UNIVERSITY OF HOHENHEIM

Akademisches Auslandsamt | Referat Sprachenzentrum (AA4)

Matriculation number:

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Last name:

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First name:

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Please fold

English for Natural Sciences, UNIcert III, C1 ***Date***

Topic

Cloning and 3D Bioprinting

➤ **Situation or scenario**

You are a journalist for a scientific magazine, which is looking into advancements in cloning and bioprinting. You have been assigned to research the merits of and issues surrounding these technologies and to compile both a written report and a presentation of your findings. Your editor-in-chief is interested in your informed stance, advocating one biotechnical advancement over the other, and in their applications, and ethical considerations. You will then present your findings at Harvard University's Annual Bioethics Conference.

➤ **Tasks and goals**

Your task is (1) to listen to relevant information and answer associated questions; (2) to read additional information and answer related questions; then you will be asked (3) to research as much information as possible on the subject to prepare and produce a report on your findings; and (4) present your report to a panel and respond to their questions about your research.

LISTENING	READING	WRITING	SPEAKING	TOTAL
Introduction of topic	Development of topic	Case study - scenario & report	Case study - presentation	Exam
45 min	*45 min*	*120 min*	*30 min*	*4 hours*
25 points	**25 points**	**25 points**	**25 points**	**100 points**

I give my assurance that I will complete the exam personally and independently and will not use any unauthorized aids or tools.

Unterschrift Prüfling:

Examiner's signatures:

1st Examiner

2nd Examiner

For Examiner's Use Only

Overall Grading scheme

- **25 Punkte –Skala pro Fertigkeit**

Zwischen	25	und	25	die Note	**1,0**	Sehr gut
	24		24		**1,3**	
	22		23		**1,7**	Gut
	21		21		**2,0**	
	20		20		**2,3**	
	19		19		**2,7**	Befriedigend
	17		18		**3,0**	
	16		16		**3,3**	
	15		15		**3,7**	Ausreichend
	13		14		**4,0**	
	10		12		**5,0**	Nicht ausreichend
	8		9			
	6		7			
	4		5			
	2		3			
	0		1			

- **100 Punkte - Skala**

Zwischen	96	und	100	die Note	**1,0**	Sehr gut
	91		95		**1,3**	
	86		90		**1,7**	Gut
	81		85		**2,0**	
	76		80		**2,3**	
	71		75		**2,7**	Befriedigend
	66		70		**3,0**	
	61		65		**3,3**	
	56		60		**3,7**	Ausreichend
	50		55		**4,0**	
	41		49		**5,0**	Nicht ausreichend
	33		40			
	25		32			
	16		24			
	8		15			
	0		7			

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➤ **Tasks and goals**

Your task in this section of the exam is to listen to relevant information on the topic and answer the associated questions.

LISTENING				
Introduction of topic *45 min* **25 points**				

Examiner's signatures :

1st Examiner

2nd Examiner

PART 1: LISTENING COMPREHENSION

The following audio file will introduce the topic of this exam:

Cloning and 3D Bioprinting

Listen to the audio clip and take notes in the space provided below. Please take notes only in this examination booklet. Your notes will not be graded. Then read the comprehension questions and listen to the audio again. Answer the associated comprehension questions in paragraph form, using complete sentences. You will have 45 minutes to complete this section of the test which covers 25% of the overall exam grade.

What is Human Cloning? How to Clone a Human [00:06:38]

- David Bird Science, https://www.youtube.com/watch?v=VL8lw4i5qkM

Notes (You may also write on the back of this sheet.)

LISTENING COMPREHENSION QUESTIONS

1. What analogy does he use to explain what a clone is, and what is exactly the same in both the clone and its donor? (4 points)

2. How does cloning work? (5 points)

3. Describe what you understand by the process as “human cloning as an interventive activity” compared to “in the identical twin sort of way”? (4 points)

4. In which way is a cloned copy not identical to its donor? (4 points)

5. In order from best to worst, list the living organisms mentioned in the video that can be cloned. (5 points)

6. Inferring from what is explained in the video, why are these organisms in this particular order? (4 points)

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➤ **Tasks and goals**

Your task in this section of the exam is to read additional information on the topic and answer the related questions.

