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Review

A Bigger Toolbox: Biotechnology in Biodiversity Conservation

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Conservation biology needs a bigger toolbox to meet unprecedented challenges. Genomics, fueled by declining sequencing costs, offers novel tools with increased precision for genetic questions previously answered with a few molecular markers, as well as completely new possibilities. Metabarcoding promises quicker, cheaper, and more accurate assessments of biodiversity in groups that are difficult to assess by traditional methods, while sequencing low-quality DNA extends the range of useable materials to include museum specimens, archeological remains, and environmental samples. Genomic and transcriptomic data can be used to assess the potential of populations to adapt to new challenges. In the near future, gene-editing tools may help endangered species cope with change, while gene drives control unwanted species and help wanted ones. De-extinction has become a serious prospect.

Trends

Conservationists increasingly recognize the need for a bigger toolbox and the potential of the novel tools offered by genomics and related technologies.

Current applications of genomics in conservation increase the precision and resolution obtainable from traditional conservation genetics, but truly novel applications are still rare.

Metabarcoding and environmental DNA are beginning to enter conservation practice, although significant technical problems remain, and we lack a comprehensive and taxonomically reliable barcode database.

Routine assessments of adaptive potential are not yet practical, but in the future could inform many aspects of conservation management.

Gene editing, gene drives, and de-extinction of wild species are moving from theory to plausible conservation practice, but they face a host of practical, regulatory, and public perception issues.

Conservation and Biotechnology

Biodiversity conservation and biotechnology have traditionally been opposite poles of biological sciences, with little interaction [1]. However, this paradigm is changing in response to several recent developments. First, conservationists face a host of interacting challenges, including habitat loss, overexploitation, climate change, and invasive species, and most practitioners recognize that they need a bigger toolbox [2]. Second, a new generation of young conservation biologists is more comfortable with biotechnology through their own academic training: indeed, students entering graduate programs in conservation often know more about modern genomic methods than about organismic biology. Third, the ability to outsource much of the work makes the new molecular tools more accessible than many earlier techniques. Fourth, the development of real-time sequencing with relatively cheap, pocket-sized devices using nanopore technology promises to massively increase opportunities for applying these tools in the muddy, biodiverse, real world [3]. Finally, there are techniques under development that could make the genetic manipulation of wild populations practical for the first time [4]. This review of current trends in the application of biotechnology in conservation aims to inform biotechnologists of conservation needs and concerns, and show conservationists what biotechnology has to offer (Table 1).

Conservation Genomics

A range of *in vitro* techniques from biotechnology have found applications in conservation biology [5], but this review focuses largely on 'conservation genomics', a term applied, rather loosely, to conservation applications of data originating from **next-generation sequencing** (NGS) (see Glossary) techniques [6,7]. Despite the steady reduction in the cost of NGS (five orders of magnitude in 10 years [7]), the routine application of genomic techniques in conservation is still too expensive, except for commercially important species, such as salmon [8,9].

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Table 1. Conservation Problems with Actual or Potential Genomic Solutions

Conservation Problem	Actual and Potential Applications of Genomics	Refs
Identifying cryptic lineages to conserve	RADseq, ancient DNA	[13,14]
Delimiting conservation units	RADseq	[17]
Optimizing *ex situ* conservation	RADseq, RNAseq	[21]
Monitoring pathogens	RADseq	[23]
Identifying pathogen-resistant individuals	Associative transcriptomics	[60]
Selecting populations for reintroduction	RADseq, RNAseq	[16,18,54]
Assessing past and present connectivity	Various NGS techniques, ancient DNA	[19,42]
Assessing biodiversity	Metabarcoding, environmental DNA	[27–29]
Detecting invasive species	RADseq, metabarcoding, environmental DNA	[24,44]
Establishing baselines for restoration	Ancient DNA	[41,42]
Assessing adaptive potential	Genome-wide association studies, associative transcriptomics	[21,38,59,60]
Assessing acclimation potential	Transcriptional profiling	[54]
Controlling invasive species	CRISPR-based gene drives	[65]
Genetic rescue of inbred populations	RADseq, cellular and reproductive technologies	[9,70]
Reversing extinction	Synthetic biology	[1,68]

