性種として確立します。固定した座位 SS は減数分裂を経て S に半減しても接合相手も S を持っているのでゲノム希釈は起こらない（図 3）、すなわち生殖モード座位に関しては減数分裂のコストは生じないことになります。S から N への復帰突然変異が起こって SN ヘテロ個体が生じ、SN 同士の交配で無性個体 NN が復

活しても、彼らは交配しないので有性遺伝子プールから切り離されることになり有性プールの S 固定は維持されます。生殖モード遺伝子座以外の座位も皆自殖により固定するので、遺伝的変異＝進化可能性は大きく失われますが、有害遺伝子が致死臨界を超えて死ぬよりましなのです。

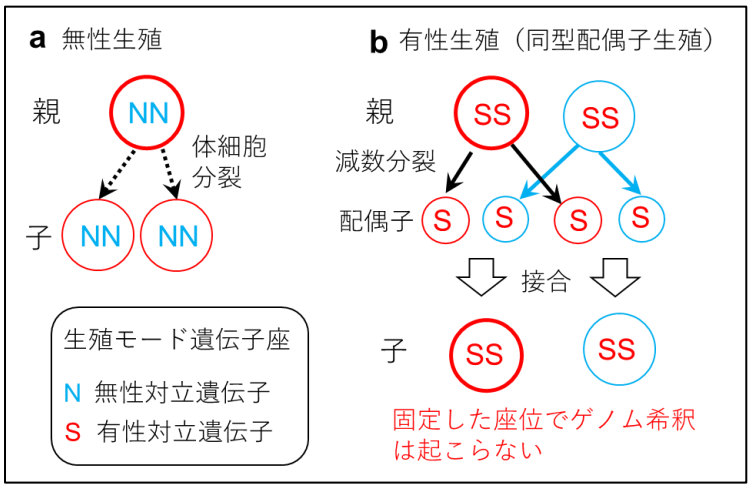

図 3　固定した遺伝子座では減数分裂があってもゲノム希釈は起こらない。有性モード遺伝子 S を持つもの同士の間でだけ交配は起こるので、S の固定は維持される。

CS+CS になる確率は 50%なので DS+DS（*dms* = 60 + 60 = 120 > 100 = *dmt*）になって死ぬ場合もあります（図 2b）が、有性突然変異 S が独立に生じる機会が何度もあれば、その約半数では S が C ゲノムに入り、CS+CS 配偶子生殖の進化が達成されます。シーソー効果の利点は減数分裂のコストを負わないだけでなく、増殖率の点にも現れます（図 4）。第 1 世代では 1 匹の親が CS 配偶子 2 個と DN 配偶子 2 個を作り、CS+CS は 1 個体が生き残るので適応度は 1 ですが、2 世代目以降は CS 配偶子が 4 個作られるので CS+CS は 2 個体生き残り、適応度は 2 になり、無性二分裂増殖と同じになります。しかし無性系統は有害遺伝子を臨界近く保持したままなのでマラーのラチェットが回転し、いずれ死滅します。その結果、有性系統は無性個体群を置き換えることができます。

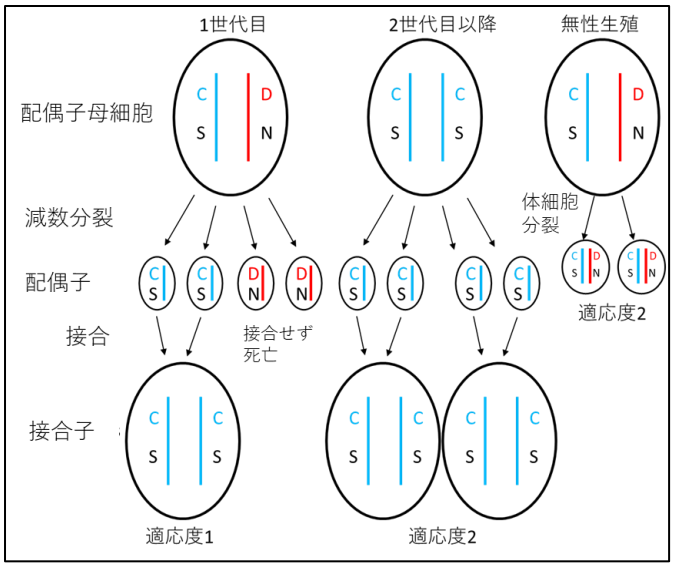

図 4　自殖 2 世代目以降は増殖率（適応度）においても、有性生殖は無性生殖と対等になる。同型配偶子（雄がいない）なので「雄生産コスト」はかからないことに注意。

有性個体が増え、有性個体群が確立すると生殖モード遺伝子座以外の座位に独立した突然変異を持つ者が現れ、進化可能性とゲノム希釈コストが復活しますが、S を持つ者の間でだけ交配が起こるので有性個体群における S の固定は揺るぎません。最初は自殖だった配偶子有性生殖は、血縁者間の近親交配、後に遠縁者間での外交配へと発展したと考えられます。自殖が一度起こると全ての座位はホモ接合になり、2 ゲノム間で有害遺伝子保有数は同じになるので、シーソー効果は連続世代では働かず新たな有害突然変異が非対称に蓄積するのを待つ必要があります。交配集団が大きくなることで独立した突然変異により有害変異保有数の異なる配偶子間の接合が起こり、次世代でシーソー効果を復活させます。さらに最初の減数分裂時にはまだ存在していなかった第 1 減数分裂中期（4 量体期）における内腕組み換え（染色分体の交差）が進化することで、より大きな *dms* 非対称が作り出されます。シーソー効果は突然変異が 2 ゲノム間に非対称に起こるというランダム性にのみ基づいているのに対して、組換えが可能になると積極的に一方のゲノムに有害遺伝子を集中させ、その個体を死なせることで集団から除去するコンドラショフ効果へ進化していったと考えられます。両者に共通する原理は、有害変異を 2 つのゲノムへ均等に残すのではなく一方へ偏らせることで、他方を浄化することです。

配偶子有性生殖の起源：シーソー効果のまとめ
これまで無性生殖の集団に生じた有性突然変異が何らかの理由で配偶機会を得て、性のもたらす利益により何世代もかけて徐々に頻度を増やし、集団を置き換えると考えられてきたのに対して、シーソー効果は、オートミクシス自殖によって外部の配偶者を必要とせず、2、3 回の試行で CS の組み合わせが生じれば 1 世代で配偶子有性生殖を進化させることが可能です。これにより「どうやって 2 倍不利なはずの最初の有性個体は配偶者を得て、生き延びて、無性集団中で頻度を増やし定着することができたのか」という誰も解けなかった難問に答えました。

第 2 仮説　アニソガミー（雌雄二極化）の起源（inflated isogamy）
前述のように配偶子有性生殖は同型配偶子アイソガミーで始まったと考えられます。アイソガミーでは両親ともが繁殖資源を同じだけ出し合う（割り勘状態）ため「雄を作るコスト」がかかりません（「資源を消費しながら子供を産まない雄」がそもそも存在しない）。一方、有害遺伝子の除去や病原体への抵抗といった有性生殖の利点は全て備えるためアイソガミーは理想的な生殖モードといえます。しかし自然界ではアイソガミーは出芽酵母、クラミドモナス、中心目珪藻などの限られた単細胞生物に限られ、脊椎動物などの複雑な多細胞生物ではアニソガミーが広く観察されます。理想的なはずのアイソガミーが進化的に不安定で、そこからアニソガミーが進化し、維持されていることは 2 倍のコストを生じても雄を作る理由があることを示唆します。どのようにして同型配偶子から卵と精子へ二極化する進化が起きたのでしょうか。

図 5 は各生殖様式の経済状況の概念図です。ここでは「配偶子 1 個あたりの資源量」と「親 1 個体が繁殖に使う総資源量」を区別して考えます。一匹の親が $2R$ の資源（＝母細胞の大きさ）を生殖に費やし、子（娘細胞または接合子）の生存または発育が可能な最小の大きさが R である

と考えます。単細胞の無性生殖生物（分裂直後のサイズ R）は外界から資源を取り入れ、サイズ $2R$ に成長した後、体細胞二分裂によりサイズ R の二つの娘細胞に分かれます（図 5a）。同型配偶子生殖アイソガミー（図 5b）では、サイズ $2R$ の成熟した母細胞がサイズ $0.5R$ の同型配偶子に 4 分裂し、他の配偶子と接合（$0.5R$+$0.5R$）してサイズ R の接合子が一つでき、サイズ $2R$ の成熟細胞に成長して再び繁殖します。以降、このような性の様式をスマートアイソガミーと呼びます。「スマート」とは、胚の生存に必要な最小限の資源(R)を、両配偶型が「割り勘」で支払うことを意味します。無性生殖（図 5a）とスマートアイソガミー（図 5b）はどちらも $2R$ の資源を負担してサイズ R の子を作るので経済的には同等（雄を作るコストが生じない）であり、シーソー効果も働くので 5a から 5b への進化は容易だったと思われます。しかしスマートアイソガミーからアニソガミーへと進化しようとすると、雄が資源を負担しないため雌が代わりに全額を出す（$0.5R$ から R へ支出が倍増）ことになり「2 倍のコスト」を負うことになります。なぜこれが可能だったのでしょうか。