	READING			
	Development of topic *45 min* **25 points**			

Examiner's signatures :

1st Examiner

2nd Examiner

READING COMPREHENSION

The following article will develop the topic of this exam:

Cloning and 3D Bioprinting

Read the article. Take notes only in this examination booklet. Your notes will not be graded. Then answer the associated comprehension questions concisely using complete sentences. You will have 45 minutes to complete this section of the test which covers 25% of the overall exam grade.

Medical Applications for 3D Printing: Current and Projected Uses

- Ventola CL. Medical Applications for 3D Printing: Current and Projected Uses. P T. 2014 Oct;39 (10):704-11. PMID: 25336867; PMCID: PMC4189697.

Notes (You may also write on the back of this sheet.)

Article

Medical Applications for 3D Printing: Current and Projected Uses

WHAT IS 3D PRINTING?

Three-dimensional (3D) printing is a manufacturing method in which objects are made by fusing or depositing materials—such as plastic, metal, ceramics, powders, liquids, or even living cells—in layers to produce a 3D object.[1,8,9] This process is also referred to as additive manufacturing (AM), rapid prototyping (RP), or solid free-form technology (SFF).[6] Some 3D printers are similar to traditional inkjet printers; however, the end product differs in that a 3D object is produced.[1] 3D printing is expected to revolutionize medicine and other fields, not unlike the way the printing press transformed publishing.[1]

There are about two dozen 3D printing processes, which use varying printer technologies, speeds, and resolutions, and hundreds of materials.[9] These technologies can build a 3D object in almost any shape imaginable as defined in a computer-aided design (CAD) file (Figure 1).[9] In a basic setup, the 3D printer first follows the instructions in the CAD file to build the foundation for the object, moving the printhead along the x–y plane.[5] The printer then continues to follow the instructions, moving the printhead along the z-axis to build the object vertically layer by layer.[5] It is important to note that two-dimensional (2D) radiographic images, such as x-rays, magnetic resonance imaging (MRI), or computerized tomography (CT) scans, can be converted to digital 3D print files, allowing the creation of complex, customized anatomical and medical structures (Figure 2).[3,5,10]

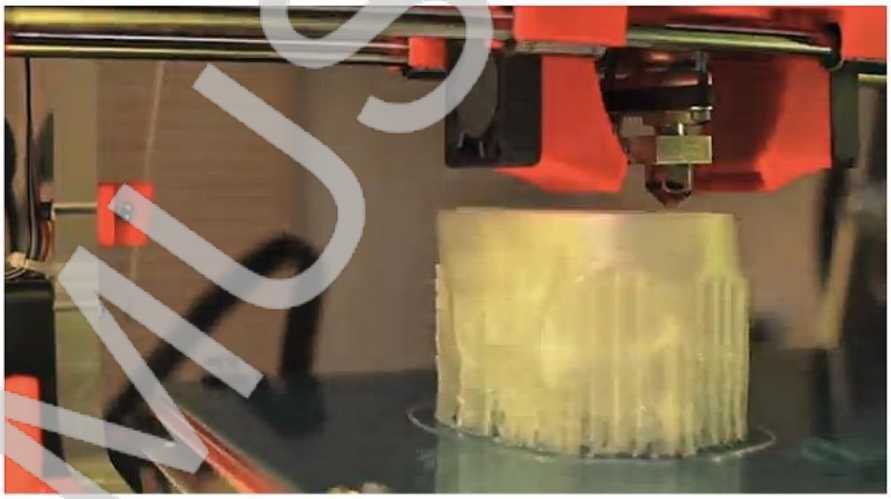

Figure 1 A 3D printer uses instructions in a digital file to create a physical object.[12]