Moreover, the necessary bioinformatics capability for data analysis is not yet part of the skill set of most conservation biologists [10]. However, NGS techniques have the advantage of broad applicability, in contrast to the species- or clade-specific markers used previously in conservation genetics; thus, outsourcing is common in conservation-related studies and can include bioinformatic assistance. Genomic techniques are already being used by some nonacademic labs, including governmental and nongovernmental organizations [8,11], and costs are falling so fast that routine use is likely to spread more widely over the next few years. Meanwhile, the rapidly growing sequence archive provides an increasingly valuable resource for the future.

Until recently, applications of modern biotechnological tools in conservation (Box 1; Table 1) were largely limited to the use of genomic data from NGS for things previously done with smaller numbers of (putatively neutral) molecular markers that sampled far less of the genome (e.g., allozymes, RAPDs, AFLPs, microsatellites, etc.). Recent examples of such studies include identifying unrecognized, morphologically cryptic, lineages worthy of conservation attention [12–14] (Figure 1); wildlife forensics [15,16]; delineating conservation units [17]; identifying source populations for translocations or genetic rescue [12,18,19]; estimating gene flow [20]; detecting inbreeding in small populations [21]; optimizing collections for *ex situ* conservation [19,21]; managing captive populations [22]; monitoring pathogens in wild and captive populations [16,23]; and detecting hybridization with invasive aliens [24] (Figure 1).

In most cases, the major advantage of the new approaches has been increased resolution and precision, rather than qualitatively novel findings, although many studies have novel extensions that would have been impractical before [16,25]. However, the increased power of NGS to detect subtle differences between populations also raises the important issue of when these differences are considered large enough to be of conservation relevance [25]. It is not practical to treat every genetically diagnosable difference between populations as significant. Another related issue is that of replication: increasing sequencing depth is no substitute for an adequate number of true biological replicates, although these multiply costs [16,26].

Glossary

CRISPR/Cas9: 'clustered regularly-interspaced short palindromic repeats/CRISPR associated protein-9' is a bacterial adaptive immunity system that is used as a genome-engineering tool to induce site-directed double-strand breaks in DNA in a range of organisms. These breaks can inactivate the gene or allow the insertion of new genes. Guide RNAs ensure target specificity.
Epigenome: chemical changes in the DNA and histone proteins that do not change the gene sequence but influence the function of the genome; often used more broadly to include other regulatory layers, such as chromatin packaging and small RNAs. Epigenomes have a major role in phenotypic plasticity.
Gene drives: genetic systems that circumvent the rules of Mendelian inheritance so that both offspring of an edited parent receive a copy of the edited gene. This allows genes to spread to all members of a population even if they reduce individual fitness. Gene drives occur in nature, but the CRISPR/CAS9 system allows the engineering of drives to spread edited genes.
Genome: the DNA of an organism, including both coding and noncoding regions.
Next-generation sequencing (NGS): recent technologies that enable sequencing of DNA and RNA more quickly and cheaply than the previously used Sanger sequencing; also called high-throughput sequencing, massively parallel sequencing, and second-generation sequencing.
Proteome: the proteins in a cell, tissue, or organism at a certain time.
Transcriptome: the messenger RNA molecules in a cell, tissue, or organism at a certain time.

Box 1. Genomic Tools Currently Used in Conservation Biology

Few of the conservation applications mentioned in this review require whole-genome sequences, so most use reduced-representation sequencing (RRS) approaches that target a relatively large (around 1%), unlinked, representative subset of the genome, reducing costs per sample and allowing greater depth of coverage per locus and/or larger numbers of individuals [76] (Table 1, main text). Most studies currently use restriction site-associated DNA sequencing (RADseq), a family of techniques that sequence fragments adjacent to sites cut by restriction enzymes [77]. RADseq does not require prior genomic information (although it is useful to have some), so its use is not restricted to model organisms. Microsatellites can be mined from genomic data, but single-nucleotide polymorphisms (SNPs) are abundant and spread across the genome, and thousands of genome-wide SNPs can be identified for the cost of developing a few microsatellites, so they are currently the marker of choice [12]. Moreover, SNPs are directly comparable between labs, which is a major advantage for collaborative studies [49].

