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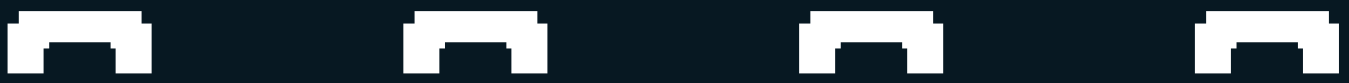
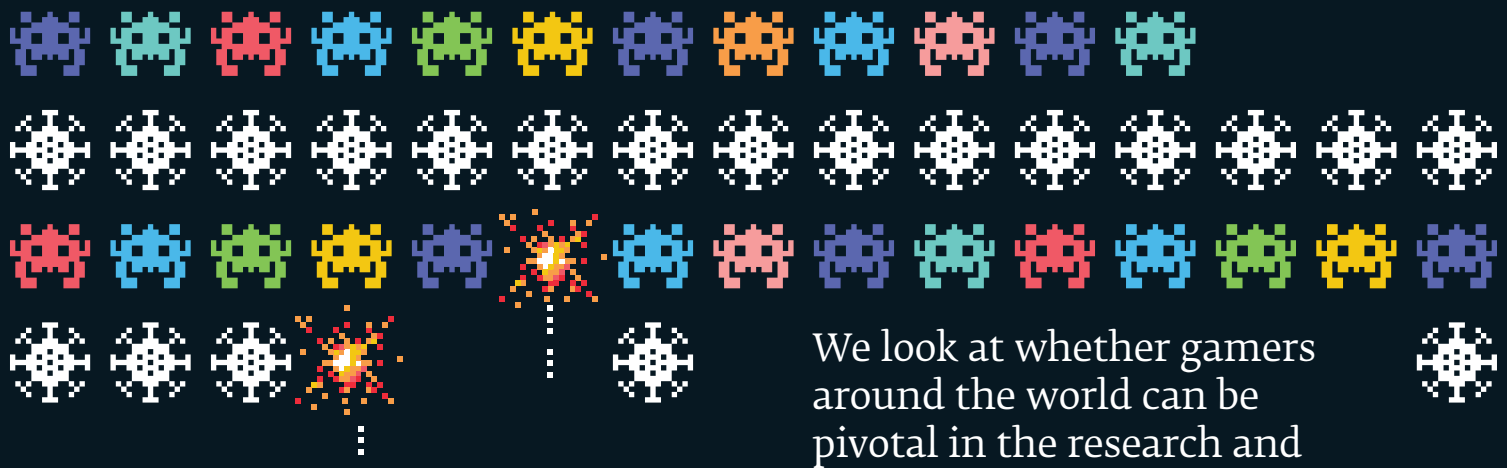


CAN COMPUTER GAMES REVOLUTIONISE PATHOLOGY?



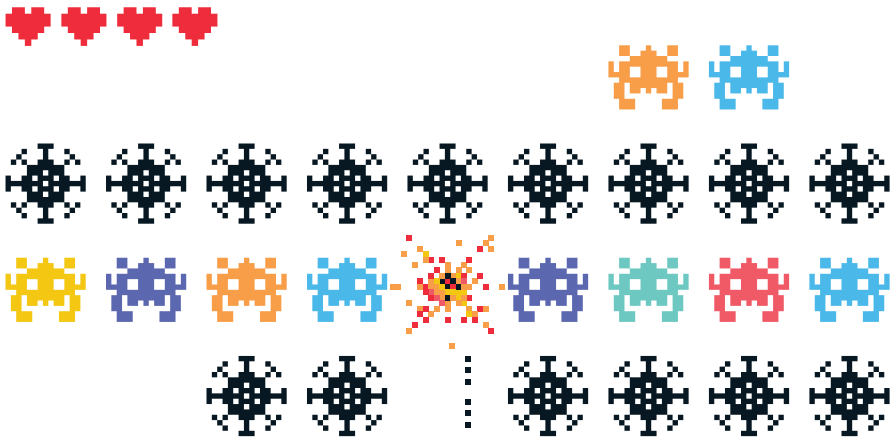
We look at whether gamers around the world can be pivotal in the research and innovation that forms the basis of our fight against diseases.