OVERVIEW OF CURRENT APPLICATIONS

Commercial Uses

3D printing has been used by the manufacturing industry for decades, primarily to produce product prototypes.[1,9] Many manufacturers use large, fast 3D printers called “rapid prototyping machines” to create models and molds.[11] A large number of .stl files are available for commercial purposes.[1] Many of these printed objects are comparable to traditionally manufactured items.[1]

Companies that use 3D printing for commercial medical applications have also emerged.[2] These include: Helisys, Ultimateker, and Organovo, a company that uses 3D printing to fabricate living human tissue.[2] At present, however, the impact of 3D printing in medicine remains small.[1] 3D printing is currently a $700 million industry, with only $11 million (1.6%) invested in medical applications.[1] In the next 10 years, however, 3D printing is expected to grow into an $8.9 billion industry, with $1.9 billion (21%) projected to be spent on medical applications.[1]

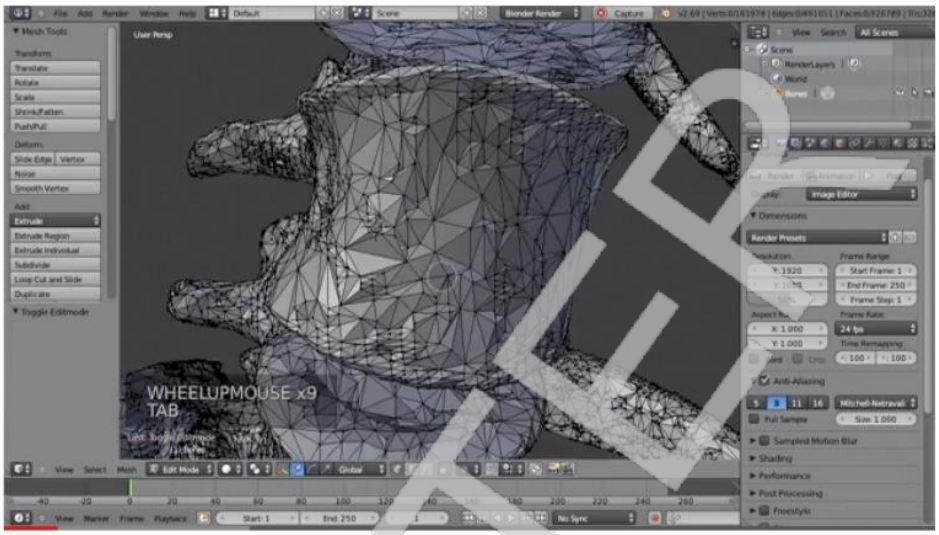

Figure 2 Radiographic images can be converted to 3D print files to create complex, customized anatomical and medical structures.[12]

Consumer Uses

3D printing technology is rapidly becoming easy and inexpensive enough to be used by consumers.[9,11] The accessibility of downloadable software from online repositories of 3D printing designs has proliferated, largely due to expanding applications and decreased cost.[2,4,11] It is now possible to print anything, from guns, clothing, and car parts to designer jewelry.[2] Thousands of premade designs for 3D items are available for download, many of them for free.[11]

Since 2006, two open-source 3D printers have become available to the public, Fab@Home (www.fabathome.org) and RepRap (www.reprap.org/wiki/RepRap).[6,9] The availability of these open-source printers greatly lowered the barrier of entry for people who want to explore and develop new ideas for 3D printing.[9] These open-source systems allow anyone with a budget of about $1,000 to build a 3D printer and start experimenting with new processes and materials.[9]

This low-cost hardware and growing interest from hobbyists has spurred rapid growth in the consumer 3D printer market.[11] A relatively sophisticated 3D printer costs about $2,500 to $3,000, and simpler models can be purchased for as little as $300 to $400.[8,11] For consumers who have difficulty printing 3D models themselves, several popular 3D printing services have emerged, such as Shapeways, (www.shapeways.com), Thingiverse (www.thingiverse.com), MyMiniFactory (www.myminifactory.com), and Threeding (www.threeding.com).[11]

