Journal of Advanced Health Informatics Research (JAHIR)
Vol. 1, No. 1, April 2023, pp. 1-9
DOI: https://doi.org/10.59247/jahir.v1i1.1

A Review of Bioinformatics for Primatologists: A Note for Reducing Living Primate Model and Supporting The Conservation

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ARTICLE INFO

Article history:

Received November 28, 2022
Revised December 28, 2022
Published January 15, 2023

Keywords:

Molecular Biology;
Big Data;
DNA Forensic;
Primate Model;
Omics.

ABSTRACT

The problem is that bioinformatics, as a part of health informatics, plays a role in studying molecular things and genetic studies. Primatologists who studied primates, as well as non-human primates (NHPs), found a dilemma relating to biomedical studies and conservation. Which one to achieve, the goal of being a model animal or their conservation efforts, of course, has very few boundaries. **The solution** in this study tries to review how to seek to reduce the quantity of NHPs model animals but not reduce their quality, on the other hand, considerations of conservation efforts. **The research contribution** in this paper proposed authors' perspectives according to the context of the NHPs model as well as conservation efforts, which are considered for dry or wet materials, which means that the genetic resources come. This study would give the 3Rs principle idea, reducing, which contributes to its conservation efforts. **This review method** used literature surf, scientific selection, and report writing. **The result** proposed the discussion about related scientific sources as well as the authors' perspective to solve the problem of animal model uses in NHPs. **The conclusion** is that NHPs are fortunate to receive special attention outside their studies as animal models, even though they are still used in research to benefit humans. Of course, the benefits and drawbacks of using genetic samples—whether wet or dry—are only relevant when used as research materials for medical and bioinformatics investigations. So that there are no more instances of increasing conservation status brought on by the volume of research on the use of model animals, efforts to conserve NHPs as a component of wildlife in nature must be considered.

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1. INTRODUCTION

In the era of digitalization, the role of artificial intelligence (AI) is the most important thing [1]. As part of an intelligent system, AI can be contributed to applied science as well as biological sciences. Besides, molecular biology is commonly known as a minor thing in the biological sciences [2]. Since DNA was established as the heredity role of living things [3], then also used for evolutionary reconstruction [4]. DNA

was used for genetic analysis, a needed platform, software, and intelligent computer called high-throughput computing [2]. Within the high development of this high-performance computing, also with AI support, genetic analysis (genomics) has been studied as a bioinformatics subject [5]. Besides, the kinds of genetic analysis not only use DNA as a hereditary tool, such as RNAs [6], [7], as well as mitochondria were commonly used as the basis for genomic sampling for collecting the genetic sources [8], then this method also stated as mitogenomic [9]. All the -omics methodologies used bioinformatics and AI-based genetic sequencing methods.

One of the branches of biological science is primatology which studies all about living primates. The role of primatology also studied genetics, anatomy, physiology, behavior, ecology, evolution, and conservation. Their biological aspects have been used bioinformatics approach. In contrast, primates were one of the wildlife that needed further action and research for their sustainability. So, in the era of molecular biology, all research also used the omics method, which is part of bioinformatics studies [10], including the primatology field.

Living primates (known as non-human primates, NHPs) are the animal model for studying human disease and its treatment [11]–[13], as well as the development of the omics era in the field of biomedicine [14] and bioinformatics [10]. Besides, bioinformatics (omics method), also commonly known as high-throughput, can be used for studying evolution [15], [16], wildlife trade tracking [17], and vaccine development [18]. Meanwhile, many primate species are indicated as endangered and critically endangered for several reasons [19], [20]. An example is a long-tailed macaque (cynomolgus macaque, crab-eating macaque) as an animal model. Now, the current conservation status by IUCN Red List is endangered [21], increased from vulnerable [22], while most factors such as population decreased and animal models used [23].

In the era of sustainability of primate biodiversity, conservation efforts must be action [24]–[26], as well as optimization for the animal model in biomedicine [27], [28]. So, this paper aims to review the bioinformatics approach's role in studying primatology as well as the development of omics methods, which can be applied to primatology and primates as human disease models are also cited. This paper focus on biomedicine, biology, and conservation, as well as the human and wildlife sustainability perspectives. This paper can explain our perspectives on reducing the living primate model and supporting conservation.

2. REVIEW METHOD

This study used several phases for the review method. First of all, literature searching as well as online scientific surf in several databases such as Scopus (Sciencedirect), PubMed, IEEE, Dimensions AI, Lens, Web of Science (MJL Clarivate), and DOAJ. The tool for internet surfing used Publish or Perish 8. Keywords used with Boolean variation such as *non-human primate OR animal model AND bioinformatics OR high-throughput OR gene editing OR gene expression AND laboratory OR breeding OR housed OR cage OR captive.* Second, scientific selection, as well as full-text readiness. Third, the final phase is the review report, which is written in this paper.