NGS can also be used to sequence messenger RNA (RNAseq): that is, the transcriptome [26]. While the potential advantages of focusing on only the functional parts of the genome are obvious, RNA-seq requires high-quality tissue samples, since RNA is rapidly degraded, which has restricted its use in conservation studies. Moreover, individual transcripts vary hugely in relative abundance, increasing sequencing costs, while the transcriptome varies between tissues and over time in the same organism, so many replicates are needed [26]. The common practice of pooling samples before sequencing reduces the risk of bias from an unrepresentative sample, but only true replication allows for statistically robust conclusions. **Proteomes** can sometimes be used in the same way as transcriptomes, and may be preferred because proteins are longer lived and have a direct impact on cell function, but proteomic technologies currently lag behind NGS in both throughput and comprehensiveness [78].

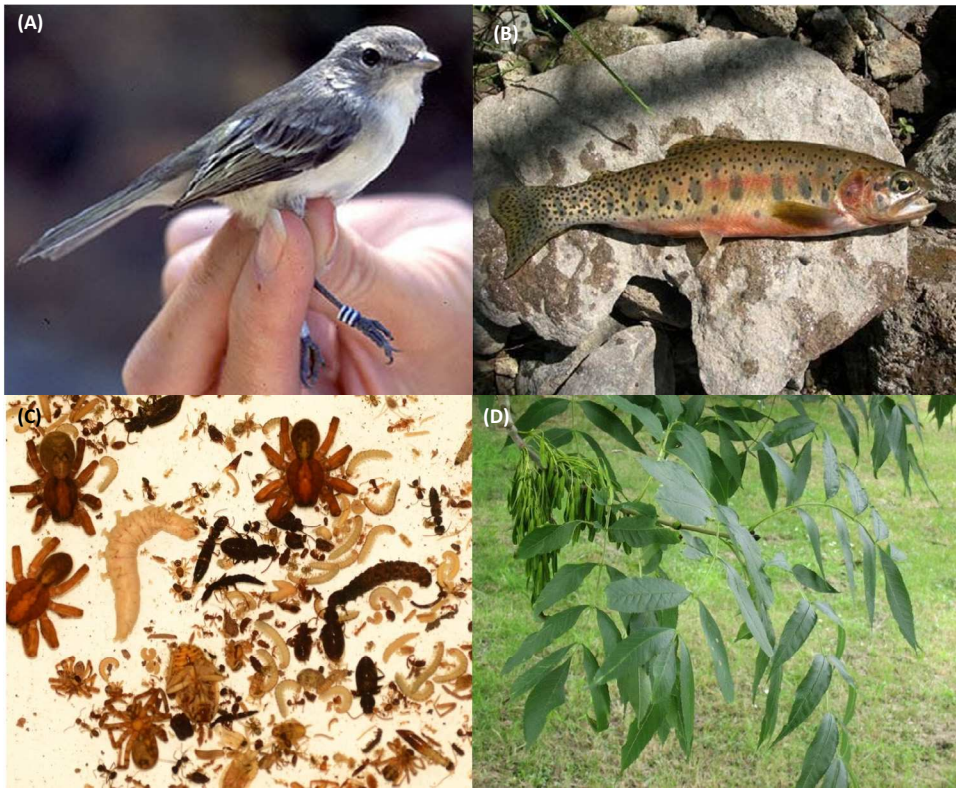
The same NGS platforms can also be used to assess DNA methylation, a major mechanism of epigenetic modification [53]. Pretreatment with sodium bisulfite ensures that methylated and unmethylated cytosine bases are distinguished during sequencing (bsRADseq). Other epigenetic modifications, involving histone and chromatin, are not heritable and, thus, of less obvious conservation interest [53]. In the future, it should become possible to integrate these various omic technologies to obtain a more complete understanding of the link between genotype, phenotype, and environment [78], although conservation applications of this 'integrated omics' have not yet been developed.