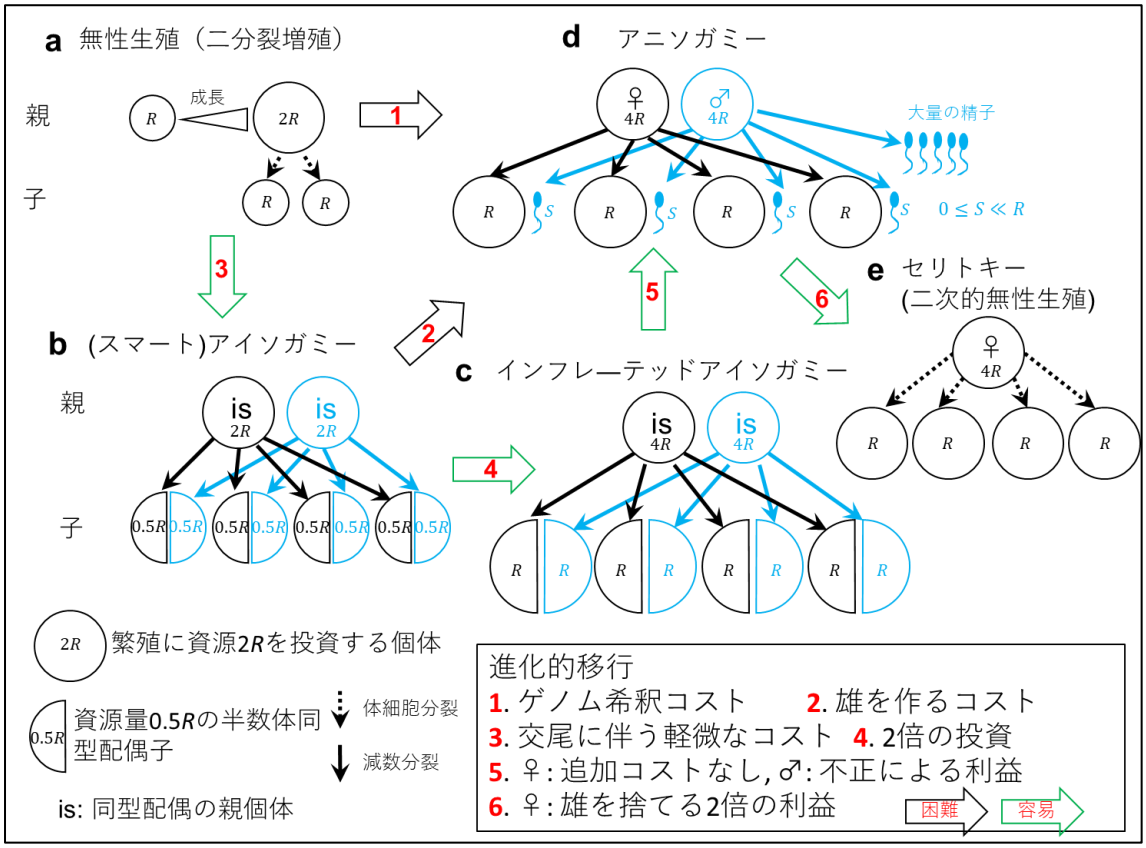

図 5　細胞分裂の経済。単細胞無性生殖(a)からスマートアイソガミー(b)への移行は、同じ $2R$ の資源を蓄えて二分割するか、四分割して二つが接合するかの違いなので比較的容易である(どちらも娘胚は R の資源を持つ)。スマートアイソガミーからアニソガミー(d)への移行は雄が資源負担しないため、雌が 2 倍($4R$)支出する必要がある(雄の 2 倍のコスト)。多細胞生物への進化に伴い資源供給に余裕が生じて両親ともに配偶子を 2 倍(R)にした膨張型アイソガミー(c)を中間段階に置くと b→c→d の移行はスムーズになる。しかし減数分裂をやめてセリトキー（e：産雌性単為生殖）に移行すると雄のコスト、減数分裂のコストともに消失する。なぜコストのかかる雄が多くの種で維持されているのかは Yasui 2026ab「性の進化第 2・第 3 論文」で取り上げる。

偉大な Parker 理論にも盲点がある

アイソガミーからアニソガミーへの進化を説明する先行理論は Parker, Baker and Smith (1972)によるいわゆる「PBS モデル」が有名です（図 6）。

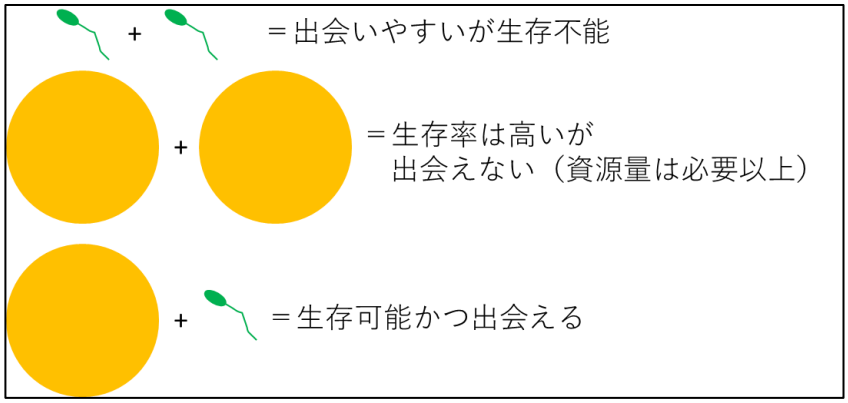

図 6　PBS モデルのコアロジック：異サイズ交配

Parker GA, Baker RR, Smith VG. The origin and evolution of gamete dimorphism and the male-female phenomenon. *J Theor Biol*. 1972 Sep;36(3):529-53. https://doi.org/10.1016/0022-5193(72)90007-0 PMID: 5080448.

配偶子集団に大小さまざまな変異があるとき、小＋小の接合は出会い確率は高くても栄養不足で死に、大＋大の接合は栄養は十分以上だが運動性が低く出会えない、結局、大＋小の接合だけが必要な栄養を備えかつ出会えるため生き残り、アニソガミーへと進化した。同時に同型配偶子生殖では 3 つ以上存在していた性別が大小両極端だけが残ったため雄と雌の 2 つになったという説明は科学史上最も感動的な「なるほど」をもたらすものです。しかしこのモデルには見過ごされてきた欠陥があります。卵から精子までのサイズ変異が集団中に存在しているならこのような異サイズ交配（size-disassortative mating）は起こるでしょう。しかし当初の集団は同型配偶子（私の言うスマートアイソガミー）で構成されていたはずで、そこに卵から精子までの大きなサイズ変異がどうやって生じたのか。PBS モデル論文では同型配偶子からまずサイズの増大が起こり、それに呼応してサイズの減少も起こり、分断淘汰が働いてサイズ変異が拡大したと簡単に触れているだけで、具体的なメカニズムは書かれていません。つまり PBS モデルには、分断淘汰が始まった後の説明はありますが、分断淘汰を開始させる最初のサイズ変異がなぜ有利になれるのかという説明がありません。分断淘汰が働くには、配偶子サイズの平均値からの少しの増加と少しの減少がそれぞれ直ちに有利でなければなりません。しかし単細胞生物は資源に余裕がありません。Smart isogamy $0.5R+0.5R=1R$（図 7a）の状態で一方が投資を減らせば胚が死ぬだけです（図 7b）。つまり一方がサイズを減らすためには相手が前もってサイズを大きく（$0.5R \rightarrow 1R$）している必要があるのです。相手にはそうするメリットがあるでしょうか。単細胞生物にとって資源獲得に時間をかけて配偶子サイズを少し大きくしても生存率はほとんど改善しません。それよりも資源量 $2R$ が貯まり次第、減数分裂したほうが増殖速度が速くなります。したがって配偶子サイズを増大させる選択圧は小さく率先して雌になるメリットはないと考えられます。では雄になるメリットはあるでしょうか。ここで想定する祖先的な単細胞生物では、1 回の減数分裂から直接配偶子を 4 個しか得られません。配偶子サイズを少し小さくしても受精率はほとんど改善しないし、最大 4 個しか受精できない。数が増やせないのにサイズを減らしたら生存率が下がるだけです。したがって配偶子サイズを縮小させる選択圧も小さ

い。それゆえ PBS モデルが想定しているようなサイズ分断淘汰は起こりにくいと考えられます。

片利共生としてのアニソガミーの進化

必要なのは、一足飛びで両親とも配偶子サイズを増大させる何らかのブレイクスルーです。私の inflated isogamy 仮説では、シーソー効果によって 1 個体から自殖由来の遺伝的にほぼ同一な子孫集団が生じ、それらが局所的に増殖することで、クローンの単細胞生物が至近距離に密集する状況を想定します。この高血縁度の細胞群では細胞間競争が小さく、協力と役割分担が成立しやすいため、細胞同士が融合して多細胞生物へと進化(multicellularization)しやすくなったと考えます。クローンの細胞（血縁度 1）同士が協力し、役割分担を行うので多細胞生物は単細胞生物よりも高度な適応を達成できます。同時に多細胞生物は胚発生のためにより多くの資源が必要ですが、複数の細胞の産生エネルギーを合算できるので十分な資源量を供給できるようになります。そのため両親が isogamy のまま配偶子サイズを 0.5R から 1R に増大させ、1R+1R=2R の同型接合により 2 R の接合子を得る inflated isogamy（膨張した同型配偶：図 5c, 7c）という状態が生じたと考えます。この場合、支出は 2 倍に増大しますが両親の間に不平等はありません。接合子がどれだけ資源を持っているかでその生存率や胚発生の到達レベルが決まるのでこれは「2 倍のコスト」ではなく価値ある「2 倍の投資」と言えるでしょう。