Since the beginning of the pandemic, scientists from all around the world have worked hard to better understand COVID-19. Immunologists in particular have been at the forefront, building crucial knowledge on how the virus triggers our immune response and why this process differs so widely between people.

Researchers at the Francis Crick Institute, King's College London and Guy's and St Thomas' NHS Foundation Trust have been conducting highly detailed analysis of the composition of immune cells in the blood of patients with COVID-19. Through their study, called Covid-IP, their goal was to see how the immune system responds to coronavirus and whether it is possible to predict at an early stage who might need additional treatments or critical care.

They managed to identify an "immune signature" that works as a good predictor of disease severity. Furthermore, their findings have also informed clinical trials into drugs that promote T cell function.

"During the COVID pandemic, we conducted important work to try to understand why some people get sicker than others – our hypothesis being that understanding the immune response would be key to understanding the disease. With our Covid-IP project, we were able to build a very comprehensive understanding of how the immune response worked and how this related to disease severity", says Adam



Laing, Postdoctoral Research Associate at King's College London.

New tools

However, this ground-breaking work was only possible because the Covid-IP team reorganised the lab to dedicate all its efforts to the pandemic. This kind of work requires analysing large sets of data, which can be very time consuming.

"The immune system is unique in the sense that we can study very many different cell types from a single blood sample. We use flow cytometry to interrogate proteins on the surface of immune cells and to classify them in different groups. This is a powerful tool in immunological research, but the data it generates are complex, with many different parameters related to every single cell. To analyse these data quickly, we relied on the collective talents of a large team working full time on this, but this is not always possible, and so we need to develop new tools", Adam Laing points out.

This is where computer games can come in. The Covid-IP team has received help from Project Discovery, an in-game citizen science project that exists within the popular massively multiplayer online computer game, EVE Online, developed by CCP Games.

Previously, this game had been used as part of a collaboration with the Human Protein Atlas as well as by the University of Geneva to help identify new exoplanets and aid in improving the mapping of millions of proteins in the human body, by using the manpower of hundreds of thousands of players to provide large-scale data analysis.

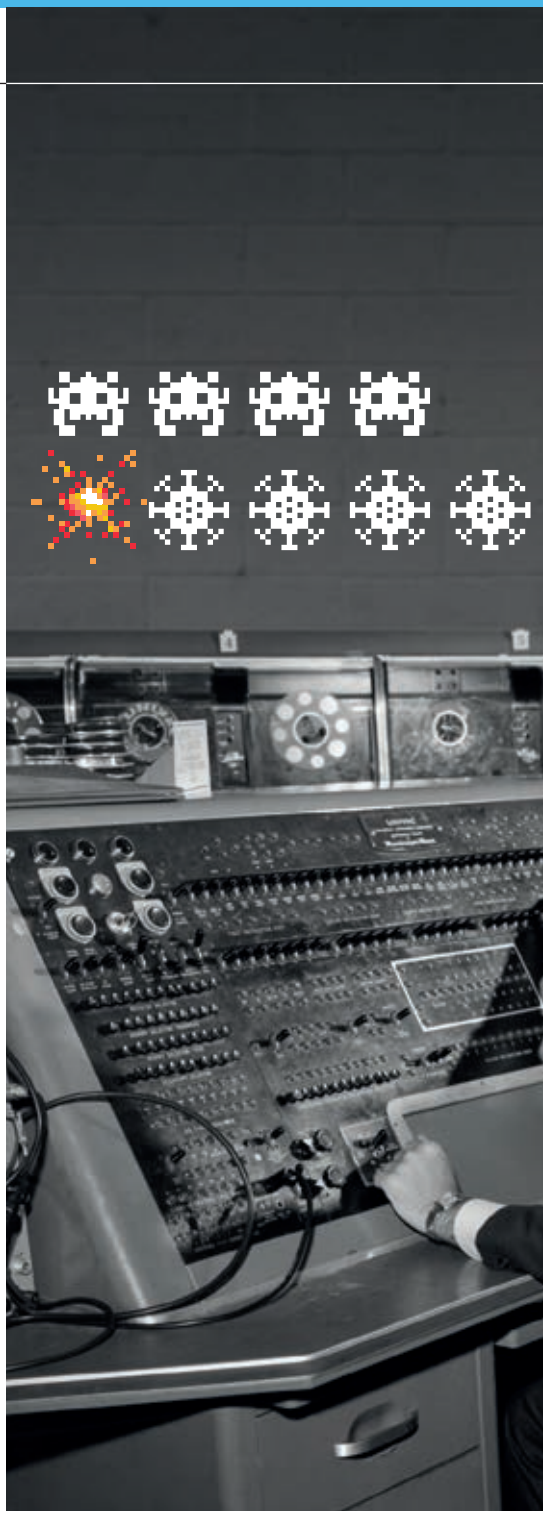
Attila Szantner, CEO and co-founder of Massively Muliplayer Online Science (MMOS), says: "Although citizen science is an amazing concept, in reality many initiatives are struggling with long-term user engagement because the tasks can be quite repetitive and people stop taking part. We founded MMOS to solve this problem. We came up with the idea of embedding mini-games focused on these citizen science tasks into already existing major videogames to answer specific research questions.