Metabarcoding

The combination of NGS with universal primers for common barcoding regions (metabarcoding) has shown considerable promise for assessing biodiversity in mixed, bulk samples of taxa that are difficult to assess with traditional methods, including microbes and a variety of invertebrates [27–29] (Figure 1). This type of data is needed for conservation assessments, land-use planning, monitoring environmental impacts, and assessing the functionality of restored ecosystems. However, some technical issues still need to be resolved, including PCR amplification biases that affect species detection, before metabarcoding becomes a routine biodiversity assessment and monitoring tool. Moreover, species-level identifications are currently limited by the lack of a comprehensive and taxonomically reliable barcode database for most of these taxa [30,31]. The same techniques can also be used on gut contents to identify trophic interactions in food webs as a basis for effective conservation management [32–34]. Biases in PCR amplification also currently limit the use of metabarcoding for the assessment of relative abundances of species, but PCR-free methods are being developed [35].

Using Low-Quality DNA

High-throughput sequencing has also been important in applications that involve degraded DNA (Box 2): in museum or herbarium specimens, in archaeological studies, in sediments, and in the wider environment [14,36,37]. Museum and herbarium specimens provide historical information that can be used to assess recent genetic changes and inform decisions on conservation interventions, such as translocations and assisted gene flow [38]. On a longer timescale, the DNA in archeological and paleontological remains (ancient or aDNA) tends to be both degraded and contaminated with microbial material, but improved DNA extraction and enrichment methods continue to push back the age limits for useable sequence data [39,40]. In conservation, aDNA is potentially useful for establishing baselines for ecological restoration and species reintroductions and, for this purpose, data from the past 100–200 years are often most relevant, as well as most likely to be available [41]. At the species level, aDNA has provided evidence for



Trends in Biotechnology

Figure 1. Examples of Conservation Studies that have Benefitted from Genomics. (A) Genomic studies have shown that least Bell's vireo populations form a distinct evolutionary lineage that needs urgent conservation action [13]; (B) genomics allowed accurate estimates of hybridization between the native westslope cutthroat trout and the introduced rainbow trout [24]; (C) metabarcoding has been used to assess the impact of land-use change on litter arthropod communities in southwest China [27]; (D) transcriptomics identified markers that can be used to select European ash seedlings with lower susceptibility to a devastating fungal disease [60]. Reproduced from Kingsley Beng (C) and Wikimedia (D).

past gene flow, with implications for the conservation management of currently isolated populations [42].

The extraction of 'environmental DNA' (eDNA) from bulk environmental samples, such as water, soil, and air, uses a similar range of techniques [43]. As a conservation tool, eDNA has been used to detect invasive alien and endangered native species at lower densities than is practical with

Box 2. Working with Degraded DNA

Researchers in biomedical and agricultural sciences usually have easy access to large quantities of fresh, intact DNA. Conservationists are rarely so lucky and many of the most exiting applications of genomic techniques in the field have required the development of methods for extracting information from fragmented, contaminated, or otherwise degraded DNA samples [14,36,37]. RADseq (Box 1, main text) does not work well with highly fragmented DNA, so most studies faced with this problem either target specific genes [79] or use 'genome skimming' (i.e., shallow sequencing of the entire genome that results in relatively deep sequencing of genetic elements that have many copies, including chloroplast and mitochondrial genomes) [80]. Targeted capture requires some prior knowledge of the genome sequence to design a set of capture probes, and several different approaches have been used for this [79]. Recent examples using NGS with low-quality DNA include a complete plastid genome for an extinct tree lineage from a single leaf of a 140-year-old herbarium specimen [81] and barcodes from century-old insect type specimens [82]. Barcoding of type specimens is particularly valuable because these have a scientific name permanently attached to them. Degraded DNA fragments are shorter than most standard barcodes (500–800 bp), but it is possible to use shorter, minibarcodes (<300 bp) for many purposes [82] or to reconstruct longer fragments before sequencing [83].

traditional sampling methods [44], as well as for surveying multispecies communities [45,46]. In the latter case, eDNA potentially allows the rapid assessment of a broad taxonomic range of organisms without complex sampling methods and expert identification, as a substitute for, or complement to, traditional biodiversity assessments [45]. Quantification of eDNA is more difficult, but could be used as way to estimate population sizes [43,44].