しかしこの状態では接合子は必要以上に大きい（必要サイズは R）ので、一方の性が、相手がすでに必要量を支出していることを見越し、親 1 個体としての総投資量を変えずに自分の配偶子サイズを半減し（1R→0.5R）数を 2 倍に増やす不正を行ったとします。多細胞化により配偶子母細胞が増え、1 個体が 5 つ以上の配偶子を作れるようになったことがこれを可能にしました。これにより「不正者」の性は 2 個体以上の配偶子を受精する（一夫多妻）メリットを得て雄に進化しました。ここに初めて、「小さくなるほど多く作れる」という PBS モデルの選択圧が作動し始めます。つまり雄は起源においてすでに一夫多妻だったのです。他方の「だまされた」性は雌となりこうして最初期段階のアニソガミーが成立します。しかし雌はこの不公平を容認しました。なぜならば雌の支出は inflated isogamy の 1R から変化しなかったからです。雄だけが子供 1 匹あたりの投資を減らすことで子供の数を増やす一夫多妻利益を得たので、すなわちアニソガミーは「一方が得をするが他方は損も得もしない」相互作用である片利共生 commensalism として進化したのです。

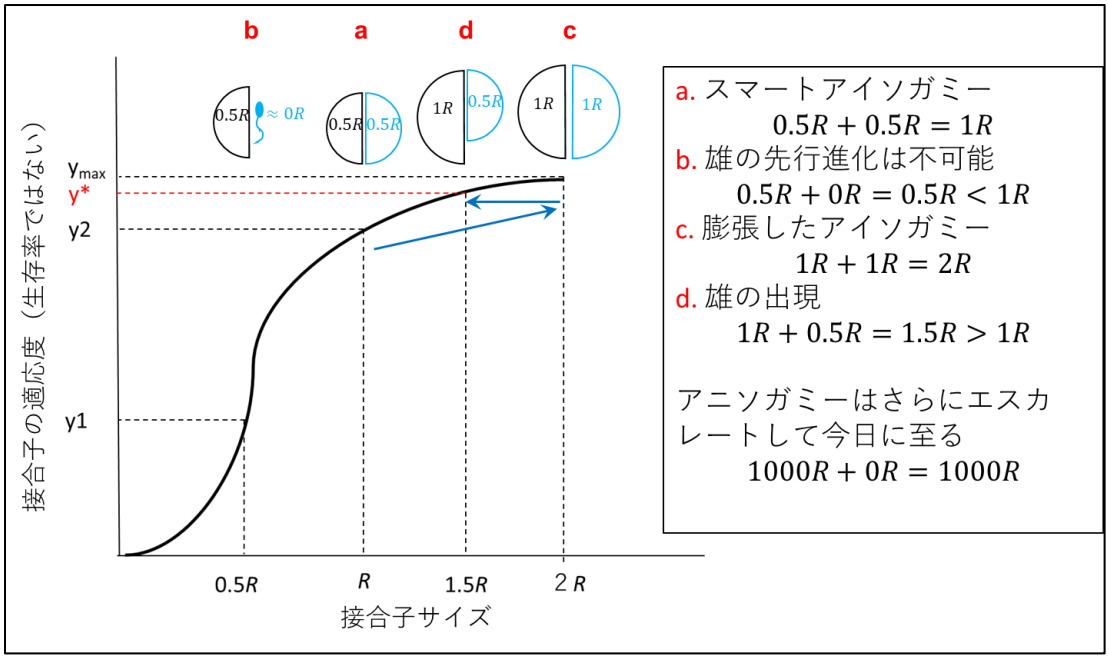

図 7　inflated isogamy 仮説：必要資源量 *R* を両性で「割り勘」していたスマートアイソガミー状態(a：適応度 y2)では資源の余裕がないため、一方の性が投資を減らす（雄化する）と適応度は激減する(b：適応度 y1)のでアニソガミー移行は不可能である。多細胞化に伴い両性ともに配偶子を増大させた inflated（膨張した）アイソガミー(c)では適応度は最大化(y_{max})するがスマートアイソガミーからの増分はわずかで 2 倍の投資（0.5*R*→1*R*）には見合わない。この資源の冗長性に便乗して一方の性が配偶子を縮小しても適応度はほとんど下がらない(y*)。小さな配偶子は多く作れるので一夫多妻メリットが生じ、「不正者」は雄へと進化した。だまされた「正直者」である雌は自己の投資量が 1*R* のまま変化しないためこれを容認し、片利共生として最初期段階のアニソガミーが起源した。以後配偶子のサイズ差は拡大し、今日のアニソガミー（雌と雄の二極化）が完成した。

受精率の改善：片利共生から相利共生へ

このように接合子への資源投資に関する不平等を容認する形でアニソガミーは成立しています。そもそも配偶子の大きさ（資源投資）が異なることをもって雌雄を定義するのですから、平等になったらそれは雄・雌とは呼べなくなります。しかし雄の存在は雌にとってコストをもたらすばかりなのでしょうか。配偶子生殖に固有の問題は卵が未受精のまま死ぬことです。特に配偶子が大きい inflated isogamy の状況では未受精で残される同型配偶子が相当あったものと考えられます。異性が対等の栄養投資をしてくれたとしても未受精で死ぬのでは意味がありません。ここで雄の裏切りによって生じた小配偶子（精子）は運動性と数の多さによって受精率を改善した可能性があります。Yasui and Hasegawa (2022)はコンピュータシミュレーションによってこの可能性を検討しました（図 8）。

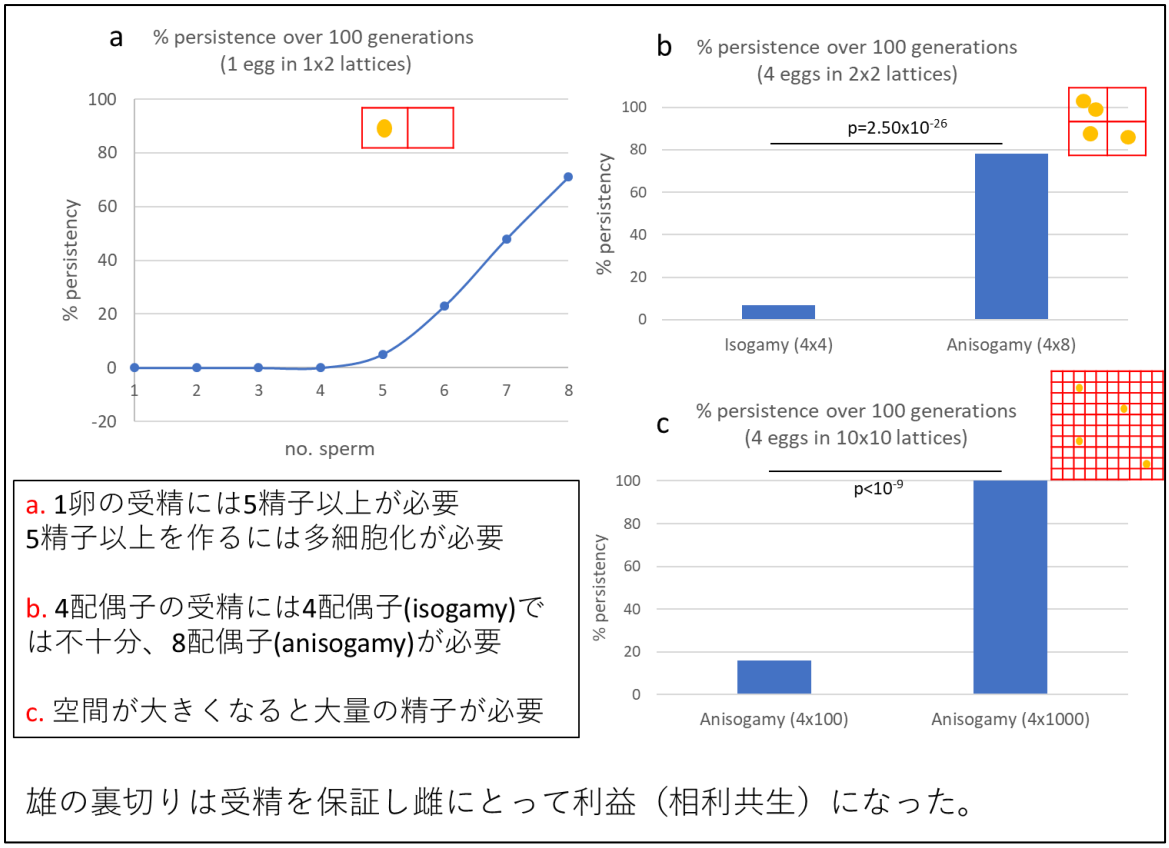

図 8　シミュレーション

a. 1 x 2 の格子に 1 卵

b. 2 x 2 の格子に 4 卵

c. 10 x 10 の格子に 4 卵　がランダムに入っている状況を想定し、そこにランダムに精子が散布され同じ升目に入ると受精する。 1 つでも受精卵が得られれば次世代に継続する。100 世代持続するのに必要な精子数を求めた。

シミュレーション（図 8）では、 1 × 2 の最小の空間構造で、1 つの母細胞から減数分裂で作られる 4 配偶子では 100 世代の系統存続率がほぼ 0 であり、多細胞化して 5 つ以上の精子を作ると初めて存続可能性が生じること、 2 × 2 の空間では 4 配偶子（対等の条件、つまりアイソガミー）の 100 世代存続率はきわめて低いのに対し、2 つの母細胞から作られる 8 配偶子（最小限のアニソガミー）では存続率が大幅に上昇すること、10×10 と空間が拡大すると 100 精子でも存続率は低く、1000 精子でほぼ 100%に達することが示されました。このシミュレーションでは精子数の効果だけを検証していて運動性の効果は考慮していないので、実際にはさらに受精率が上がることが期待されます。これらの結果から、当初雄の不正を雌が容認した片利共生によってスタートしたアニソガミーが、受精率の改善という利益を雌にもたらし相利共生 mutualism へと進化したことが理解できます。

アニソガミー：寄生から共生へ

従来、アニソガミーは精子（雄）による卵（雌）に対する寄生であると考えられてきました。しかしそれは子供に対する資源投資だけに注目した見方です。両者は異なる問題においてお互

