

AN ETHICAL ANALYSIS OF BIOTIC GAMES

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Microbes and sometimes more complex living things can be turned into pieces in games that,

though they may have educational purposes, may also just be played for fun. Should we be troubled?

In 2011, Ingmar Riedel-Kruse's bioengineering laboratory at Stanford University publicized an application that uses paramecia for what the researchers termed "biotic games." These games make use of living organisms, computer programs, and lab equipment to implement games like Pong, Pac-man, and soccer. Several media outlets covered the lab's work, which resulted in discussion online; the response was mixed, and the intensity of statements of opposition prompted Riedel-Kruse to engage with bioethicists in order to evaluate these objections and obtain guidance for future work, which led to this jointly authored analysis.

Biotechnology is advancing at such a pace that we can expect a variety of commercial, academic, and

educational uses of technology that make increasingly radical alterations of organic matter and living things. The use of living things in "games" enabled by biotechnology is a special case, as "games," "entertainment," "play," and related activities are often considered nonserious or trivial, whereas life, biological systems, and science are treated very seriously in moral analysis and public perception. The manipulation of living matter frequently engenders at least some controversy in the marketplace of ideas, and using living things in games is no exception. Some of the objections lodged against biotic games have appeared in the ethics literature on similar topics; however, the addition of an entertainment element introduces some objections distinct from those about similar cases, as the online comments vividly illustrate. We aim to explore and address the objections in this paper, using the comments to organize and launch the discussion. In scientific work, there is

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typically a presumption of some prospect of translation and application of generated knowledge for public benefit. In the case of biotic games, these applications are not self-evident. Because of this, a serious analysis of the justifications, limitations, and features of biotic games is warranted. To this end, we outline key ethical limits that ought to be placed on these activities as well as the obligations that these activities generate for researchers, other professionals, and lay people who design, implement, use, and play them.

What Are Biotic Games?

) iedel-Kruse's group defined a bi-Notic game "as any activity including the necessary equipment (i) that falls under the concept of games, (ii) that has one or more humans interacting as active players with biological materials or processes, and (iii) where the game design and human experience depends on modern biotechnology."1 This means that biotic games include some playful or competitive component governed by rules, and that they differ from the familiar use of animals in sport and games (such as dog racing or polo) by relying on biotechnological techniques to enable interaction between humans and biological material.

Riedel-Kruse and his bioengineering lab at Stanford University have developed a series of biotic gamesincluding Ciliaball, PAC-mecium, Microbash, and Pond Pong-in which players control the movements of paramecia in a fluid-filled dish by applying electric fields or chemical stimuli via a handheld controller that resembles traditional videogame controllers. Players interact using the controller and observe the reactions of the paramecia on a screen with a superimposed game environment. Riedel-Kruse's lab has also made biotic games that rely on polymerase chain reaction and yeast cultures, but these projects have received little treatment in the media. It is important to note that games simulating biological processes are not considered biotic games; only those that use actual biological materials have that label.² To focus still more precisely on the issues of using biological materials in games, we restrict the concept of biotic games to the introduction of biological material into games, omitting the gamification of biology research. This means that efforts to crowd-source research through games like Foldit or EteRNA, wherein users design protein and RNA structures, will not be considered typical cases of biotic games for this paper.³

Biotic games are subject to certain normative considerations that follow from the very idea of being observations in order to identify winning strategies.⁵

The association of organisms with new technologies is an ancient phenomenon. The use of animals for transportation, protection, pest control, and food can be seen as the early development of biological technologies. The use of animals for games and sport can be viewed as providing examples of interaction between biology, technology, and society. More modern efforts to incorporate technology and biological processes are myriad. B. F. Skinner's operant conditioning chamber used technology to influence animal behavior, and around World War II, Skinner and

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a game. They should be fun, engaging, and intrinsically motivating for their players. These features are considered thoughtfully in game-design literature.⁴ These features, however, are not the sole justificatory criteria for games. Although there are reasons to believe that games and play activities are important, some games, such as gambling or violent contact sports, are ethically dubious. Suffice it to say that a well-designed game is not always an ethically justified one.