In addition to the specific uses mentioned above, techniques for dealing with low-quality DNA samples have a broad application in conservation biology. DNA from wild populations, particularly of endangered species, must often be extracted from non-invasively collected samples, such as hairs, feathers, and feces [47,48]. The same techniques can also be used in a variety of special situations, such as identifying the source of saliva in carnivore bite-marks on livestock [49]. These are all situations where rapid sequencing under field conditions would often be valuable, particularly at remote sites where samples cannot be returned quickly to the lab [3].

Beyond the Genome

NGS is also be used to analyze **transcriptomes** (RNAseq) (Box 1). Transcriptomic studies in lab animals typically use large amounts of RNA sampled from various tissues, but tiny, nonlethal blood samples can be used for genome-wide studies on even small endangered species [50]. Transcriptome data have been used to assess the ability of target species to acclimate by modifying gene expression [38,51], and transcriptome responses of lab-reared animals to field-collected water or sediment samples have been used in environmental assessments [52]. NGS can also be used to analyze some components of **epigenomes** (Box 1). There is evidence that, at least in some circumstances, DNA methylation can be involved in local adaptation and that it can remain stable over multiple generations [53]. However, the extent to which methylation variants are independent of changes in the underlying genotype and, thus, potentially worthy of conservation in their own right, is still unclear [53].

Identifying Adaptive Potential

Genomic and transcriptomic data are potentially particularly useful for identifying adaptive (i.e., fitness-related) loci. This strategy would allow conservation to move beyond conserving 'genetic diversity' to targeting the parts of the genome that are responsible for local adaptation and, thus, survival. This approach could then inform many aspects of conservation management, including the identification of conservation units and the choice of individuals for reintroduction programs [6,16,18,54], genetic rescue of isolated, inbred populations [55], and identification of climate-resilient populations for conservation [56]. Where genome-wide sequencing data are available from multiple individuals, it is possible to use statistical techniques to identify alleles that appear to be under selection and, thus, are likely to be of functional relevance [38,57]. Genome-wide association studies (GWAS) look for associations between single nucleotide polymorphisms (SNPs) and traits or environmental variables to identify regions putatively subject to divergent selection [21,38,57].

Identifying the precise target of selection is more difficult, particular where selection targets multilocus combinations, some with small individual effects. Functional evidence is usually needed to confirm statistically derived hypotheses. A recent study of the valley oak in California identified SNPs potentially under spatially divergent selection correlated with climate gradients [58]. Common garden experiments are needed to confirm these results, but this study provides an initial basis for predicting responses to climate change in this species. New methods and new data are likely to make the functional interpretation of genome-wide sequence variation easier in the future, but currently the best practice is probably to also use neutral markers and/or phenotypic information to ensure that important contributions to adaptive variation are not overlooked [16].

A key issue in conservation is the need to identify and prioritize populations that have the capacity to adapt to novel threats [59]. Where these threats are well understood, it may be possible to target specific adaptive traits. For example, associative transcriptomics (GWAS with transcriptomes) was used to identify markers strongly associated with resistance to a devastating fungal pathogen in European ash (Figure 1), making possible the rapid identification of genetically diverse tolerant trees that can be used to replace dead trees before the associated ecosystems are irreversibly lost [60]. However, in most situations, it is probably still best to screen for genome-wide variation as a generalized measure of evolutionary potential in the face of an uncertain future [59]. A refinement of this approach is to consider only SNPs in coding regions (cSNPs), since these are more likely to be associated with function than are those outside these regions [54].