BENEFITS OF 3D PRINTING IN MEDICAL APPLICATIONS

Customization and Personalization

The greatest advantage that 3D printers provide in medical applications is the freedom to produce custom-made medical products and equipment.[3] For example, the use of 3D printing to customize

prosthetics and implants can provide great value for both patients and physicians.[3] In addition, 3D printing can produce made-to-order jigs and fixtures for use in operating rooms.[4] Custom-made implants, fixtures, and surgical tools can have a positive impact in terms of the time required for surgery, patient recovery time, and the success of the surgery or implant.[4] It is also anticipated that 3D printing technologies will eventually allow drug dosage forms, release profiles, and dispensing to be customized for each patient.[5]

Increased Cost Efficiency

Another important benefit offered by 3D printing is the ability to produce items cheaply.[1] Traditional manufacturing methods remain less expensive for large-scale production; however, the cost of 3D printing is becoming more and more competitive for small production runs.[1] This is especially true for small-sized standard implants or prosthetics, such as those used for spinal, dental, or craniofacial disorders.[3] The cost to custom-print a 3D object is minimal, with the first item being as inexpensive as the last.[1] This is especially advantageous for companies that have low production volumes or that produce parts or products that are highly complex or require frequent modifications.[4]

3D printing can also reduce manufacturing costs by decreasing the use of unnecessary resources.[5] For example, a pharmaceutical tablet weighing 10 mg could potentially be custom-fabricated on demand as a 1-mg tablet.[5] Some drugs may also be printed in dosage forms that are easier and more cost-effective to deliver to patients.[5]

Enhanced Productivity

"Fast" in 3D printing means that a product can be made within several hours.[4] That makes 3D printing technology much faster than traditional methods of making items such as prosthetics and implants, which require milling, forging, and a long delivery time.[3] In addition to speed, other qualities, such as the resolution, accuracy, reliability, and repeatability of 3D printing technologies, are also improving.[3]

Democratization and Collaboration

Another beneficial feature offered by 3D printing is the democratization of the design and manufacturing of goods.[4] An increasing array of materials is becoming available for use in 3D printing, and they are decreasing in cost.[4] This allows more people, including those in medical fields, to use little more than a 3D printer and their imaginations to design and produce novel products for personal or commercial use.[4]

The nature of 3D printing data files also offers an unprecedented opportunity for sharing among researchers.[6] Rather than trying to reproduce parameters that are described in scientific journals, researchers can access downloadable .stl files that are available in open-source databases.[6] By doing so, they can use a 3D printer to create an exact replica of a medical model or device, allowing the precise sharing of designs.[6] Toward this end, the National Institutes of Health established the 3D Print Exchange (3dprint.nih.gov) in 2014 to promote open-source sharing of 3D print files for medical and anatomical models, custom labware, and replicas of proteins, viruses, and bacteria (Figure 3).[12]

MEDICAL APPLICATIONS FOR 3D PRINTING

3D printing has been applied in medicine since the early 2000s, when the technology was first used to make dental implants and custom prosthetics.[6,10] Since then, the medical applications for 3D printing have evolved considerably. Recently published reviews describe the use of 3D printing to produce bones, ears, exoskeletons, windpipes, a jaw bone, eyeglasses, cell cultures, stem cells, blood

vessels, vascular networks, tissues, and organs, as well as novel dosage forms and drug delivery devices.[1,3,11] The current medical uses of 3D printing can be organized into several broad categories: tissue and organ fabrication; creating prosthetics, implants, and anatomical models; and pharmaceutical research concerning drug discovery, delivery, and dosage forms.[2] A discussion of these medical applications follows.