3. DISCUSSION

Bioinformatics is the role key for genetic engineering, as well as molecular study, which needs wet or dry material (in this case: DNA, gene, mitochondria, chromosome). The wet material means that the genetic sources can be adopted from original biological living things, such as fecal, hair, urine, secretory, blood, as well as fresh resources. Besides, the dry material means that the genetic sources are available in online resources. If talk about wet material and the fresh sample collected from living tissue is also needed for sample collection methods, such as invasive and non-invasive methods. Besides, invasive methods commonly must be with some 'invasive treatment' to the animal, including injection for blood sample collection, as well as any other living tissue. For example, a recent study published in a preprint version talks about a highly versatile and non-invasive method for collecting a DNA sample from a fresh buccal cell [29], this can be assumed that this proposed method for collecting a good-quality of DNA from the buccal cell, as well as fecal DNA sample which probably contains allelic dropout [30], inside the risk of contamination if infectious-probable. Besides, the significant collected fresh genetic sample from living tissue, as well as in primates, is fecal, while this method is commonly used for conservation efforts [30] instead of urine samples [31].

This section discusses more applied bioinformatics in the role of primate biodiversity as well as evidence-based, with a particular focus on conservation efforts.

3.1. Bioinformatics for Primate Model for Humans

Known as non-human primates (NHPs), they were used for human disease studies [32], [33], as well as in vitro studies [34]. Bioinformatics is commonly used as genetic sequences [35], [36], i.e., translation process [18]. Besides determining the locus (specific gene location) for a particular human disease, in NHPs model also used the bioinformatics approach [37], i.e., with whole genome sequencing [38]. There are many studies about NHPs as a human disease model and its prevention (like a vaccine or drug candidate [39]), including Parkinson's disease [40], SARS-CoV-2 (Covid-19) [41], adenovirus infection [42], human development study [43], as well as studies about the metabolic disease [44]. Currently, studying human disease, human disease infection, and human disease prevention optimized or before clinical trials using the NHPs model [14].

If NHPs are used as a human disease model, experimental study, or laboratory research, they must be approved by the commission of ethics for the animal model [45], [46], as the 3Rs technique is needed to do the NHPs model research as one of the ethical clearances requirements [47], [48]. Several studies about NHPs for human disease are proposed by the bioinformatics approach, as well as health informatics science. For the justification for this statement, as stated before, sampling collection with a non-invasive method (e.g., fecal, urine, buccal cell, hair, secretory) is also required to fill in ethical clearance requirements [49]. When considered for animal welfare, a non-invasive method is better than an invasive method [50].

Health informatics, as well as bioinformatics study, are required to adopt the ethical research requirement. Some cases are needed for several ethical considerations to reduce harm-level to the animal, increase their welfare, as well personnel safety. In addition, some studies do not have ethical approval nor wet material, which comes from open-source databases for genetic sources [51], as well as genomic resources [52], also called dry material, which is evenly used in ecology or conservation study.

3.2. Primate As wildlife Needs Conservation Focus

As stated in previous research [53], [54] as well as Primates in Peril [19], [20], most non-human primates (NHPs) species are needed for conservation efforts. E.g., Tapanuli Orangutan, the newest Pongoid NHP species, has been critically endangered (CR status by IUCN Red List) since it was founded [55]–[58]. Meanwhile, new Tarsier species were found [59]. The role of bioinformatics is required for determining this new species, as well as the phylogenetic condition, undoubtedly. Besides, to support its conservation also with bioinformatics approach [60]–[62]. In addition, this approach also contributes to conservation efforts [63].

As computational intelligence [64], bioinformatics is the primary role of primate mitogenomics study [9], [65], [66], evolutionary study [67]–[69], phylogeography study [70]–[72], biodiversity study [73]–[75], distribution to conservation plan [76]–[78], as well as help the conservationist and geneticist to work together. Supriatna [79] stated that every single person would help and work together to save the biodiversity, including non-human primates (NHPs) species. Besides, transdisciplinary science is also required to improve the conservation plan [25] as well as primates species [80], including intelligent computing approaches such as bioinformatics and health informatics.

3.3. Cases from Forensics

Forensic science needed biological samples to collect DNA from living things [81], [82] (evenly called wet materials). Several papers reported that they used a bioinformatics approach with high-throughput computing to prove the wildlife trade [17], [70], [83]–[86]. This intelligent computing can prove that genetic evidence-based would explain the wildlife's origin [17], [83]. Forensics in wildlife (also called wildlife forensics and animal forensics) can be challenging in the following decades in the endangered or CR status of non-human primates (NHPs) species.