Adaptation is not the only mechanism for coping with environmental stress: organisms can also show phenotypic flexibility (acclimation) [37,51]. He *et al.* proposed combining an estimate of functional genetic variation (from known functional SNPs and/or a genome-wide scan of cSNPs) to assess the adaptive potential, with transcriptional profiling (of candidate genes and/or the whole transcriptome) to assess the acclimation potential [54]. For species with little or no genomic information, these assessments will require additional work, including comparing the transcriptional profile before and after exposure to relevant stresses. However, this approach is likely to be particularly useful in selecting source population for reintroductions, when the high cost may be justifiable if it increases the currently low success rates. Moreover, reintroduced populations must often adjust to novel environmental conditions, as a result of changes in climate and other factors [2], putting a premium on adaptive and acclimation potential.

Genetic Modification, Genome Editing, and Gene Drives

Despite the obvious potential for transferring adaptive genes within or between species to solve conservation problems, such as inbreeding and threats from invasive pests and diseases, rising temperatures, or increasing droughts, transgenic organisms have not yet been released into the wild for conservation purposes. Conservationists have been wary of using genetic modification for wild species because of both restrictive government regulations and continued public suspicion, as well as lingering concerns in the conservation community itself. The new genome-editing tools can modify genes of interest without inserting foreign DNA, which may help with both regulatory issues and public perceptions [61]. Over the past 2 years, **CRISPR/Cas9** has largely displaced alternative tools, including transcription-activator-like effectors nucleases (TALENs) and zinc-finger nucleases, because of its simplicity and low cost [62]. Genome editing with CRISPR/Cas9 is cheap and easy enough for any molecular biology lab to perform and is versatile, which is a key attribute for conservationists, who have little interest in model organisms. The apparent precision of CRISPR is another attractive feature. Some of the applications currently being explored in agricultural crops [63] and livestock [64] have potential relevance in conservation. Gene editing for disease resistance could protect endangered plant or animal species from emerging infectious diseases, while editing for drought resistance could allow keystone plant species to continue functioning in a changing climate. However, precision editing will not necessarily avoid unexpected and undesirable outcomes with traits that that are controlled by many genes or involved in complex gene–environment interactions.

CRISPR-based **gene drives**, where all the offspring of an edited parent have two copies of the edited gene so that even deleterious genes can spread, could allow the genetic transformation of wild populations in a way that controls harmful invasive species or enhances the survival of threatened natives [4]. There are currently many barriers, both technical and regulatory, to field applications of gene drive systems, but the prospect of tackling some of the worst diseases in the world by modifying their mosquito vectors, is likely to spur the rapid removal of these barriers [64]. The most obvious application for gene drives in conservation is the control of invasive

species by spreading deleterious genes through their populations [65]. In species with short generation times, this could be a cheap and effective control measure, although the drives will spread slowly in long-live species. The biggest concern is that, once a gene drive is released, it may be impossible to stop, although 'reverse gene drives' that cancel the original mutation are being developed [64]. There is also the possibility that the deleterious trait could spread into the natural range of the species, leading to its global extinction [65].

Currently, the risks of using gene drives outside the lab are far from being fully understood [66], and the first applications in conservation are likely to target invasive species on isolated oceanic islands [65]. Most attention so far has focused on doing bad things to unwanted species, but it may also be possible to use gene drives to do good things to wanted species, such as helping the survival of threatened species by increasing resistance to novel biological or abiotic threats [4]. However gene drives are used, an agreed international regulatory framework is urgently needed. It is also important that scientists communicate the risks and advantages to a skeptical general public, to avoid the unselective backlash that has limited the applications of earlier means of genetic modification [64,66].

Synthetic Biology

Synthetic biology is a broad and ill-defined emerging field that takes an engineering approach to biology, with emphasis on 'the design and construction of new biological parts, devices, and systems, and the redesign of existing, natural biological systems for useful purposes'[i]. The potential is huge, but applications in conservation are still limited. Genetically modified bacteria and yeasts can be used as biosensors for detecting pollutants in bioavailable forms [67] and it is becoming practical to engineer bacteria to degrade pollutants [1]. Modifying more complex organisms is a greater challenge, but it may eventually be possible to engineer novel resistance to emerging infectious diseases in the wild species that they threaten [1].