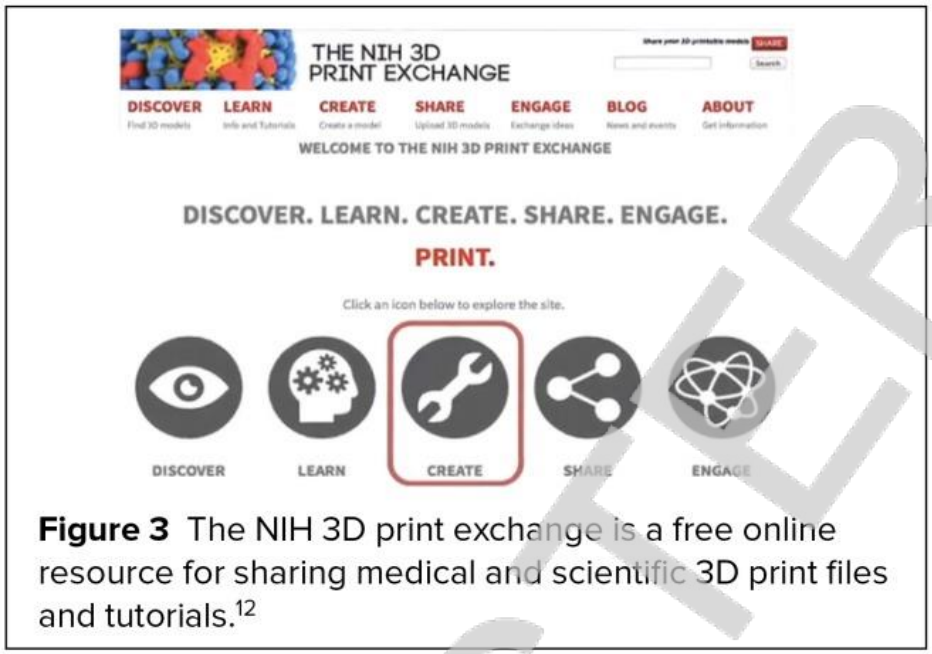

Figure 3 The NIH 3D print exchange is a free online resource for sharing medical and scientific 3D print files and tutorials.[12]

Bioprinting Tissues and Organs

Tissue or organ failure due to aging, diseases, accidents, and birth defects is a critical medical problem.[10] Current treatment for organ failure relies mostly on organ transplants from living or deceased donors.[10] However, there is a chronic shortage of human organs available for transplant.[1,10] In 2009, 154,324 patients in the U.S. were waiting for an organ.[10] Only 27,996 of them (18%) received an organ transplant, and 8,863 (25 per day) died while on the waiting list.[10] As of early 2014, approximately 120,000 people in the U.S. were awaiting an organ transplant.[1] Organ transplant surgery and follow-up is also expensive, costing more than $300 billion in 2012.[10] An additional problem is that organ transplantation involves the often difficult task of finding a donor who is a tissue match.[1] This problem could likely be eliminated by using cells taken from the organ transplant patient's own body to build a replacement organ.[1,13] This would minimize the risk of tissue rejection, as well as the need to take lifelong immunosuppressants.[1,13]

Although 3D bioprinting systems can be laser-based, inkjet-based, or extrusion-based, inkjet-based bioprinting is most common.[13] This method deposits "bioink," droplets of living cells or biomaterials, onto a substrate according to digital instructions to reproduce human tissues or organs.[13] Multiple printheads can be used to deposit different cell types (organ-specific, blood vessel, muscle cells), a necessary feature for fabricating whole heterocellular tissues and organs.[13] A process for bioprinting organs has emerged: 1) create a blueprint of an organ with its vascular architecture; 2) generate a bioprinting process plan; 3) isolate stem cells; 4) differentiate the stem cells into organ-specific cells; 5) prepare bioink reservoirs with organ-specific cells, blood vessel cells, and support medium and load them into the printer; 6) bioprint; and 7) place the bioprinted organ in a bioreactor prior to transplantation.[13] Laser printers have also been employed in the cell printing process, in which laser energy is used to excite the cells in a particular pattern, providing spatial control of the cellular environment.[13]