He continues: "These mini-games should be designed by industry experts who know the gaming community and who can work hand in hand with researchers. We identified CCP Games as an ideal partner for several reasons, one being EVE is a science fiction game and this theme creates many opportunities to connect with very different kinds of research. CCP immediately embraced the idea, and half a year later Project Discovery was born."

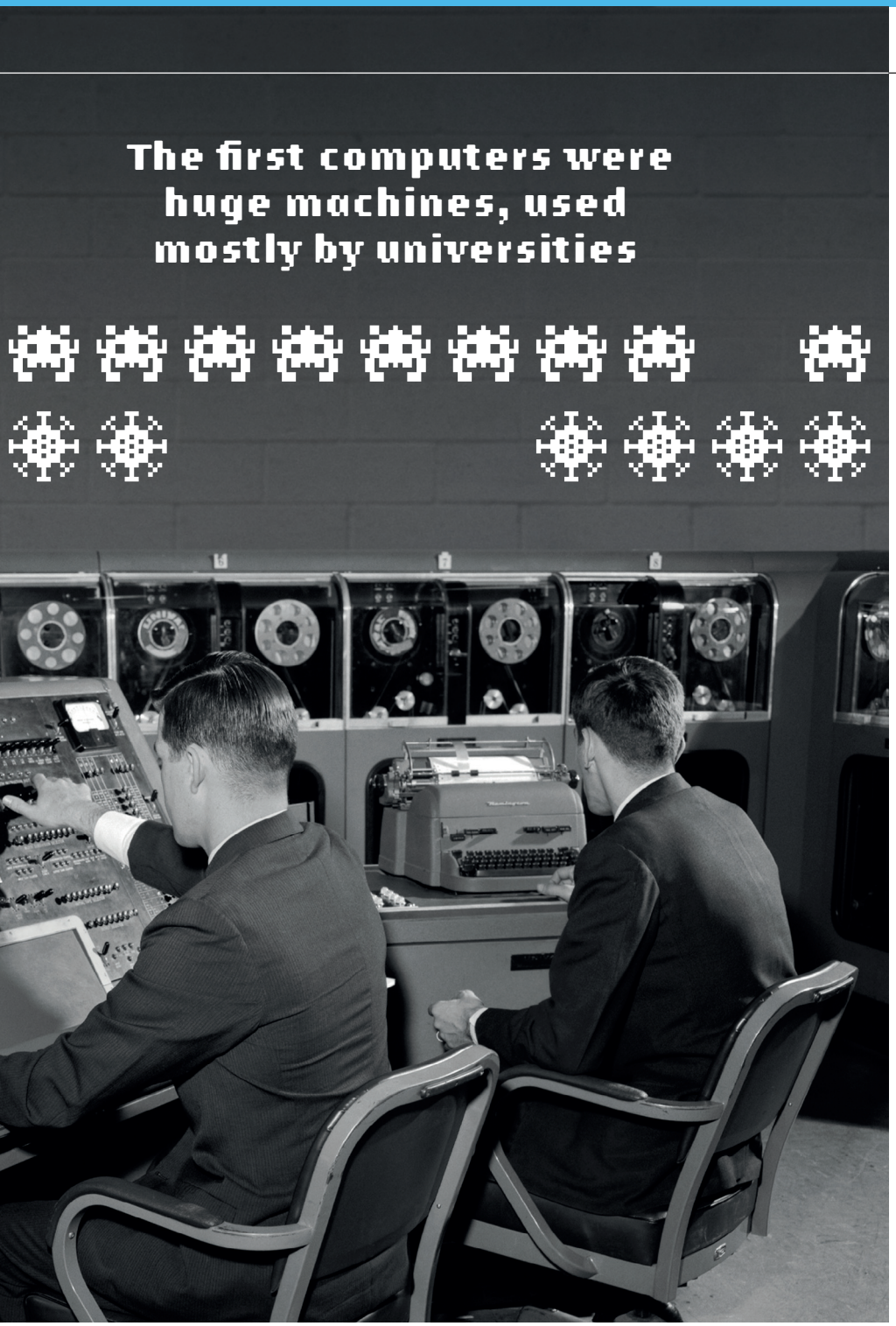
At the beginning of the pandemic, the infrastructure was already in place, and the Project Discovery team decided early on that they wanted to join the fight against COVID-19. It took only 5 weeks from idea to launch, joining forces with the research team and developing the game.