いの弱点を補い合っているのです。卵にとっての弱点は大きくて動けないために出会いの確率が低いことであり、精子にとっての弱点は小さいために子供（受精卵）に栄養を供給できないことです。両者の共生が成立したことで、精子はさらに小さく多くなり、卵は単独で全ての栄養を賄うためにさらに大きくなり、雌雄の性的役割 sex role が確立し、今日の生物多様性が構築されたと考えられます。

アニソガミー（雌雄二極化）の起源：inflated isogamy のまとめ
PBS モデルが明示していなかった同型配偶子集団にサイズ変異が生じ、分断淘汰へとつながる具体的なシナリオを本稿は提示しました。雌は（スマート）アイソガミーからアニソガミーに進化する過程で 2 倍のコストを負うことは変わりないが、inflated isogamy という緩衝プロセスを想定することで移行がスムーズになったと考えられます。

考察
性のコスト論 3 つの注意点
１．減数分裂は常にゲノム希釈コストを生じるわけではない
CS（きれいで有性）配偶子同士のオートミクシス自殖（シーソー効果）により生殖モード遺伝子座は S で固定し、固定した座位では希釈は起こりません。突然変異と外交配により他の座位でヘテロ接合が生じゲノム希釈が復活しても、それらは絶滅回避と進化可能性のために有性生殖の存続を容認せざるを得ない。全遺伝子座は有性システムの下で妥協するしかないのです。

２．投資とコストを混同してはならない
スマートアイソガミー→インフレーテッドアイソガミー→アニソガミーと変遷する間に雌が負担する資源量は 2 倍に増えましたが、これは採算が合う投資でした。コストは常に減らすべきだが投資は利益が出る限り増やすべきです。当初はパートナーも同額を投資し、途中で雄化して撤退しアニソガミーになった後でも、卵投資は雄による受精保証があれば雌にとって採算の合う投資なのです。

３．複雑な多細胞生物はどうしてもアニソガミーを必要とする（以下は「性の進化第 3 論文」（Yasui 2026b）と一部重複して論じています。）
単細胞生物では両配偶型は同じだけの資源を出し合っていました(isogamy)。すなわち両配偶型は資源投資において平等でした。多細胞生物に進化すると、胚発生（細胞分裂して大きく複雑な体を作る）のためにより多くの資源が必要となります。だから接合子（受精卵）は大きくなる必要がある。しかし大きな接合子を半分に割った量の資源を両配偶型が出し合うことは物理的に不可能（動けない、出会えない、細胞質が邪魔になる）。ハーフサイズのダチョウの卵 2 つがくっつくかどうか想像してみてください。したがって一方が大きくなって栄養を担い、もう一方はその細胞質を潜り抜けられる小さなサイズになるほかはないのです。それゆえ雌と雄に二極化するのは機械的必然であり、数理モデルで解析する必要などありません。複雑な多細胞生物はアニソガミー（大型配偶子と小型配偶子への二極化）で

しか存在しえないのです。卵の大型化による栄養供給は爬虫類（恐竜）・鳥類（ダチョウ）で限界に達しました。これ以上大きくすると陸上環境では重力に卵が耐えられません。重力でつぶれないように殻を厚くしたら今度は孵化できなくなります。それゆえ哺乳類は胎生すなわち小さな受精卵を胎盤を通じた栄養供給で育てる方法に移行しました。まさにこの理由により、象がメートルサイズの卵を割って孵化するということはないのです。哺乳類に至ると、胎盤経由の栄養供給および授乳という雌の巨大な投資に比べれば配偶子サイズの雌雄差はもはや性のコストを表していません。配偶子サイズに基づく性のコスト論はここで終焉を迎えます。
しかし雄を作るコストは無くなりません。数が多くて運動性の高い精子がいくら受精率を高めても、産雌性単為生殖セリトキーに移行すれば受精自体が不要になるので受精率向上メリットは失われます。また胎生でも雌ばかりを産むような突然変異が生じれば、雌雄を 1：1 で産む有性個体群は世代あたり 2 倍の増殖率の差により乗っ取られることになります。しかし多細胞生物の世界でアニソガミーが大半を占めること、今日まで無性生殖の哺乳類は知られていないことを説明する必要があります。（第 2 論文、第 3 論文に続く）

Author’s Introduction to the Paper

Yukio Yasui

The Origin of Gametic Sexual Reproduction and Anisogamy

Yasui, Y., Hasegawa, E. The origination events of gametic sexual reproduction and anisogamy. *Journal of Ethology* 40, 273–284 (2022). https://doi.org/10.1007/s10164-022-00760-3

“The Twofold Cost of Sex”

Most eukaryotes undergo gametic sexual reproduction, in which two gametes produced by meiosis fuse to form a new individual. However, in this system, only half (n) of the parental genome (2n in the case of diploids) is passed on to the offspring; thus, the efficiency of gene transmission is halved compared to asexual reproduction (thelytoky), in which clonal offspring (2n) are produced without meiosis. This inefficiency is referred to as the “cost of meiosis” or the “genome dilution cost.” It is believed that at the stage when gametic sexual reproduction first arose, gametes of nearly the same size fused (isogamy); however, today many multicellular organisms practice anisogamy, in which a large gamete called an egg is fertilized by a small gamete called a sperm. Since the sex that produces eggs is defined as female and the sex that produces sperm is defined as male, the transition from isogamy to anisogamy is nothing less than the evolution of males and females. In anisogamous organisms, half the population typically consists of males—who consume resources but do not produce offspring themselves—resulting in a growth rate per generation that is half that of a population consisting solely of females (thelytoky). This demographic disadvantage is referred to as the “male production cost.”

The "cost of meiosis" and the "cost of male production" are collectively referred to as the "twofold cost of sex," and the reason why sex has evolved and is maintained in the vast majority of organisms despite this cost is considered one of the greatest mysteries in evolutionary biology.

The Benefits of Sex

If sexual reproduction provides benefits that can offset these costs, the maintenance of sex becomes understandable. The benefits of sexual reproduction have been proposed from various perspectives. Notable examples include the prevention of the accumulation of deleterious mutations (Muller's ratchet hypothesis), the combination of mutations arising in different individuals to create new adaptations (the Fisher–Muller effect), and the ability to respond to an arms race with pathogens (the "Red Queen" hypothesis). However, the existence of benefits is a separate issue from whether they are sufficient to offset the twofold cost (it is the subject of the second and third papers of Yasui's "The Evolution of Sex Trilogy").

Genome Size and the Presence or Absence of Sex

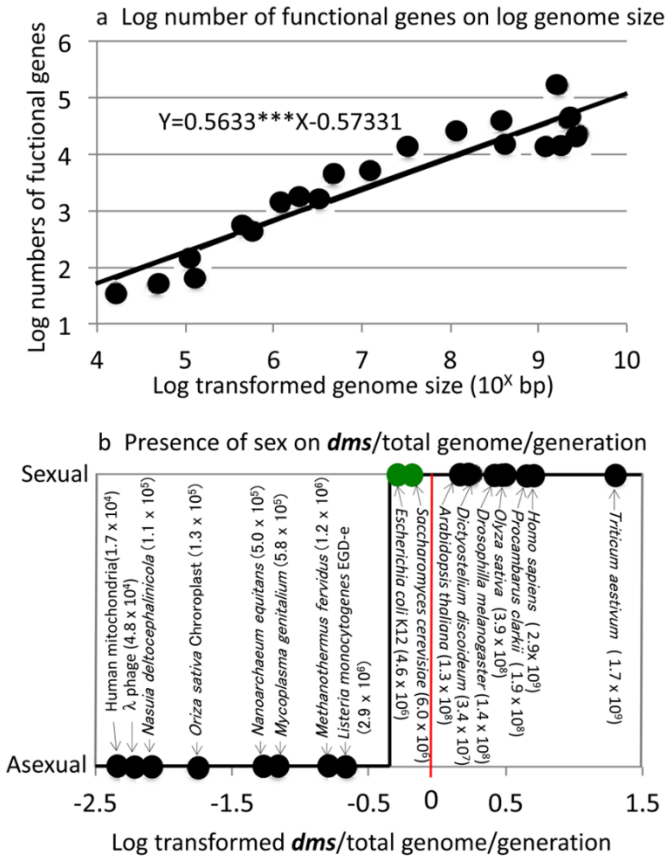

Figure 1. Relationship between genome size and the number of functional genes (**a**), and relationship between the number of deleterious genes arising per genome per generation and the presence or absence of obligate sexual reproduction (**b**). The mutation rate across all organisms is on the order of approximately 10^{-8} to 10^{-9} per base pair per generation (or replication). In other words, for the Muller's ratchet to turn (with one mutation occurring per generation), a total functional sequence length of at least 10^8 to 10^9 base pairs is required (the Kondrashov threshold: red line). Beyond the Kondrashov threshold, obligate sex arises, and eukaryotes and gametic reproduction also begin (yeast and *E. coli*, which are near the threshold, exhibit facultative sex).

Figure 1 shows that, across 21 organisms ranging from human mitochondria to common wheat, genome size and the number of functional genes are positively correlated; organisms with a higher number of genes are more prone to deleterious mutations, and once a certain threshold (the Kondrashov threshold) is

exceeded, deleterious genes arise in every generation, causing the “Muller’s ratchet” to inevitably turn. At the same time, it indicates that a shift from asexuality to obligate sexuality is occurring. This suggests that the primary function of sex is the removal of deleterious genes, while the “Red Queen” effect is a secondary function (since some bacteria, despite being parasitized by phages, do not possess obligate sexuality).