Although tissue and organ bioprinting is still in its infancy, many studies have provided proof of concept. Researchers have used 3D printers to create a knee meniscus, heart valve, spinal disk, other types of cartilage and bone, and an artificial ear.[4,6,7] Cui and colleagues applied inkjet 3D printing technology to repair human articular cartilage.[13] Wang et al used 3D bioprinting technology to deposit different cells within various biocompatible hydrogels to produce an artificial liver.[13] Doctors at the University of Michigan published a case study in the *New England Journal of Medicine* reporting that use of a 3D printer and CT images of a patient's airway enabled them to fabricate a precisely modeled, bioresorbable tracheal splint that was surgically implanted in a baby with tracheobronchomalacia.[7] The baby recovered, and full resorption of the splint is expected to occur within three years.[7]

Challenges in Building 3D Vascularized Organs

Proof-of-concept studies regarding bioprinting have been performed successfully, but the organs that have been produced are miniature and relatively simple.[1,9,10] They are also often avascular, aneural, alymphatic, thin, or hollow, and are nourished by the diffusion from host vasculature.[1,6,9,10] However, when the thickness of the engineered tissue exceeds 150–200 micro meters, it surpasses the limitation for oxygen diffusion between host and transplanted tissue.[10] As a result, bioprinting complex 3D organs will require building precise multicellular structures with vascular network integration, which has not yet been done.[6]

Most organs needed for transplantation are thick and complex, such as the kidney, liver, and heart.[11] Cells in these large organ structures cannot maintain their metabolic functions without vascularization, which is normally provided by blood vessels.[13] Therefore, functional vasculature must be bioprinted into fabricated organs to supply the cells with oxygen/gas exchange, nutrients, growth factors, and waste-product removal—all of which are needed for maturation during perfusion.[10,13] Although the conventional tissue engineering approach is not now capable of creating complex vascularized organs, bioprinting shows promise in resolving this critical limitation.[10] The precise placement of multiple cell types is required to fabricate thick and complex organs, and for the simultaneous construction of the integrated vascular or microvascular system that is critical for these organs to function.[10]

Customized Implants and Prostheses

Implants and prostheses can be made in nearly any imaginable geometry through the translation of x-ray, MRI, or CT scans into digital .stl 3D print files.[2,3,6] In this way, 3D printing has been used successfully in the health care sector to make both standard and complex customized prosthetic limbs and surgical implants, sometimes within 24 hours.[3,7,9] This approach has been used to fabricate dental, spinal, and hip implants.[3] Previously, before implants could be used clinically, they had to be validated, which is very time-consuming.[3]

The ability to quickly produce custom implants and prostheses solves a clear and persistent problem in orthopedics, where standard implants are often not sufficient for some patients, particularly in complex cases.[3] Previously, surgeons had to perform bone graft surgeries or use scalpels and drills to modify implants by shaving pieces of metal and plastic to a desired shape, size, and fit.[3,7] This is also true in neurosurgery: Skulls have irregular shapes, so it is hard to standardize a cranial implant.[3] In victims of head injury, where bone is removed to give the brain room to swell, the cranial plate that is later fitted must be perfect.[9] Although some plates are milled, more and more are created using 3D printers, which makes it much easier to customize the fit and design.[3]

BARRIERS AND CONTROVERSIES

Unrealistic Expectations and Hype

Despite the many potential advantages that 3D printing may provide, expectations of the technology are often exaggerated by the media, governments, and even researchers.[3] This promotes unrealistic projections, especially regarding how soon some of the more exciting possibilities—such as organ printing—will become a reality.[3] Although progress is being made toward these and other goals, they are not expected to happen soon.[3,4] 3D printing will require vision, money, and time for the technology to evolve into the anticipated applications.[3] While it is certain that the biomedical sector will be one of the most fertile fields for 3D printing innovations, it is important to appreciate what has already been achieved without expecting that rapid advances toward the most sophisticated applications will occur overnight.[3]