Even more ambitious is the idea of bringing extinct species back to life [1,68]. This could transform conservation by allowing the reintroduction of keystone species lost decades to millennia ago and, thus, the restoration of truncated natural ecosystem processes [2]. For recently extinct species with well-preserved tissues available, it is potentially possible to transfer the nucleus of a somatic cell (i.e., not a germ cell) into a denucleated egg of the nearest living relative, which is then used as surrogate mother (interspecies somatic cell nuclear transfer [69]). A similar method could be used within a species for the 'genetic rescue' of inbred wild populations using genetic material from preserved specimens [70]. The expanding potential for combining genomic, cellular, and assisted reproduction biotechnologies to rescue critically endangered and recently extinct species reinforces arguments for the urgent, global, cryopreservation of gametes, embryos, and other tissues from endangered species [71].

Where only degraded DNA is available, as will be true for most extinct taxa, the best approach may be to reconstruct as complete a genome sequence as possible and either use this to edit the genome of an extant relative or, conceivably in the future, create an entire synthetic genome. De-extinction has gone from science fiction to a serious prospect within the past few years, with the passenger pigeon, great auk, woolly mammoth, thylacine, and others under current discussion [68].

Risk Assessment and Minimization

An apparently fundamental cultural distinction between conservationists and biotechnologists is that the former have traditionally been reactive and risk-averse, viewing almost any change as potentially bad, while the latter are proactive and willing to experiment, with a generally positive attitude to change [1]. This is reflected in the vast literature in recent decades on assessing the potential ecological risks from genetically modified organisms (GMOs), despite the absence of

evidence that these risks are any greater than with other changes in agricultural practices [72]. Yet, the same decades have seen an unprecedented assault on the biodiversity on the Earth from forces (land-use change, logging, hunting, pollution, climate change, invasive species, etc.) that have nothing to do with GMOs. Using the new toolbox to mitigate some of these impacts will require compromises that both risk-averse conservationists and risk-taking biotechnologists may initially be uncomfortable with.

Agricultural GMOs are not designed to spread into the natural environment, while gene-edited wild species, gene drives, and de-extinct organisms will be. Therefore, the risks are greater and of a different nature. These risks cannot be entirely eliminated and some uncertainties will always remain, but this is true of all the conservation tools in use today, from herbicides to reintroduction. Practical conservation requires that practitioners balance the risks of active intervention with those of doing nothing. With endangered species, the risks of doing nothing are, by definition, high. However, before using any new technology, practitioners need clear guidance.

The widespread adoption of stringent guidelines in the field of biological control, which also seeks to release organisms into the natural environment, was partly a response to high-profile disasters in the past [73]. These guidelines, which are already in place, could usefully form a basis for guidance on the application of biotechnology in conservation. However, while a flexible and enforceable regulatory framework is essential, the rapidity of change, which challenges any bureaucratic procedure, and the global spread of biotechnological techniques and their potential impacts, which requires international agreement, will make this difficult. The prospect of amateur biohackers editing genomes at home adds to these problems [74].

The Cartagena Protocol on Biosafety to the United Nations Convention on Biological Diversity (CBD) is designed to manage the risks from 'living modified organisms [LMOs] resulting from modern biotechnology', but it is not clear whether the concept of LMO includes all gene-edited organisms. The CBD has established an Ad Hoc Technical Group on Synthetic Biology which will report to the 13th Conference of Parties in Mexico in December 2016, but the USA is not a Party and will not be covered by any new agreement. With the prospects for uniform global governance poor, both researchers and practitioners will have to work within a changing patchwork of national and subnational regulations. In this situation, it is crucial that scientists work with regulatory authorities, potential users, and conservation groups to assess not only the science, but also its social, ethical, and legal implications [66].