Riedel-Kruse's lab notes that it expects its biotic games to be effective tools for teaching microbiology and biophysics. Many American high schools already use paramecia in an observational or experimental setting, and biotic games may help motivate and engage students. Riedel-Kruse et al. postulate that students might discuss and understand their scientific others aimed to use pigeons to guide missiles, dogs to guide torpedoes, and seals to deploy underwater mines to submarines.6 Advances in technology have led to nonlethal but still somewhat strange ways of interacting with living matter. The Metazoa Ludens project at the Mixed Reality Lab, based in Singapore, uses digital media to enable playful human-animal interactions, allowing people to exercise hamsters remotely.7 Another project from the Mixed Reality Lab is aimed at allowing remote interaction between humans and poultry via technologically mediated petting.8

Although all of these examples demonstrate interaction between technology and living things, biotic games fall into a different category insofar as they "biologize" games, meaning that they aim to implement entertainment modalities by manipulating life using biotechnology. The key difference between biotic games and the examples above is the game element. Biotic games are designed to produce an enjoyable interaction with biological systems; Riedel-Kruse and colleagues write, "[W]e hope that biotic games will be played for fun."9 This means that any application of biotic games toward a goal such as education must to some degree also just be fun. This consideration is the crux of evaluating biotic games from an ethical standpoint-although they can be used for education or other purposes, they should be fun, and we must discern to what degree manipulating organic, sometimes living, matter for fun is acceptable and what constraints ought to be placed on such activity. To some degree, our analysis in this paper poses and responds to the question, when is it acceptable to have fun with biology?

It is worth mentioning that other groups have produced similar gamelike activities, and although they are not referred to as "biotic games," nor even always as games of any sort, they either meet the definition of biotic games or could be minimally altered to do so. These examples make use of a variety of organisms, including cockroaches and crickets, to implement many of the same designs that Riedel-Kruse et al. have developed into games similar to Pac-man and Pong.¹⁰ There is even an effort to fund and commercialize home kits for controlling cockroaches with smart phones.11 It is easy to envision using these techniques to create and play games. There is a considerable difference between cockroaches, crickets, and other more complex animals, on the one hand, and paramecia, on the other, but these differences should be considered through careful ethical analysis. We intend for our analysis to apply to biotic games broadly construed.

What People Say

Because the work by Riedel-Kruse et al. has been featured in numerous articles that incorporate online communities, we decided to use the comments on these sites (see sidebar) to informally gauge public response and connect representative public responses to topics already in the ethics literature. From the comments, several points became clear. First, comment sections on websites are not brimming with sophisticated arguments, unsurprisingly. Second, nevertheless, many comments fit with arguments and positions treated in the bioethics literature. Concerns about animal welfare, respect for life, playing God, slippery slopes, and whether this kind of work is worthwhile were all ubiguitous in comments, as were visceral responses. In the following section, we give examples of these comments and connect them to the relevant discussions in the literature. Some of the comments may contain a degree of sarcasm or irony; the fact that these ethical concerns are voiced at all, though, whether seriously or sarcastically, suggests that there is something ethically charged about biotic games.

• Animal Welfare

"This sounds a bit like dog fighting. Wait till PETA hears about this."

—At Scientific American, *January 23, 2011*

Animal welfare is an important ethical consideration, but it's not applicable to the biotic games so far developed. Because paramecia are single-celled organisms without nervous systems, not animals, they are incapable of feeling pain.¹² Yet many comments seemed to anthropomorphize paramecia and indicate a lack of understanding of their nature, suggesting a persistent belief in the possibility that they might be sentient and have the ability to suffer, showing that even readers of popular scientific publications can lose track of the differences between single-celled organisms and dogs or roosters.