Understand complex data

EVE players were mobilised to analyse large sets of data to build a picture of how the virus affects the immune system, via flow cytometry, and therefore teach a learning algorithm to automate the process entirely. Their efforts will help immunologists on the Covid-IP team to understand and characterise immune responses associated with the disease.



The project is also shedding light on how citizen science and computer games can contribute more widely to the research world. "In communities, such as EVE online, we find well-organised people that share a few attributes," says Max Birk, an Assistant Professor in the Department of Industrial Design at Eindhoven University of Technology. "They understand complex data, and they know how to collaborate and build out functional hierarchies. The openness to respect games as contributors is where I see the innovation here. Instead



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of disregarding game play as child's play, the research sees gaming as a way to identify a group with similar interests that matched their research problem using games in the research world."

The origins

Using video games to advance research projects with complex data analysis is not new. Citizen science has successfully leveraged game behaviour before to support a number of studies. One of the earliest and most successful examples is FoldIt – an online puzzle about protein folding, developed by the University of Washington. It asks players to fold proteins and then selects novel contributions to be further analysed by experts. "The example of FoldIt, where players were able to solve how one HIV protein folds is very interesting as it shows how the collective brainpower of many gamers who see things in different ways can help advance research" says Mary Ann Comunale, an Assistant Professor in Microbiology and Immunology at Drexel University College of Medicine.

While computer games and online community have been used to facilitate data analysis and to understand biological processes, other uses are also emerging.

Innovative iuses

Scientists are, for example, looking at whether they can leverage and analyse players' behaviours during games to identify early indicators of diseases, to help support diagnosis, or track recovery. To do

A SHORT HISTORY OF VIDEO GAMES

The history of video games is tightly linked to innovative scientific research. The early computer programmers were not just wasting time or looking for new ways to have fun by creating games. They had practical reasons to do so.

During the 1940s and 1950s, the first computers were huge machines, used mostly by universities. People had no idea what they could do, so creating games was a way to raise awareness and gain support. One of the earliest games was William Higinbotham's Tennis for Two, in 1958.