The Origin of Gametic Sexual Reproduction and the Origin of Anisogamy

While there is a wealth of theoretical and empirical research on the benefits of sex, it is still not well understood how gametic reproduction originated and how it evolved into anisogamy (male-female dimorphism). Since there is no fossil record of events believed to have occurred in the oceans approximately 1 billion years ago, the validity of a hypothesis is determined by its logical persuasiveness.

In 2022, Professor Yukio Yasui (Evolutionary Biology and Entomology) of the Faculty of Agriculture at Kagawa University, together with Associate Professor Eisuke Hasegawa of the Faculty of Agriculture at Hokkaido University, presented two novel hypotheses that have shaken up this long-standing puzzle.

Hypothesis 1: The Origin of Gametic Reproduction—The “Seesaw Effect”

It is unlikely that, when the first sexual individual underwent meiosis, the same sexual mutation occurred simultaneously in another individual who was close enough to undergo fusion. Furthermore, the “genome dilution cost” arises immediately upon meiosis. How was the first sexual individual—which should have been at a twofold disadvantage—able to survive, increase its frequency within the asexual population, and become established?

The authors first posited a single-celled, diploid eukaryote as the ancestral type [Note 1](Figure 2). Through generations of repeated asexual binary fission, they evolved increasing complexity and expanding genome size. As a result, the total gene length surpassed the Kondrashov threshold, causing Muller’s ratchet to turn and accumulate deleterious genes in both genomes. We hypothesize that when the total number of damaged genes, *dms*, exceeds the lethal threshold, *dmt*, the organism dies [Note 2](threshold response). For example, if *dmt* = 100, the organism remains normal up to *dms* = 100 but dies when *dms* reaches 101. However, since mutations occur independently in the two genomes, it is unlikely that the deleterious genes will be distributed evenly, with 50 on Genome 1 and 50 on Genome 2, even if dms = 100. Instead, a random deviation is expected. For example, if the DMS is divided 60 to 40, the 60 would be called “dirty” Genome D and the 40 would be called “clean” Genome C.

We hypothesize that the locus determining the mode of reproduction consists of a wild-type allele N, which governs asexual reproduction, and a sexual mutant S, which governs meiosis and fusion and is dominant over N [Note 3].

Note 1 The events assumed here occurred in the ocean approximately 1 billion years ago, and there is no evidence (such as the fossil record) that the ancestral form was diploid. However, for meiosis to occur, the organism must be diploid (even-ploidy).

Note 2 In other words, the assumption is that "mutation meltdown"—the accumulation of lethal mutations—is a quantitative trait. At this ancient stage, functional differentiation between loci is not yet sufficient; rather than a single locus having a strong effect, numerous loci function complementarily. Consequently, there is no concept of dominance or recessiveness at individual loci. The Muller's ratchet and the Kondrashov effect are also based on this assumption.

Note 3 Of course, there are cases where S is recessive; in such cases, NS is selectively neutral, spreading through genetic drift within the population, and it is necessary to wait for S mutation to reoccur. This takes a long time. For simplicity, we assume S to be dominant here.

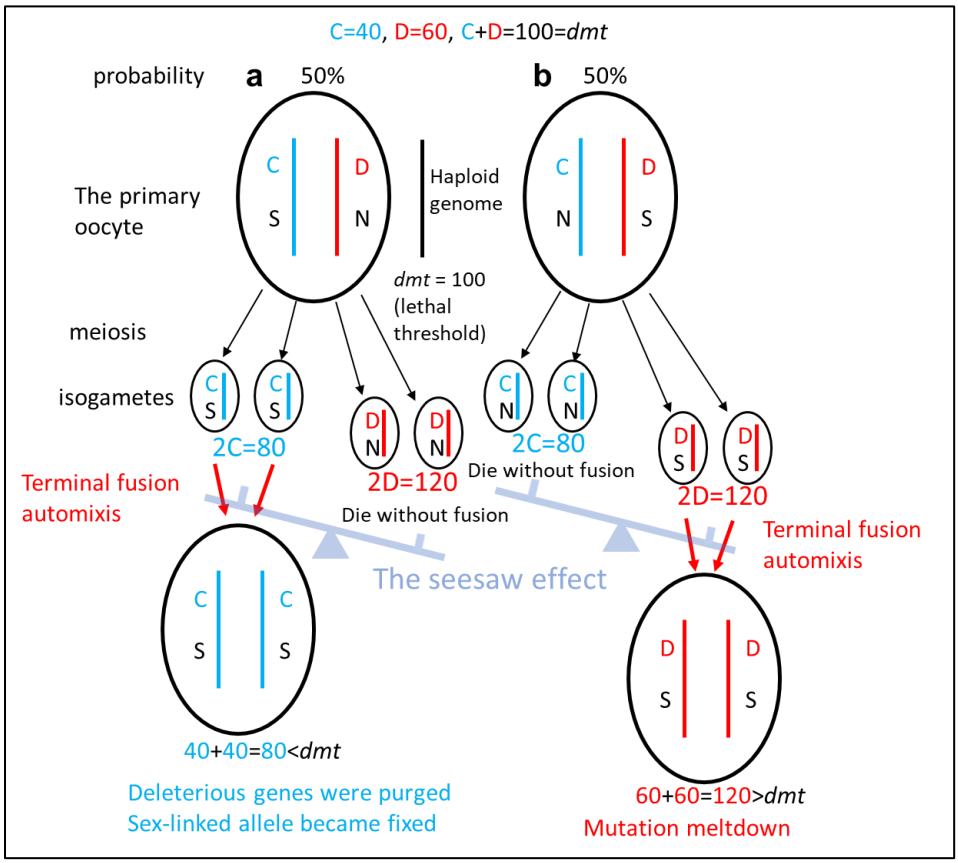

Figure 2: Seesaw Effect

In a situation where deleterious genes are asymmetrically distributed across two genomes, if a sexual mutation S occurs in the "clean" genome C, terminal fusion automixis between CS gametes takes place, simultaneously achieving a reduction in the total number of deleterious genes and the fixation of the sexual allele S in a single step.

When a sexual mutation S occurs, the probability of it entering genome C and the probability of it entering genome D are each 50%. If it enters C, two CS (clean and sexual) gametes and two DN (dirty and asexual)

cells are produced (Figure 2a). The very first sexual individual had no mate, but these two CS gametes were able to fuse. In other words, the first gametic reproduction was self-fertilization. This corresponds to a process called terminal fusion automixis, which is also observed in modern parthenogenetic organisms. Although self-fertilization usually has a negative connotation because recessive deleterious genes become homozygous, in this case, *dms* = 40 + 40 = 80. This results in fewer deleterious genes than the lethal threshold of 100. The DN haploid cells produced simultaneously carry the asexual allele N and therefore lack the ability to fuse; unable to restore diploidy, they simply die. We have named this process the "seesaw effect," in which the harmful genes carried by the mother are unevenly distributed across the two genomes, thereby increasing the genetic burden on one while reducing it on the other. Crucially, during CS × CS mating, the S allele becomes fixed at the reproductive mode locus. As a result, the offspring population derived from this individual is established as a sexual species. Even if the fixed SS genotype is halved to S through meiosis, genome dilution does not occur because the mating partner also carries the S allele (Figure 3); in other words, there is no cost of meiosis with respect to the reproductive mode locus. Even if a back mutation from S to N occurs, producing SN heterozygotes, and asexual NN individuals are restored through mating between SN individuals, these NN individuals do not interbreed with SS sexual individuals and are thus isolated from the sexual gene pool, thereby maintaining the fixation of S in the sexual gene pool. Since all loci other than the reproductive mode locus are also fixed through self-fertilization, genetic variation—and thus the potential for evolution—is greatly reduced; however, this is preferable to harmful genes exceeding the lethal threshold and causing death.

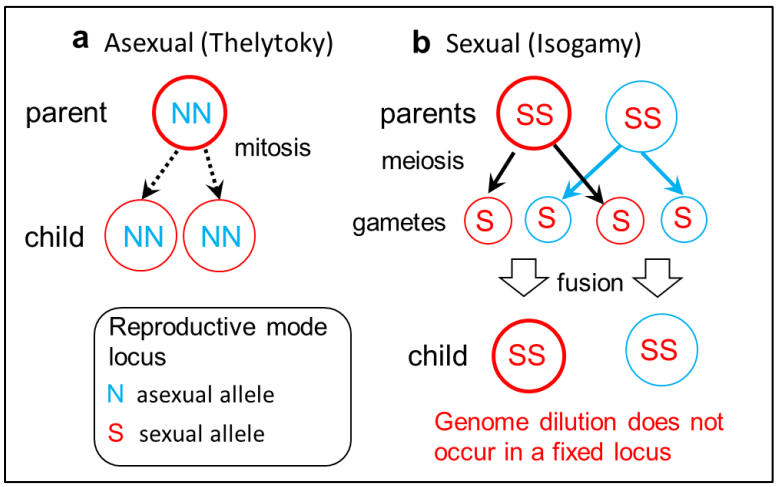

Figure 3: At fixed loci, genome dilution does not occur even during meiosis. Since mating occurs only between individuals carrying the sexual mode gene S, the fixation of S is maintained.

Since the probability of producing CS+CS is 50%, there are cases where the result is DS+DS (*dms* = 60 + 60 = 120 > 100 = *dmt*), leading to death (Figure 2b); however, if sexual mutation S arises independently on repeated occasions, then in approximately half of them S will occur in genome C, allowing CS+CS gametic reproduction to become established. The advantage of the seesaw effect is not only that it avoids the cost of meiosis but also manifests in terms of reproduction rate (Figure 4). In the first generation, a single parent produces two CS gametes and two DN gametes; since only one CS+CS individual survives,

the fitness is 1. However, from the second generation onward, four CS gametes are produced, so two CS+CS individuals survive, bringing the fitness to 2—the same as in asexual binary fission. However, since asexual lineages retain deleterious genes at levels close to the lethal threshold, the Muller's ratchet engages, eventually leading to their extinction. As a result, sexual lineages can replace asexual populations.