Safety and Security

3D printing has given rise to safety and security issues that merit serious concern.[8,11] 3D printers have already been employed for criminal purposes, such as printing illegal items like guns and gun magazines, master keys, and ATM skimmers.[7,11] These occurrences have highlighted the lack of regulation of 3D printing technology.[7] In theory, 3D printing could also be used to counterfeit substandard medical devices or medications.[12] Although 3D printing should not be banned, its safety over the long term will clearly need to be monitored.[7]

In 2012, in response to the news that a functioning plastic handgun had been 3D printed, several local and state legislators introduced bills banning access to this technology.[8] However, such fear-based policy responses could stifle the culture of openness necessary for 3D printing to thrive.[8] Such a ban could push 3D printing underground at the expense of important scientific, medical, and other advances.[8] There have already been reports of "garage biology" being conducted that could potentially lead to innovations in the life sciences.[8] However, it is being conducted in secrecy to avoid interference from law enforcement—even though the research is legal.[8]

READING COMPREHENSION QUESTIONS

1. What is "bioprinting" and how does it work? (4 points)

2. Describe the mechanism by which "bioprinting" works? (5 points)

3. Summarize the benefits 3D printing can offer in the medical field. Give a concrete example of each. (6 points)

4. What is the biggest issue to date with bioprinting living organs? Why is it a problem? (5 points)

5. Discuss why there is such a hype around 3D printing and bioprinting. Include evidence from throughout the article. (5 points)

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➤ **Tasks and goals**

Your task in this section of the exam is to research as much information as possible on the subject to prepare and produce a report on your findings.

		WRITING		
		Case study - scenario & report *120 min* **25 points**		

Examiner's signatures :

1st Examiner

2nd Examiner

PART 3: WRITING

Case study - Scenario and Report

Read, watch, and listen to background information which builds on the general theme of this exam. Please take notes on the following video and articles and do so only in this examination booklet. Your notes will not be graded. The background information and the scenario lead into the writing section of the test.

You are a journalist for a scientific magazine, and you have been asked to write a report outlining the merits of, and issues with, cloning and bioprinting. State your stance and support by citing from the studies you have read. Then, include a section in which you advocate one biotechnical advancement over the other, and discuss whether there are moral/ethical differences or similarities.

Your report structure must include the following

- Introduction, thesis statement and stance
- Findings
- Preferred technology
- Conclusion

You will have 120 minutes to study the research materials provided and to write your report.

LISTENING

- *What is Human Cloning? How to Clone a Human* [00:06:38]
  David Bird Science, https://www.youtube.com/watch?v=VL8lw4i5qkM

READING

- *Medical Applications for 3D Printing: Current and Projected Uses*
  Ventola CL. Medical Applications for 3D Printing: Current and Projected Uses. P T. 2014 Oct;39 (10):704-11. PMID: 25336867; PMCID: PMC4189697.

WRITING

- Seeker 24.12.2020, The first full-size 3D print of a human heart is here: https://www.youtube.com/watch?v=_rfeCSQxDBg
- Colossal Biosciences 07.04.2025, The Making of the Colossal Dire Wolves - World's First De-Extinction https://www.youtube.com/watch?v=F5uCuOwK_VE
- MIT Technology Review, 08.04.2025, Game of Clones: Colossal´s new wolves are cute, but are they dire?

Article:

Game of Clones: Colossal´s new wolves are cute, but are they dire?

Colossal Biosciences claims it has revived an extinct species, but scientists outside the company are skeptical.

By Antonio Regalado, April 8, 2025, MIT Technology Review

Andrew Zuckerman/Colossal Biosciences

Somewhere in the northern US, drones fly over a 2,000-acre preserve, protected by a nine-foot fence built to zoo standards. It is off-limits to curious visitors, especially those with a passion for epic fantasies or mythical creatures. The reason for such tight security? Inside the preserve roam three striking snow-white wolves—which a startup called Colossal Biosciences says are members of a species that went extinct 13,000 years ago, now reborn via biotechnology.

For several years now, the Texas-based company has been in the news for its plans to re-create woolly mammoths someday. But now it's making a bold new claim—that it has actually "de-extincted" an animal called the dire wolf. And that could be another reason for the high fences and secret location—to fend off scientific critics, some of whom have already been howling that the company is a "scam" perpetrating "elephantine fantasies" on the public and engaging in "pure hype."