Anthropomorphic responses to biotic games are more likely a product of natural human tendencies than of the games, per se, so these responses are unlikely to disappear, especially for biotic games that make use of living things.13 This is not to endorse a defeatist attitude on whether the public can come to understand animal welfare, however. The tendency to anthropomorphize animals, even microbes, is compatible with correct beliefs about biology. Surely, even neuroscientists sometimes attribute mental content to cartoon characters, toys, and so on-when playing with their children, for example-but that is a far cry from believing that the cartoon characters are feeling things. The anthropomorphic tendency can certainly correspond with incorrect beliefs about images and organisms, but it need not; the attributions and the beliefs are separable. And in fact, it would be impossible, and undesirable, to eliminate anthropomorphic tendencies. A world in which it was epistemically incorrect for children to attribute attitudes to their toys would be strange and unpleasant. Whether or not biotic games can accomplish the goal of educating the public about the comlexity of animal welfare, there ought to be a broader goal of education through other means.

Of course, animal welfare is a legitimate moral concern, and efforts should be undertaken to prevent animal suffering in biotic games.

• Respect for Life

"But isn't this microslavery?" —At Boingboing, January 19, 2011

Respect for life was a basis for numerous objections in online comments. Respect for life appears in philosophical positions that are related to concerns about animal welfare, insofar as those concerns typically rely on some justification for respect. The Kantian view, in the Metaphysics of Morals, is that "cruelty to animals is contrary to man's duty to himself, because it deadens in him the feeling of sympathy for their sufferings, and thus a natural tendency that is very useful to morality in relation to other humans is weakened."14 Kant's view here is not based on respect for life per se, but rather on the notion that

failing to respect animals capable of experiencing suffering erodes respect for persons. Other arguments concerned with respect for life avoid Kant's anthropocentrism, however. Peter Singer argues that sentience is the basis for the ability to experience pleasure or pain, and he advocates a utilitarian approach for respecting life.¹⁵ Singer's view would not apply to games played with paramecia, given that they are far from sentient, but it certainly applies to biotic games in general. Still others argue in various ways for the much more radical claim that *all* life has some moral status.¹⁶

Certainly, interesting arguments can be made to expand the moral community beyond the traditional anthropocentric concepts and justifications of agency and autonomy, and these radically biocentric views surely have something to say about biotic games. At the same time, these positions constitute a radical departure from the Western moral tradition. Especially in the field of bioethics, rational autonomy and accompanying political commitments are foundational. A radically biocentric position might tend to undercut the moral status of humans, depending on how human interests would be balanced against the interests of other living things. If only because of pragmatic considerations, it seems that the implications of a radically biocentric ethics for the political and legal treatment of human beings and other complex animals require quite a bit of careful thought, and that it would be premature to apply such an ethics to biotic games. In addition, it's not yet clear why respect for life provides a compelling reason not to engage in biotic games, given the very wide and historically well-established range of permissible scientific and social activities that involve interacting with nonhuman living things in some capacity.

In our view, respect for life is an intuition that represents a starting place for evaluating interactions with living things, and a value that may inform or guide decision-making alongside other considerations and values. But any use of the value of respect for life requires an account of why *this* kind of life ought to be respected in *this* case and what actions are motivated or proscribed by those considerations. In short, the value must be accompanied by additional, substantial reasons.

• The Promethean Objection "So we are the Gods, and the single celled organisms are the romans." —On youtube.com, "The Bold New World of Biotic Games," February, 2011

Other objections to biotic games reflect various moral views and taboos

they must identify the features of activities that overstep the bounds of acceptable human "meddling," so to speak, and demonstrate why the activities are unacceptable. If they do so, adherents of the "playing God" argument would make their position more compelling to those who do not necessarily share their intuitive starting point.