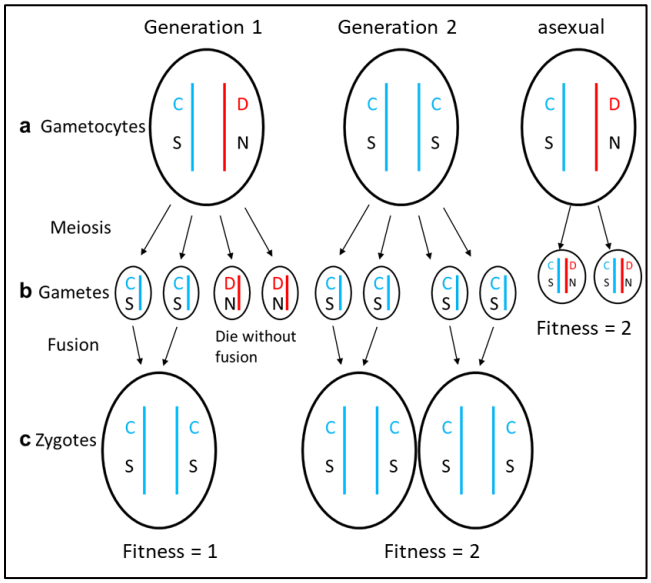

Figure 4: After the second generation of self-fertilization, sexual reproduction becomes equivalent to asexual reproduction in terms of growth rate (fitness). Note that since the gametes are isogamous (there are no males), there is no "male production cost."

As the number of sexual individuals increases and a sexual population becomes established, individuals carrying independent mutations at loci other than the reproductive mode locus begin to appear, and evolutionary potential and the genome dilution costs are reinstated. However, since mating occurs only among individuals carrying S, the fixation of S within the sexual population remains unaffected. It is believed that gametic sexual reproduction, which began as self-fertilization, evolved from inbreeding among relatives to outbreeding among distantly related individuals. Once self-fertilization occurs, all loci become homozygous, and the number of deleterious genes held by the two genomes becomes equal; consequently, the seesaw effect does not operate across consecutive generations, and it is necessary to wait for new deleterious mutations to accumulate asymmetrically. As the mating population grows, independent mutations lead to recombination between gametes with different numbers of deleterious mutations, restoring the seesaw effect in the next generation. Furthermore, the evolution of inner-arm recombination (chromosomal crossover) during the first meiotic metaphase (tetrad stage)—which did not yet exist in the ancestral meiotic division—creates greater *dms* asymmetry. While the seesaw effect is based solely on the randomness of mutations occurring asymmetrically between the two genomes, it is thought to have evolved into the Kondrashov effect, in which, once recombination becomes possible, deleterious genes are actively concentrated in one genome, causing the individual to die and thus be removed from the population. The principle common to both processes is that deleterious mutations are not left evenly

distributed between the two genomes; instead, they are biased toward one genome so that the other is purified.

The Origin of Gametic Sexual Reproduction: A Summary of the Seesaw Effect

Whereas it has traditionally been thought that sexual mutations arising in asexual populations, for whatever reason, gain access to mating opportunities and gradually increase in frequency over many generations due to the benefits of sex, eventually replacing the population, the seesaw effect suggests that automixis—self-fertilization—eliminates the need for external mates; if a combination of CSs arises after just two or three trials, gametic sexual reproduction can evolve within a single generation. This provided an answer to the long-standing puzzle—one that no one had been able to solve—of "how the first sexual individuals, who should have been at a twofold disadvantage, were able to find mates, survive, increase their frequency, and become established within an asexual population."

Hypothesis 2: The Origin of Anisogamy (Inflated Isogamy)

As mentioned earlier, gametic sexual reproduction is thought to have begun with isogamy involving equal-sized gametes. In isogamy, both parents contribute an equal amount of reproductive resources (a "split-the-bill" arrangement), so there is no "cost of producing males" (since males "that consume resources without producing offspring" do not exist). On the other hand, since isogamy retains all the benefits of sexual reproduction—such as the elimination of harmful genes and resistance to pathogens—it can be considered an ideal reproductive mode. However, in nature, isogamy is limited to a small number of single-celled organisms, such as budding yeast, Chlamydomonas, and centric diatoms, while anisogamy is widely observed in complex multicellular organisms such as vertebrates. The fact that isogamy—which should be ideal—is evolutionarily unstable, and that anisogamy evolved from it and has been maintained, suggests that there is a reason to produce males even if it incurs the twofold cost. How did the evolution from isogametes to the differentiation into eggs and sperm occur?

Figure 5 is a conceptual diagram illustrating the economic conditions of each reproductive mode. Here, resource investment per gamete is distinguished from the total reproductive investment made by one parent. Assume that a single parent expends $2R$ units of resources (equal to the size of the mother cell) on reproduction, and that the minimum size required for the survival or development of the offspring (daughter cell or zygote) is R. A unicellular asexual organism (size R immediately after division) takes in resources from the external environment, grows to size $2R$, and then divides by binary fission into two daughter cells of size R (Fig. 5a). In isogamous reproduction (Fig. 5b), a mature mother cell of size $2R$ undergoes the two-step meiotic division to produce four isogametes of size $0.5R$, which fuse with another gamete ($0.5R + 0.5R$) to form a single zygote of size R. This zygote then grows into a mature cell of size $2R$ and reproduces again. Hereafter, this reproductive mode will be referred to as "smart isogamy." "Smart" refers to the fact that both mating types "split the bill" for the minimum resources (R) necessary

for embryo survival. Since both asexual reproduction (Fig. 5a) and smart isogamy (Fig. 5b) require 2*R* in resources to produce an offspring of size *R*, they are economically equivalent (there is no cost associated with producing males); furthermore, given the seesaw effect, it seems that the evolution from 5a to 5b was relatively easy. However, when attempting to evolve from smart isogamy to anisogamy, because males do not contribute resources, females must instead cover the full cost (with expenditure doubling from 0.5*R* to *R*), resulting in a "twofold cost." Why was this possible?

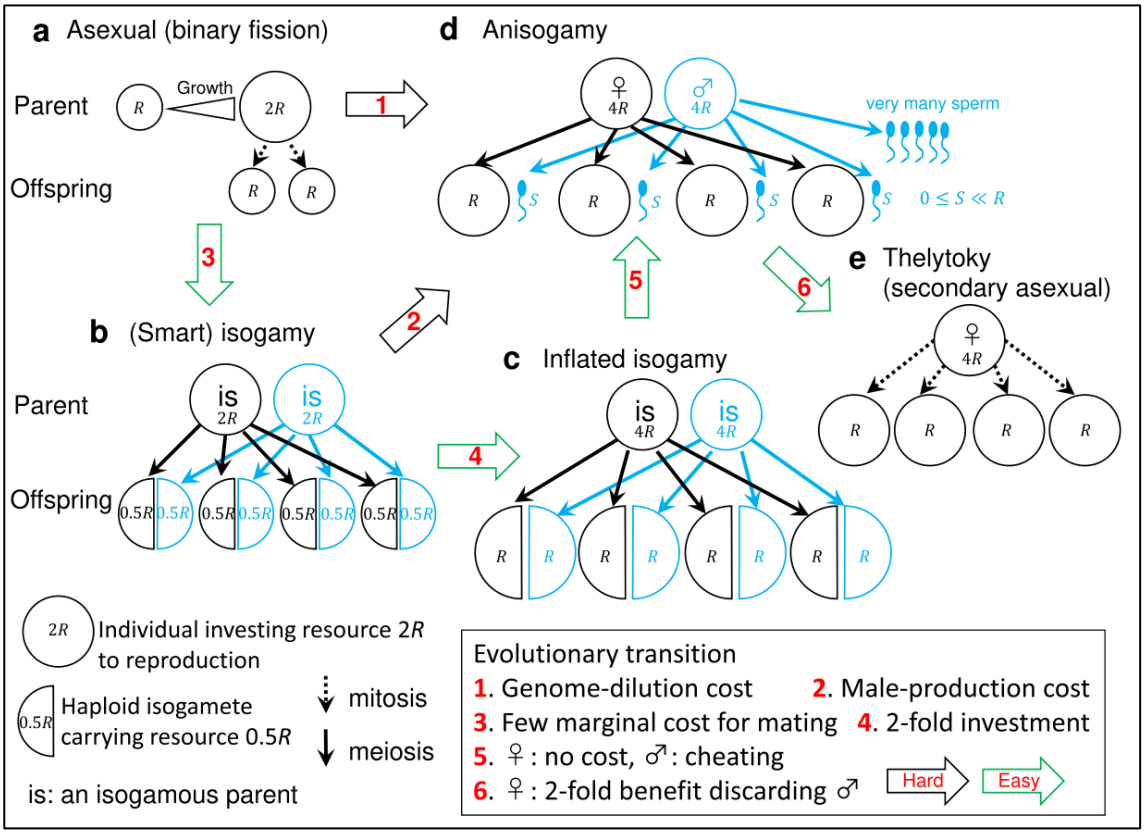

Figure 5: The Economics of Each Reproductive Mode. The transition from unicellular asexual reproduction (**a**) to smart isogamy (**b**) is relatively straightforward, as it involves either dividing a cell containing the same 2*R* of resources into two parts or dividing it into four parts, with two of those parts fusing (in both cases, the daughter cells possess *R* resources). The transition from smart isogamy to anisogamy (**d**) requires the female to expend twice as much (4*R*)— the twofold cost of males—since the male bears no resource burden. As evolution toward multicellular organisms creates a surplus in resource supply, introducing an intermediate stage of inflated isogamy (**c**), in which both parents produce twice as large gametes (*R*), makes the transition from **b** to **c** to **d** smoother. However, if meiosis is abandoned in favor of thelytoky (e: female-producing parthenogenesis), both the male production cost and the cost of meiosis disappear. The question of why costly males have been maintained in so many species is addressed in Yasui 2026ab, "The Evolution of Sex: Papers 2 and 3."