Furthermore, at the time, developing games was interesting for the early computer programmers as it allowed them to challenge the capabilities of these machines.

One of the first and most ground-breaking computer games was created at Massachusetts Institute of Technology in the 1960s. A team of students worked with a PDP-1 computer to create a programme with three aims: to use as many of the computer's resources as possible, to remain interesting after repeated viewings and to be interactive. This paved the way for Spacewar, a game involving a duel between two spaceships. But it was not until TVs became more widely used and the public was able to access these new technologies, that the development of video games really took off.

so, they need to gain an understanding of cognitive, affective, and social skills in very large samples of players.

The game Sea Hero Quest, developed by Alzheimer's Research UK in 2016, is an example of this. Researchers collect data on players' navigational abilities, which start to decline in individuals who suffer from dementia. The goal is to help scientists understand in detail how our brains navigate space, and to build the largest crowd-sourced database on human spatial navigation. The scientists used the data to build a canvas that allows them to understand individual behaviours and to create a benchmark to help determine what goes wrong in the brain for people with dementia. As a 2019 study published in *PNAS* suggests, the game may prove useful as a tool to aid diagnosis and to accurately classify spatial impairments in people at high risk of Alzheimer's disease. The goal, however, is not to use the game on its own, but rather in addition to all the traditional tests and neurological exams.

"Today, we leave so many digital traces that are reflective of cognitive, social, and affective processes – and we can leverage those to construct markers of behaviour that are indicative of our health. I think the interest in these fields is massively growing, but right now we are still a bit overwhelmed by how much data we can gather in how little time. As a diagnostic tool, I think digital data provide supplementary information – I don't think we will see accepted diagnosis just based on digital data in the foreseeable future for good reasons," says Max Birk.

Educating

However, computer games are not just an innovative way to get scientific results. They are also key to educate the public, improve science literacy and interest in research. By playing or simply by learning how games can help advance research, people may recognise the importance of science and see it as more accessible.

We leave so many digital traces that are reflective of cognitive, social, and affective processes

This is beneficial to society as a whole, but some initiatives have focused on using games to target specific demographics. At Drexel University, games are important tools to teach students about science. "As educators, we have focused on the use of mobile app games. Our Institute for Molecular Medicine and Infectious Diseases at Drexel's College of Medicine has designed several of these games. We are conducting research on their use in graduate and undergraduate populations. For example, our game Hep B-Ware teaches students about the lifecycle of the hepatitis B virus. It's all about targeting the game so it helps students understand complex topics they might be having a hard time visualising", says Mary Ann Comunale.

These tools may also be very useful in a clinical setting, to promote collaboration and efficient decision-making. "Games can be helpful to train medical students in decision-making processes and coordination of care. For example, a game called ElderQuest is teaching medical students to care for geriatric patients, by teaching them how to coordinate care and use a team-based approach to achieve the best outcome," she adds.

Future collaboration

While computer games and citizen science initiatives in general are far from being systematically integrated into research projects, their importance is gradually being recognised. Many challenges remain, notably the fact that to be successful projects involving video games require experience, finances, and teams that produce games that people actually want to play. There are hopes for the future, however. "In the coming years we might see video game companies open up again to work with researchers and scientists on larger societal issues. Currently, the history of using video games as a scapegoat for societal issues and the legitimate revenue focus of game companies makes it challenging to collaborate – but we see more and more collaboration emerge and that's wonderful to see," says Max Birk.

These collaborations have the potential to have an impact on a wide range of scientific topics, from mental health, genetics and space science to emerging diseases, such as COVID-19, always with the objective of generating results, but also raising public awareness. "For example, we have seen how vaccines are essential to save lives, but also how conspiracy theories can threaten these efforts. Games can be an effective tool to combat this by engaging the public and getting them to understand how the immune system– or a range of other topics – works," Adam Laing concludes. BMS

GAME OVER