On the other hand, the DNA-forensic approach, which is based on bioinformatics, as well as high-throughput computing, was also reported for studying the mitogenomic of the endangered primate species [87]. DNA-forensics supported by bioinformatics methodology, undoubtedly [81].

4. REDUCE CHALLENGE FOR INCREASE CONSERVATION EFFORT

The discussion in this paper explains the critical role of bioinformatics as part of health computing, high external computing, and intelligent computing, especially in the field of primatology. The role of primatologists as part of biomedical experts, environmentalists, and conservationists, as well as intelligent computational experts, must be wise in choosing non-human primates (NHPs) subjects as subjects or objects to be studied. Considering that the NHPs species are mainly threatened status [53], [88]–[93].

Lesson from most NHP animal models, *Macaca fascicularis* (long-tailed macaque, cynomolgus macaque, crab-eating macaque, or Javanese macaque) [13], which is mainly used as a laboratory experiment, human disease model, infection experiment, drug and vaccine development, has increased the conservation status from vulnerable (VU) [22], [94] to endangered (EN) [21]. Besides, found a paper that discusses the impact of its conservation species with Covid-19 research [23]. Meanwhile, the last IUCN Red List status (EN) reported that population decrease is the most influential factor in IUCN's status [21]. Besides, in Javanese culture, primate exploitation, a dancing monkey or *Topeng Monyet* [95], can be another factor for its high conservation status.

In fact, health informatics, including in the bioinformatics approach, allows molecular research of genetic scales that generally occur at the gene level, loci, and certain types of DNA, to be harmonized by utilizing open-source available in the gene banks. If the research requires a direct genetic source of NHP live tissue, then it is undeniable that it requires sample collection, both invasive and non-invasive. However, if the required genetic information is available in the gene bank, anyone can access it freely so that the genetic research process based on dry material data can be optimized. In addition to supporting animal welfare efforts, it also contributes to conservation efforts. Alternatively, if genetic research requires a collection of live samples, it can use frozen preserved tissue samples. Although not every biomedical study can use this technique, it depended on the ethics commission's decision, which is related to the 3Rs principle [47].

In contrast to the case of phylogenetic tracing of a primate species, plus if it is possible for the study of new species, or new sub-species, to map the distribution of a primate species, of course, it is required to obtain a sample collection of wet materials (living tissue). However, suppose phylogenetic studies are still concerned with assumptions, reconstructions, and phylogenetic analyses of species already discovered (not the case of new species or sub-species or other related studies ascertaining the condition of phylogeny based on field or lab observations). In that case, it is recommended to use dry material, i.e., gene bank tracing, to be sequenced and compared with each other [96].

All studies on primates, particularly non-human primates (NHPs), do not necessarily use a bioinformatics approach, as well as health informatics. However, to know the scientific truth based on the molecular level, which allows the results of high-throughput computing, indeed, molecular scale is necessary; in this case, the role of bioinformatics as part of health informatics plays an important role. On the other hand, animal models, particularly NHPs as animal models for studies related to humans, can impact a wide variety of aspects, such as animal health, ethics, zoonotic potential, ecology, and conservation.

If the study would prioritize ethical principles such as 3Rs in biomedical research, it can be considered to use dry materials, although wet materials are still the main thing. Each party must still prioritize the ethical principles and sustainability of the species in nature, so that conservation effort can gradually occur, although they must start from a molecular scale.

5. SUMMARY AND CONCLUSION

Non-human primates (NHPs), although still part of animal model studies for humans' benefit, are blessed to get special attention beyond aspects of their studies as animal models. Of course, each of the advantages and disadvantages when considering genetic samples, whether wet or dry material, solely all act as material from health and bioinformatics studies. Efforts to save NHPs as part of wildlife in nature need to be considered in their conservation efforts so that there are no more cases of increased conservation status caused by the number of studies on the use of model animals.

Acknowledgments

This study is supported by Research Center for Natural Sciences, Eudaimonia Institute Foundation Research Center. The authors also thanked Primate Research Center, IPB University; Research Management Center, Jakarta Global University; as well as Dr. Rizaldi, Dr. Kurnia Ilham, Dr. Jeffrey V. Peterson, Dr. Erin Vogel, and Fitriya N.A. Dewi, Ph.D., for taking the time to discuss this with us. The authors also thanked anonymous reviewers who provided good feedback. The authors declare no conflict of interest and are not required for ethical approval.

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