Visceral Responses: The "Yuck" Factor
"disgusting. they are life too." —On Slashdot, January 15, 2011

Another potential response to biotic games is a "yuck" reaction. These visceral responses tend to

CONCERNS ABOUT animal welfare, respect for life, playing God, slippery slopes, and whether this kind of work is worthwhile were all ubiquitous in online comments about biotic games.

that admonish against "playing God." Such objections have cropped up reliably in response to the emergence of novel biotechnologies, especially those involving the manipulation of living things. As David Magnus and Arthur Caplan point out in a discussion of the "playing God" arguments lodged against the creation of genetically modified organisms, they represent an amalgam of concerns, ranging from simple disgust to precaution about the possible risks of manipulating living things to a commitment to responsible stewardship of nature that avoids excessive or dangerous meddling, to a kind of hubris that is evident in the wanton manipulation of creation.17 These intuitions are common immediate responses to novel abilities of biotechnology, but they are best viewed as starting points for ethical reasoning rather than stand-alone objections. If arguments that fall under the "playing God" umbrella are to be successfully employed,

evince strong reactions, but without additional argumentation, they, too, do not result in compelling moral positions.

The role of disgust in the moral appraisal of biotechnologies has been argued about notably by Leon Kass, who is echoed by Mary Midgley.18 Their positions hold that a feeling of moral repugnance is ethically significant and should not be ignored when evaluating a practice's moral status. Although these arguments are based on the attractive view that ethics should not be a strictly rational project, that it should not be entirely divorced from agents' affective states, it can be counter-argued that these feelings are analogous to intuitions, which give us a starting point in ethical deliberation, rather than being morally salient properties simpliciter.19 Repugnance has been used to justify immoral or unjust views, including support for segregation and opposition to miscegenation and

same-sex marriage, so it is not unreasonable to ask for additional reasoning to accompany arguments rooted in disgust. While people who are revolted by biotic games clearly should not be compelled to play them, it is also clear that their revulsion is not by itself an argument against any participation in biotic games, nor does revulsion alone mean that an activity is ethically impermissible. More argument is needed.

• The Slippery Slope

"Next thing you know it will be you and I in an octagon while someone tosses a single pair of rusty scissors while some Korean kids control our every action."

—On CNet, January 14, 2011²⁰

A popular line of criticism in the online comments, as well as in the ethics literature, has to do not with the case at hand but with cases to which it might lead-the potential future uses of the technologies. These kinds of objections should be familiar to scientists and bioethicists involved in the controversies over stem cell research and somatic cell nuclear transfer. Francis Fukuyama and Franco Furger voiced them when they argued that technology is moving too quickly for the current regulatory framework and that the framework is not equipped to address the "unfamiliar and difficult ethical dilemmas" that will emerge-and, moreover, that advancements in basic science were likely to be applied to human subjects.21

The slippery slope view is a captivating lens through which to analyze new technologies, given its appeal to the imagination and its parallels with popular science fiction. For precisely this reason, we need to employ it carefully. On the one hand, it is true that novel technologies have potentially unforeseen impacts and that they often stray from their original intent, meaning that some degree of anticipation is important to make educated predictions about how certain technologies should be managed. On the other, the slippery slope can lead to sensationalist arguments that undermine the development of useful technologies. It seems unlikely that games involving paramecia are the first step toward human-clone gladiatorial combat, but at the same time, the use of living things for activities that some may consider frivolous must be justified to set norms that govern these kinds of activities in the future. It is also important to consider the inverse of the slippery slope-that a technology is a step toward desirable but undemonstrated ends. Lacking convincing inductive evidence that an activity will lead to either good or bad ends, slippery slope arguments lack persuasive substance.

• Trivial Pursuit: Are These Activities Worthwhile?

"Using living things for research, I'm totally ok with that. Eating living things as we're higher in the food chain, I'm totally ok with that. Harming living things for fun is **not** cool—Uncoolness factor being proportional to living thing complexity."

—On Slashdot, January 15, 2011

Probably the objection that will enjoy the most traction in ethics, as well as policy and regulatory settings, has to do with whether and for what reasons these activities might be worthwhile. Reasons for questioning whether biotic games are worthwhile are myriad, but they generally deal with whether they are a good use of monetary resources and researchers' time and intellect, whether their educational or scientific outcomes will be significant, and whether manipulating life for the purpose of creating "games" is worthwhile.