Even the great Parker theory has its blind spots

The so-called "PBS model" proposed by Parker, Baker, and Smith (1972) is a well-known theory explaining the evolution from isogamy to anisogamy (Figure 6).

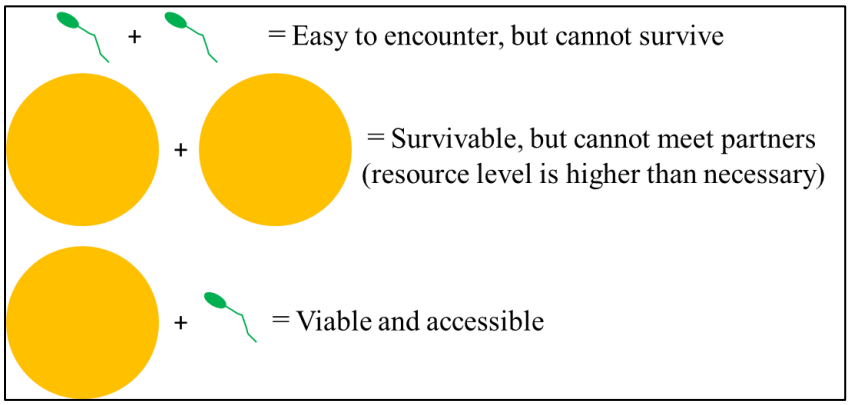

Figure 6 Core logic of the PBS model: Size-disassortative Mating

Parker GA, Baker RR, Smith VG. The origin and evolution of gamete dimorphism and the male-female phenomenon. *J Theor Biol*. 1972 Sep;36(3):529-53. https://doi.org/10.1016/0022-5193 (72) 90007-0 PMID: 5080448.

When a gamete population contains variations of different sizes, “small + small” combinations—even if they have a high probability of meeting—die due to insufficient nutrition, while “large + large” combinations—though they have more than enough nutrients—have low motility and cannot meet. Ultimately, only “large + small” combinations possess the necessary nutrients and are able to meet, so they survive, leading to the evolution of anisogamy. At the same time, the explanation that in isogamous reproduction, the three or more sexes that originally existed were reduced to just two—male and female—because only the two size extremes remained, provides one of the most inspiring “aha” moments in the history of science. However, this model has a flaw that has been overlooked. If size variation ranging from eggs to sperm exists within a population, such size-disassortative mating would indeed occur. However, the initial population must have consisted of isogamous gametes (what I call “Smart Isogamy”), so how did such a large size variation—ranging from egg to sperm—arise within it? The PBS model paper merely mentions in passing that an increase in size first occurs in isogametes, followed by a corresponding decrease in size, and that size variation expanded as a result of disruptive selection; it does not describe the specific mechanisms. In other words, the PBS model explains what happens after disruptive selection has begun, but it does not explain why the first size deviations capable of initiating disruptive selection should be advantageous. For disruptive selection to operate, a slight increase and a slight decrease from the mean gamete size must each be immediately advantageous. However, single-celled organisms do not have redundant resources. In the “smart isogamy” state of $0.5R + 0.5R = 1R$ (Figure 7a), if one parent reduces its investment, the embryo will simply die (Figure 7b). In other words, for one parent to reduce its gamete size, the other must have already increased its gamete size (from $0.5R$ to $1R$). Is there an advantage for the other parent to do so? For single-celled organisms, spending time acquiring resources to slightly increase gamete size does little to improve survival rates. Instead, once $2R$ of resources has been accumulated, undergoing meiosis results in a faster rate of reproduction. Therefore, the selective pressure to increase

gamete size is low, and there appears to be no advantage in voluntarily becoming female. So, is there an advantage to becoming male? In the ancestral unicellular system assumed here, a single meiotic event directly produces only four gametes. Slightly reducing gamete size does little to improve fertilization rates, and at most, only four partner gametes can be fertilized by those four gametes. Since the number of gametes cannot be increased, reducing their size would only lower the survival rate. Consequently, the selective pressure to reduce gamete size is also weak. Therefore, it is unlikely that size-disruptive selection, as posited by the PBS model, would occur.

The Evolution of Anisogamy as a Commensalism

What is needed is some kind of breakthrough that would allow both parents to increase their gamete size in one fell swoop. My "inflated isogamy" hypothesis posits that the seesaw effect can generate a locally expanding cluster of genetically nearly identical, self-derived unicellular descendants. In such a high-relatedness cluster, cell-cell competition is reduced and cooperation and division of labor can evolve more readily, making cell fusion and the evolution of multicellular organisms more likely (multicellularization). Because cloned cells (with a relatedness of 1) cooperate and divide labor, multicellular organisms can achieve more advanced adaptations than unicellular organisms. At the same time, while multicellular organisms require more resources for embryonic development, they can pool the energy produced by multiple cells, thereby ensuring a sufficient supply of resources. Therefore, I propose that a state referred to as "inflated isogamy" (Figure 5c, 7c) arose, in which the parents remained isogamous but increased their gamete size from $0.5R$ to $1R$, resulting in a $2R$ zygote through isogamous fusion ($1R + 1R = 2R$). In this case, the energy expenditure doubles, but there is no inequality between the parents. Since the survival rate and the stage of embryonic development are determined by how many resources the zygote possesses, this can be described not as a "twofold cost" but as a valuable "twofold investment."

However, in this state, the zygote is larger than necessary (the required size is R), so suppose one sex commits a form of cheating, without changing its total parental investment, by halving the size of its gametes ($1R \rightarrow 0.5R$) and doubling their number, anticipating that the partner has already expended the necessary amount. This was made possible by multicellularity, which increased the number of gametocytes, allowing a single individual to produce five or more gametes. As a result, the "cheating" sex gained the advantage of fertilizing the gametes of two or more individuals (polygyny) and evolved into the male. Here, for the first time, the PBS-model selection pressure—"the smaller the gamete, the more can be produced"—begins to operate. In other words, males were already polygynous at their origin. The other, "deceived" sex became the female, and thus the earliest form of anisogamy was established. However, the female accepted this inequality. This is because the female's investment remained unchanged from the $1R$ level of inflated isogamy. Since only the male reaped the benefits of polygyny—increasing the number of offspring by reducing investment per offspring—anisogamy evolved as commensalism, an interaction in which "one party benefits while the other neither gains nor loses."

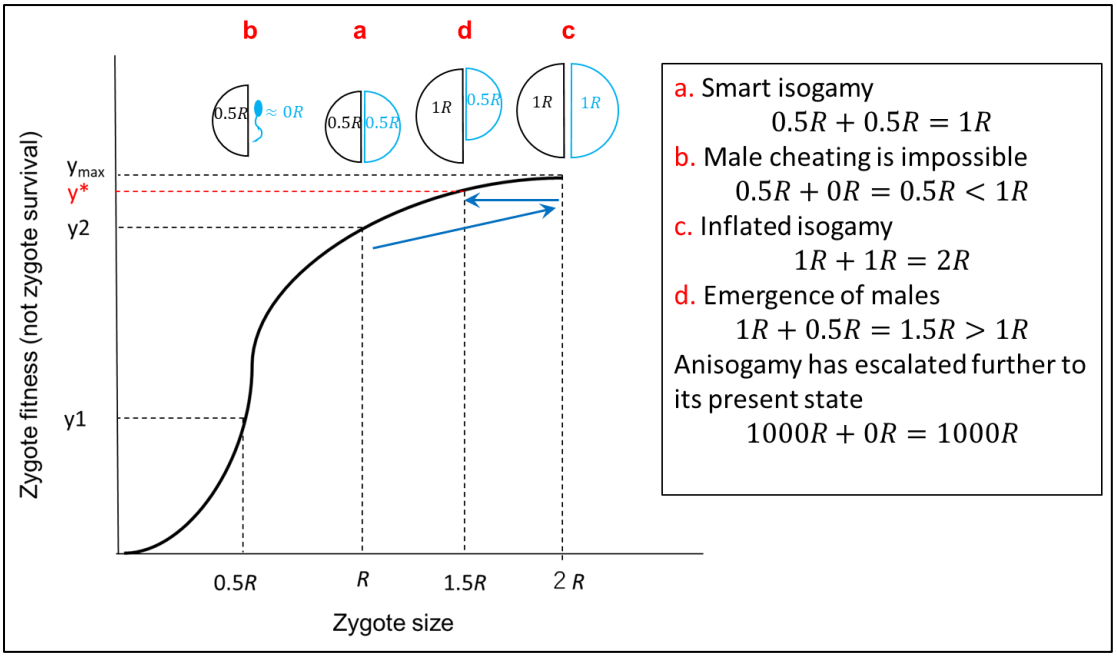

Figure 7: Inflated Isogamy Hypothesis: In the "smart isogamy" state (a: fitness y2), where both mating types "split the bill" for the required resource amount *R*, there is no surplus of resources; therefore, if one sex reduces its investment (becomes male), fitness plummets (b: fitness y1), making a transition to anisogamy impossible. In "inflated" isogamy (c), where both mating types increased their gamete size in tandem with multicellularization, fitness is maximized (y_{max}), but the gain from smart isogamy is minimal and does not justify the doubling of investment ($0.5R \rightarrow 1R$). Taking advantage of this resource redundancy, even if one sex reduces its gamete size, fitness hardly decreases (y*). Since smaller gametes can be produced in greater numbers, the benefits of polygyny arise, and the "cheaters" evolved into males. The deceived "honest" females, whose investment remains unchanged at $1R$, tolerate this arrangement, and thus anisogamy originated in its earliest stage as a commensalism. Subsequently, the difference in gamete size widened, leading to the completion of modern anisogamy (the polarization of males and females).