Concluding Remarks

This review has been about the potential of modern biotechnological tools to contribute to conservation, although many questions remain (see Outstanding Questions). As whole-genome sequencing for conservation purposes (Box 3) becomes practical over the next few years, resolution and precision will be further increased. Some of the potential of conservation genomics has been verified by demonstration projects that have used these tools to solve conservation-related problems, but there are still few examples of significant impacts on conservation itself (i.e., protecting threatened species and ecosystems on the ground).

Some authors have suggested that the uptake of the new molecular technologies in conservation has been painfully slow [9,16]. This is at least partly explained by the long (multiyear or even multidecadal) timescale on which conservation research necessarily occurs, which makes it hard to incorporate rapidly changing new techniques, but it also reflects the gap between academic research and conservation practice that exists across conservation science [75]. A demonstration of the application of a new technique can be published in the top journals, but the practical application of this technique on the conservation front line cannot and, thus, is less attractive to academics rewarded only for publication. Therefore, the key need is to make the new

Outstanding Questions

Can metabarcoding become a routine biodiversity assessment and monitoring tool?

How can assessments of the adaptation and acclimation potential of populations be simplified so that they are practical for a wider range of species?

Can the new gene-editing tools be used to enhance the survival of endangered species, and will such modifications be acceptable to both regulatory agencies and the general public?

Will gene drives work outside the lab and how can conservationists use them, both to control unwanted species and to help endangered species?

How can we best make use of the possibilities offered by de-extinction technologies?

Can we bridge the research–implementation gap between academic conservation biologists and conservation practice in the field?

How can public distrust of field applications of biotechnology be reduced?

Will the availability of cheaper, quicker, and more accurate whole-genome sequencing lead to novel applications in conservation biology over the next few years?

Box 3. Potential Applications of Whole-Genome Sequencing in Conservation

New developments, such as nanopore sequencing, are expected to make cheaper, quicker, more accurate whole-genome sequencing (WGS) available for conservation studies within the next few years. The reduced-representation sequencing (RRS) approaches that currently dominate conservation genomics (Box 1, main text) are a compromise between using a few markers, such as microsatellites, and the whole genome. Using RRS in conservation implicitly assumes that rare variants are either of little conservation value or that their distribution correlates with that of common variants. For common species in a stable environment, this may usually be true, but in threatened species with small populations, important adaptive variants may become rare by chance. In any species, rare variants with no current benefits may provide a degree of insurance against environmental changes in the future. RRS may also overlook small genomic regions of importance for adaptation [84].

WGS has yet to be applied in a conservation context, but current applications with humans, livestock, and crop plants illustrate some of the potential. In humans, the increasing amount of whole-genome data from the UK allowed the detection of selection within one lifetime (against men with an allele that makes it hard to quit smoking) and over the past 100 generations (against lactose intolerance and for fair hair and blue eyes) [85]. Both timescales are relevant to understanding how wild species are affected by rapid environmental change, and could help optimize conservation strategies. In cattle, WGS has shown the potentially massive loss of rare genetic variants when a few, optimal, individuals are selected for conservation in gene banks [86]; a frequent necessity also when optimizing *ex situ* collections of wild species. As has happened with RRS, it is likely that the wide availability of WGS will lead to both increased resolution with existing conservation applications and the development of additional, completely novel, applications.

The next generation of NGS is also likely to offer longer sequence reads than the currently dominant short-read (<300 bp) sequencing platforms [87]. These longer reads will allow the detection and mapping of structural variations >1000 bp in size, including insertions, deletions, inversions, duplications, and translocation, which are an important, but little-studied, source of genetic diversity in wild populations. This is likely to affect the current dominance of SNPs in conservation genomic studies, but it is too early to predict consequences for conservation practice.

technologies available outside academic research groups (to small labs, government agencies, and the full spectrum of conservation practitioners) while continuing to assess and minimize risks. The major gaps between researchers and practitioners have been characterized as knowledge, tools, finances, and communication [16]. The most practical way of bridging these is likely to involve three-way collaborations between academics, commercial providers, and end-users.

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Resources

[i] http://syntheticbiology.org/

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