Although Riedel-Kruse is careful to make clear the educational and scientific intent of biotic games, the label "games" connotes trivialization, subordination of life to the purpose of fun, which to some may be a basis for fundamental objections. The association between games and frivolity may be strong enough to override the educational or scientific intent of these games for some. Lacking substantial public benefit, biotic games would be vulnerable to the same kind of arguments employed in the California Fish and Game Commission's decision to ban the sale in California of the genetically modified zebra fish known as GloFish; manipulations enabled by a novel biotechnology should not be used for trivial ends.²² These kinds of objections reflect an interest in a balanced approach to the manipulation of living things. The bare ability to manipulate something is far from a justification to do so; we should take into account considerations beyond just the capabilities of science and the fun of playing with nonhuman living things.

These arguments cannot be dismissed off-hand because they refer to the attractive intuition that activities, including those that make use of advanced biotechnology, ought to provide a reasonable balance between the degree of manipulation that they require and the benefits they provide. Applications of biotechnology should not be undertaken without due consideration of their necessity and, failing necessity, utility, and should especially not be undertaken frivolously.

It is possible to clarify the purpose of biotic games to give more deference to this idea of balance. Although Riedel-Kruse et al. point to potential benefits of biotic games, such as engaging students and the public in science education, increasing economic output, and creating opportunities for open and crowd-sourced science, they are less clear, both in their press releases and academic publications, as to why these activities qua games add value to educational, scientific, and research projects, rather than trivializing them. More than adding value to the educational project, biotic games represent a step toward creating new ways of allowing humans to interact with biological systems that may allow valuable advances in scientific knowledge, or may be a step toward manipulation of living matter for poorly justified ends.

• Positive Feedback

"I think something like this might generate interest along with some 'outside the box' thinking by the public, to whom these games are being targeted." —At The Guardian, January 19, 2011

"Overall, experimenting in and researching ways to make science education more 'sticky' is just as important as furthering science. More people interested in science propagates an interest in science, which means more money for science, more scientists, et cetera."

> *—At* The Guardian, January 19, 2011

Although the objections to biotic games in online comments were intense, responses were not uniformly negative. Some online comments took more optimistic views of the biotic games project, referring to potential future applications in science, education, and interdisciplinary work.

Ethical Analysis and Discussion

The online comments should be taken seriously, yet not too seriously. Even if some are based on misunderstandings, they ultimately represent feelings and heuristic views that stand to influence uptake, additional responses, and regulation of these technologies. It is also true that they are presented in a forum that is not known for sophisticated analysis and that should not replace substantive ethical analysis.

It is worth pointing out that some lines of objection that have appeared in literature on related topics did not appear in the comments that we analyzed. For example, although there is considerable controversy regarding the positive or detrimental effects of video games on society, no one objected that biotic games are inherently bad or harmful to the socialization of children.²³ Also, no one objected that biotic games would desensitize individuals to the suffering of nonhuman organisms, though that thought may have been implicit in some comments. Finally, very few considered these activities to pose direct dangers to the public by way of, say, the organisms escaping the controlled environment of the game to cause ecological damage or public health problems—a view that has been considered in the literature on synthetic biology²⁴—though some believed them to be a step toward other, more dangerous activities.

We believe that there are four central ethical considerations that set limits to these kind of activities: the duty to minimize the suffering of sentient creatures, the responsibil-

animal suffering is permissible for the sake of technological or educational advancement, we offer a rule of thumb: the degree of animal suffering should be commensurate with some concrete benefit or necessity. This is consequentialist thinking, but not straightforwardly utilitarian. The mere experience of pleasure, for however many, is not enough to justify suffering, but other measurable benefits may be able to. We agree with those who hold that animal suffering for pure entertainment is prima facie unacceptable from a moral point of view.27 Going forward, we should keep in mind that the duties based on animal consciousness will change due

HUMAN ACTIVITIES should not be wanton manipulations of the natural world but, rather, purposive efforts to improve the human condition. The question of whether biotic games promote scientific or educational goals remains to be answered.

ity to balance our manipulation of nature with some notion of benefit and necessity, the duties of scientists to justify their work to the public, and finally, duties emerging uniquely from these activities qua games.