Improvement in Fertilization Rates: From Commensalism to Mutualism

Thus, anisogamy is established by accepting this inequality in resource investment into the zygote. Since the very definition of male and female is based on differences in gamete size (resource investment), if equality were achieved, they could no longer be called male and female. However, does the existence of males merely impose costs on females? A problem inherent to gametic reproduction is that eggs die unfertilized. Particularly in situations of "inflated isogamy," where the gametes are large, it seems that a significant number of isogametes were left unfertilized. Even if the opposite sex provided an equal nutritional investment, it would be meaningless if the gametes died unfertilized. In this context, the small gametes (sperm) produced by male "betrayal" may have improved the fertilization rate through their motility and greater numbers. Yasui and Hasegawa (2022) examined this possibility using computer simulations (Figure 8).

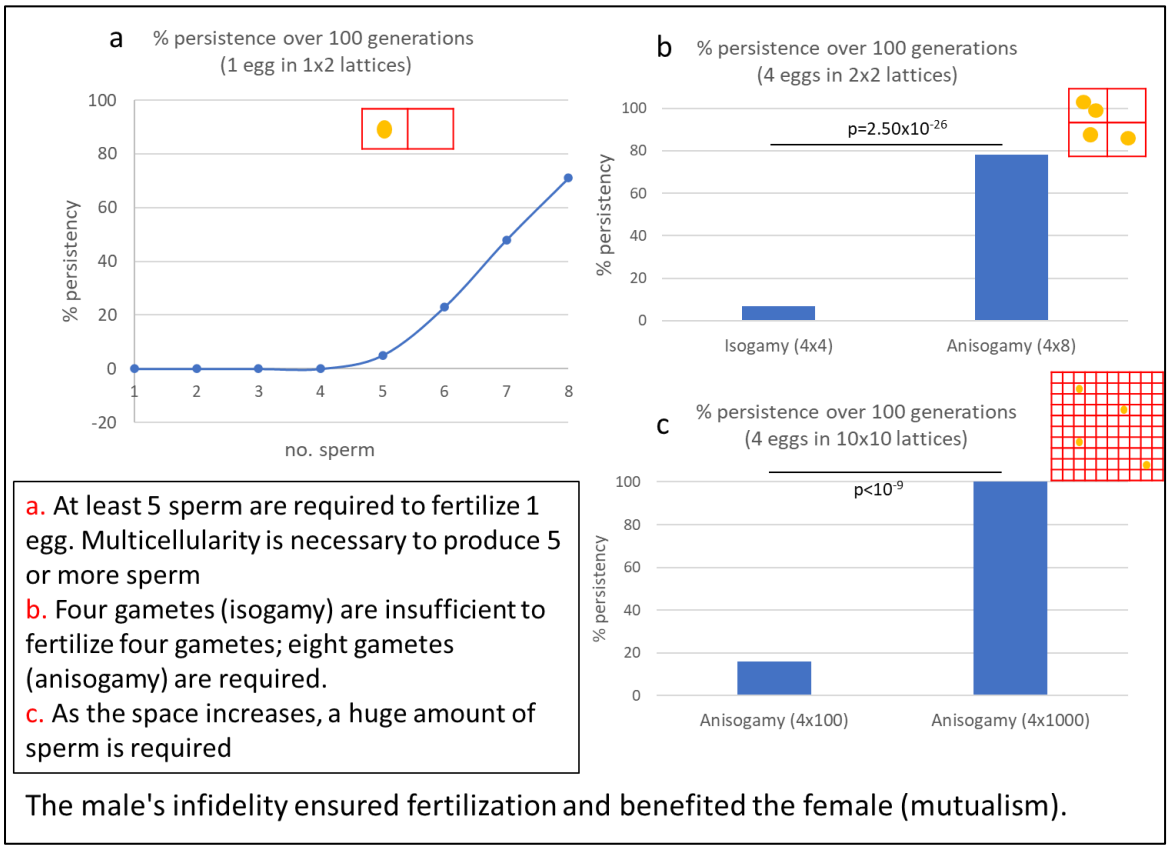

Figure 8 Simulation results

a. One egg on a 1×2 lattice

b. Four eggs on a 2×2 lattice

c. Four eggs randomly distributed on a 10×10 lattice. Sperm are randomly scattered over the grid, and fertilization occurs when a sperm enters the same cell as an egg. If even a single fertilized egg is produced, the lineage continues to the next generation. The simulations determined the number of sperm required to sustain the lineage for 100 generations.

The simulation (Figure 8) showed that, in the smallest spatial structure (1×2), four gametes produced by meiosis from a single mother cell yielded virtually no persistence over 100 generations, whereas persistence first became possible when multicellularity allowed five or more sperm to be produced. In a 2×2 space, four gametes (equal investment, i.e., isogamy) gave a very low probability of 100-generation persistence, whereas eight gametes produced from two mother cells (minimal anisogamy) greatly increased persistence. As the space expanded to 10×10, persistence remained low even with 100 sperm but approached 100% with 1,000 sperm. Since this simulation examined only the effect of the number of sperm and did not consider the effect of motility, it is expected that the fertilization rate would actually be even higher in reality. These results help us understand how anisogamy—which initially began as a commensalism in which females tolerated male exploitation—evolved into mutualism, bringing the benefit of improved fertilization rates to the females as well.

Anisogamy: From Parasitism to Symbiosis

Traditionally, anisogamy has been viewed as a form of parasitism by sperm (males) on eggs (females). However, this perspective focuses solely on resource investment in offspring. The two sexes complement each other's weaknesses in different respects. The egg's weakness is that it is large and immobile, resulting in a low probability of encountering partners, while the sperm's weakness is that it is too small to supply nutrients to the offspring (the fertilized egg). Therefore, the establishment of this symbiosis allowed sperm to become even smaller and more numerous, while eggs grew larger to provide all necessary nutrients on their own. This led to the establishment of distinct male and female sexual roles and laid the foundation for today's biodiversity.

The Origin of Anisogamy: A Summary of "Inflated Isogamy"

This paper presents a specific scenario in which size variation arises in a population of isogametes—a phenomenon not explicitly addressed by the PBS model—leading to disruptive selection. While females still bear a twofold cost during the transition from (smart) isogamy to anisogamy, the transition is thought to be smoother by assuming a buffering process of "inflated isogamy."

Discussion

Three cautions regarding the cost of sex

1. Meiosis does not always result in genome dilution costs

Through automixis (seesaw effect) between CS (clean and sexual) gametes, the reproductive mode locus is fixed at S, and dilution does not occur at this fixed locus. Even if heterozygosity arises at other loci due to mutations and outcrossing, leading to the resumption of genomic dilution, these loci must tolerate the persistence of sexual reproduction to avoid extinction and ensure evolutionary potential. All loci must inevitably compromise under the sexual system.

2. Investment and cost must not be confused

As the system evolved from smart isogamy to inflated isogamy to anisogamy, the amount of resources borne by the female doubled, but this was a profitable investment. Costs should always be minimized, but investment should be increased as long as it yields a profit. Initially, the partner invested an equal amount; even after one sex became male and withdrew, resulting in anisogamy, egg investment remains a profitable venture for the female as long as fertilization is guaranteed by the male.

3. Complex multicellular organisms inevitably require anisogamy (The following discussion partially overlaps with "The Third Paper on the Evolution of Sex" (Yasui 2026b).)

In single-celled organisms with isogamy, both mating types contributed equal amounts of resources. In other words, the two mating types were equal in resource investment. As organisms evolve into multicellular beings, more resources are required for embryonic development (cell division to form a large, complex body). Therefore, the zygote (fertilized egg) must become larger. However, it is physically impossible for both mating types to contribute resources equivalent to half the size of a large zygote (they cannot move, cannot meet, and cytoplasm gets in the way). Try to imagine whether two half-sized ostrich eggs could fuse together. Consequently, there is no alternative but for one sex to grow larger to provide the nutrients, while the other remains small enough to pass through its cytoplasm. Therefore, the polarization into male and female is a mechanical necessity; there is no need to analyze it using mathematical models.
Complex multicellular organisms can exist only with anisogamy—the polarization of gametes into a large resource-providing type and a small fertilizing type. The supply of nutrients through larger eggs reached its limit in reptiles (dinosaurs) and birds (ostriches). If eggs were made any larger, they would be unable to withstand gravity in a terrestrial environment. If the shells were thickened to prevent them from being crushed by gravity, the eggs would then be unable to hatch. Consequently, mammals transitioned to viviparity—that is, raising small fertilized eggs by supplying nutrients through the placenta. Indeed for this very reason, elephants do not hatch from meter-sized eggs. In mammals, compared to the enormous investment made by the female—namely, nutrient supply via the placenta and lactation—the difference in gamete size between the sexes no longer represents a cost of sex. The theory of sexual costs based on gamete size comes to an end here.

However, the cost of producing males does not disappear. No matter how much a large number of highly motile sperm increase the fertilization rate, if the species shifts to female-only parthenogenesis (thelytoky), fertilization itself becomes unnecessary, so the benefit of improved fertilization rates disappears. Furthermore, even in viviparous species, if a mutation arises that causes the production of only females, a sexual population that produces males and females in a 1:1 ratio would be overtaken due to the twofold difference in reproduction rates per generation. However, it is necessary to explain why anisogamy predominates in the world of multicellular organisms and why no mammals capable of asexual reproduction have been identified to date. (Continued in Papers 2 and 3)