First, we should look at the moral status of the organisms used in biotic games and the duty to minimize suffering. It is widely accepted that the moral status of living things results in part from their status as sentient beings with the ability to experience sensations like pain or pleasure.²⁵ Because relatively little is understood about the bases of subjective experience, it is difficult to concretely determine which organisms are sentient and capable of experiencing pain. However, some degree of neurological complexity is required, and it is evident that even some invertebrates, such as insects, are sufficiently neurologically complex that we cannot rule out sentience.26 In order to avoid categorical claims about whether any to developments in the understanding of consciousness, and duties to minimize suffering should be responsive to our best present explanations of the bases of subjective experience. Finally, since paramecia, being singlecelled organisms, have no neurological complexity, their use cannot be evaluated from the standpoint of sentience or suffering.

Second, as the "trivial pursuit" comments indicated, we have an obligation to balance our manipulation of nature with some measure of concrete positive outcome. As a related consideration, we should not undertake research that is unnecessarily risky or dangerous; for example, it is obviously unacceptable to play biotic games that carry the risk that virulent pathogens or ecologically harmful organisms will escape. This notion that the manipulation of nature is justified by its concrete positive outcomes was explicit in the decision to ban Glo-Fish in California, and it underwrites to a large degree the justification for funding research projects.28 It is important that human activities are not wanton manipulations of the natural world but, rather, purposive efforts to improve the human condition. In this light, it is difficult to judge the moral status of biotic games, since, as games, they do not appear to be purposive in the same sense as other activities. The philosophical literature on games often emphasizes that games are governed by rules yet are nonpurposive, playful activities, and that any positive externalities are unrelated to an activity's status as a game.²⁹ Moreover, the game design literature adds and emphasizes interactivity, internal (or intrinsic) value, and challenge.30

Taking these definitions into account alone, there is little justification for using living things in biotic games. However, games and play activities may sometimes have beneficial effects beyond the intrinsic pleasure that playing them can afford. Games are thought to be intrinsically motivating and rewarding, and intrinsic motivation is very valuable when one is exploring and learning.³¹ Further, biotic games can be specifically designed to incorporate rules that promote the understanding of biological activities and capitalize on the players' intrinsic motivation; if so, they may not be frivolous after all. They may be useful scientific or didactic tools. And if so, then they will be justified, so long as sentient organisms are not exploited. Ultimately, the proof will be in the pudding: whether they promote scientific or educational goals is an empirical question that remains to be answered.

What is perhaps most evident in the data we collected is that the responses of the public can be contrary to the enthusiasm of scientists. Examples of this phenomenon are numerous in the history of bioethics, from the advent of recombinant DNA to recent H5N1 research and work in synthetic biology, and despite much discussion, there is little agreement on the obligations of scientific researchers to justify their work to the public. However, given our first two recommendations, as well as the moral factors highlighted by the comments, we can construct a third obligation for scientists when communicating their work to the public through press releases, videos, and media coverage. We can look at these communications as not only disseminations of scientific work to the public but also as a mode of articulating the justification for scientific activities. The keystone to this consideration is that members of the scientific community, by virtue of their curiosity and professional specialization, have a unique standard for value when compared to the heterogeneous values of the public, which means that special care must be taken in communicating the motivations and justifications for research to the public. Even if sociological factors make it difficult or impossible to produce complete agreement on the value of scientific activities, our first two recommendations (to minimize suffering and justify scientific activities that manipulate life) can be viewed as generating an obligation to justify the ethics of, and reasons for, scientific activities to the public.

Finally, it is worth considering the connection between the social, scientific, and educational value of biotic games and their special nature as games meant to be played and enjoyed. Although enjoyment or fun is not traditionally a difference-making feature from a moral standpoint, it is also true that humans of all ages (as well as nonhuman animals) derive significant meaning and pleasure from play. Although the ethical literature on the value of play is relatively sparse, some have argued persuasively that play and competition are important social and cultural activities.32 Moreover, play is an important element of childhood development and socialization.³³ However, these should be treated only as pro tanto arguments for games; they are not, as we argued above, absolute justifications for all games. If biotic games have

educational benefit, which we see as plausible though uncertain, they have it insofar as they are fun and engaging. This generates further recommendations: Biotic games ought to be good games-enjoyable, engaging, challenging, and exciting-both in order to produce their intended outcomes and because games should be those things. They should also be respectful of the emotional responses of players, especially if they are to be used in educational settings. Biotic games should not cause the players undue discomfort. Furthermore, the organized use of such games should be optional; students are exempted from classroom dissections, for instance, for emotional reasons, and there should be similar exemptions available to individuals who feel uncomfortable playing or building biotic games. If these and the above considerations are taken seriously, biotic games stand to uphold both the values of ethics and scientific practice as well as values internal to the practice of playing and producing games.

We conclude that, as yet, there are no persuasive objections in principle to biotic games, as they are found in Riedel-Kruse's work, and, moreover, that they can plausibly result in new, interesting, and productive forms of research, education, and entertainment. Moreover, since there is reasonable evidence that game-playing can enhance learning and since the public at large has an interest in a scientifically literate citizenry, we believe that efforts to use biotic games as a means of disseminating knowledge should be pursued, although certainly within the limits of both ethical recommendations and strong public objection. With this in mind, we recommend cautious and continued work on the development and use of biotic games, as well as efforts to observe and quantify their impact.

Disclosure

One of the authors, Ingmar Riedel-Kruse, owns a patent on biotic games and leads the lab discussed in this article that develops biotic games at Stanford University.

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List of Online Sources for Comments on Biotic Games

The following is the complete list, with URLs, of the sites from which we collected comments. Since the time we collected our data, many more comments have been added, and several of these pages are no longer accessible. Portable document format versions of the pages and our raw data are available upon request.

D. Pescovitz, "Videogames with Paramecia Players," *Boingboing*, January 19, 2011, http://boingboing.net/2011/01/19/video-games-with-para.html.

E. A. Moore, "Biotic' Video Games: Play with Microorganisms," *CNET News*, January 14, 2011, http://news.cnet. com/8301-27083_3-20028589-247.html.

"Forget Nintendo 3DS, Biotic Video Games May Be the Future," *Aussie Gamer*, January 31, 2011, http://aussie-gamer.com/ forget-nintendo-3ds-biotic-video-games-future/.

J. Presler, "Biotic Games Played with Living Micro-organisms," *GamrFeed*, January 31, 2011, http://gamrfeed.vgchartz.com/ story/83809/biotic-games-played-with-living-micro-organisms/.

J. Schell, "Biotic Games," *Gamepocalypse Now*, January 24, 2011. http://gamepocalypsenow.blogspot.com/2011/01/biotic-games.html/.

labonachipVideos, "Biotic Games—Movie 1 of 3," You-Tube, November 19, 2010, http://www.youtube.com/ all_comments?v=Pdx7BkYSCq4.

"More Than a Game: Researchers Design Video Games that Feature Real Microorganisms," *Scientific American*, January 20, 2011, http://www.scientificamerican.com/blog/post.cfm?id=morethan-a-game-researchers-design-2011-01-20#comments. "New Video Game Played with Living Organisms" (video), *Abovetopsecret.com*, January 31, 2011, http://www.abovetopsecret.com/forum/thread657487.

"Paramecium Video Games," *The Guardian*, January 19, 2011, http://www.guradian.co.uk/science/punctuated-equilibrium/2011/jan/19/1.

"Play Pacman, Pinball, and Pong with a Paramecium," *Slashdot*, January 15, 2011, http://science.slashdot.org/story/11/01/15/149225/ Play-Pacman-and-Pong-With-A-Paramecium#comments.

S. Ceurstemont, "Play Pacman, Pinball and Pong with a Paramecium," *New Scientist*, January 14, 2011, http://www.newscientist.com/blogs/nstv/2011/01/play-pacman-pinball-and-pong-with-a-paramecium.html.

Stanford University, "The Bold New World of Biotic Games," YouTube, January 11, 2011, http://www.youtube.com/all_comments?v=f2Ux4pQH7KY.

T. Staedter. "Video Game Stars Paramecium as Protagonist," *Discovery News*, January 19, 2011, https://news.discovery.com/tech/video-game-stars-paramecium-as-protagonist. html#view-comments/. (Lebanon, NH: University Press of New England, 2007), 150-54.

20. Several comments referred to the 2009 film *Gamer*, which depicted convicts controlled by "players" forced to fight to the death to secure their freedom.

21. F. Furger and F. Fukuyama, "A Proposal for Modernizing the Regulation of Human Biotechnologies," *Hastings Center Report* 37, no. 4 (2007): 16-20.

22. S. Schuchat, "Why GloFish Won't Glow in California," *San Francisco Chronicle*, December 17, 2003.

23. N. L. Carnagey, C. A. Anderson, and B. J. Bushman, "The Effect of Video Game Violence on Physiological Desensitization to Real Life Violence," *Journal of Experimental Social Psychology* 43 (2007): 489-96; B. Bastian, J. Jetten, and H. R. M. Radke, "Cyber-Dehumanization: Violent Video Game Play Diminishes our Humanity," *Journal of Experimental Social Psychology* 48 (2011): 486-91.

24. M. K. Cho et al., "Ethical Considerations in Synthesizing a Minimal Genome," *Science* 286 (1999): 2087-90; M. A. Bedau et al., "Social and Ethical Checkpoints for Bottom-up Synthetic Biology, or Protocells," *Systems and Synthetic Biology* 3 (2009): 65-75.

25. L. Gruen, "The Moral Status of Animals," *Stanford Encyclopedia of Philosophy*, 2010, http://plato.stanford.edu/entries/ moral-animal/.

26. P. Low, "Cambridge Declaration on Consciousness," paper presented at the Francis Crick Memorial Conference on Consciousness in Human and Non-Human Animals, Churchill College, University of Cambridge, July 7, 2012, http://fcmconference.org/img/CambridgeDeclarationOn-Consciousness.pdf.

27. P. Singer, "All Animals Are Equal"; T. Regan, *The Case for Animal Rights* (Berkeley, CA: University of California Press, 1983).

28. S. Schuchat. "Why GloFish Won't Glow in California."

29. B. Suits, "What Is a Game?," *Philosophy of Science* 34 no. 2 (1967): 148-56.

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31. T. W. Malone, "Toward a Theory of Intrinsically Motivating Instruction," *Cognitive Science* 4 (1981): 333-69; D. W. Shaffer, *How Computer Games Help Children Learn* (New York: Palgrave MacMillan, 2006), 131-32.

32. J. Huizinga, Homo Ludens: A Study of the Play-Element in Culture, trans. R. F. C. Hull (Boston: Beacon Hill Press, 1955); D. Dombrowski, Contemporary Athletics and Ancient Greek Ideals (Chicago: University of Chicago Press, 2009), 75-76; R. Feezell, Sport, Play and Ethical Reflection (Chicago: University of Illinois Press, 2004).

33. K. Ginsburg, "The Importance of Play in Promoting Healthy Child Development and Maintaining Strong Parent-Child Bonds," *Pediatrics* 119, no. 1 (2007): 182-91; F. Gardner et al., "The Role of Mother-Child Joint Play in the Early Development of Children's Conduct Problems," *Social Development* 12 no. 3 (2003): 361-78.