Dire wolves were large, big-jawed members of the canine family. More than 400 of their skulls have been recovered from the La Brea Tar Pits in California. Ultimately they were replaced by smaller relatives like the gray wolf. In its effort to re-create the animal, Colossal says, it extracted DNA information from dire wolf bones and used gene editing to introduce some of those elements into cells from gray wolves. It then used a cloning procedure to turn the cells into three actual animals. The animals include two males, Romulus and Remus, born in October, and one female, Khaleesi, whose name is a reference to the TV series *Game of Thrones,* in which fictional dire wolves play a part.

Each animal, the company says, has 20 genetic changes across 14 genes designed to make them larger, change their facial features, and give them a snow-white appearance. Some scientists reject the company's claim that the new animals are a revival of the extinct creatures, since in reality dire wolves and gray wolves are different species separated by a few million of years of evolution and several million letters of DNA.

Two of the “dire wolves” at three months old. COLOSSAL BIOSCIENCES

“I would say such an animal is not a dire wolf and it’s not correct to say dire wolves have been brought back from extinction. It’s a modified gray wolf,” says Anders Bergström, a professor at the University of East Anglia who specializes in the evolution of canines. “Twenty changes is not nearly enough. But it could get you a strange-looking gray wolf.”

Beth Shapiro, an expert on ancient DNA who is now on a three-year sabbatical from the University of California, Santa Cruz, as the company’s CSO, acknowledged in an interview that other scientists would bristle at the claim. “What we’re going to have here is a philosophical argument about whether we should call it a dire wolf or call it something else,” Shapiro said. Asked point blank to call the animal a dire wolf, she hesitated but then did so. “It is a dire wolf,” she said. “I feel like I say that, and then all of my taxonomist friends will be like, ‘Okay, I’m done with her.’ But it’s not a gray wolf. It doesn’t look like a gray wolf.”

Dire or not, the new wolves demonstrate that science is becoming more deft in its control over the genomes of animals—and point to how that skill could help in conservation. As part of the project, Colossal says, it also cloned several red wolves, an American species that’s the most endangered wolf in the world.

But that isn’t as dramatic as the supposed rebirth of an extinct animal with a large cultural following. “The motivation really is to develop tools that we can use to stop species from becoming extinct. Do we need ancient DNA for that? Maybe not,” says Shapiro. “Does it bring more attention to it so that maybe people get excited about the idea that we can use biotechnology for conservation? Probably.”

Secret project

Colossal was founded in 2021 after founder Ben Lamm, a software entrepreneur, visited the Harvard geneticist George Church and learned about a far-out and still mostly theoretical project to re-create woolly mammoths. The idea is to release herds of them in cold regions, like Siberia, and restore an ecological balance that keeps greenhouse gases trapped in the permafrost. Lamm has unexpectedly been able to raise more than $400 million from investors to back the plan, and *Forbes* reported that he is now a multibillionaire, at least on paper, thanks to the $10 billion value assigned to the startup.

From left to right: Beth Shapiro, George Church, and Ben Lamm pose with the pups. COLOSSAL BIOSCIENCES

As Lamm showed he could raise money for Colossal's ideas, it soon expanded beyond its effort to modify elephants. It publicly announced a bid to re-create the thylacine, a marsupial predator hunted to extinction, and then, in 2023, it started planning to resurrect the dodo bird—the effort that brought Shapiro to the company. So far, none of those signature projects have actually resulted in a live animal with ancient genes.

Each faces dire practical issues. With elephants, it was that their pregnancies last two years, longer than those in any other species. Testing out mammoth designs would be impossibly slow. With the dodo bird, it was that no one has ever figured out how to genetically modify pigeons, the family of birds to which the dodo belonged and from which a new dodo would have to be crafted. One of Lamm's other favorite targets—the Steller's sea cow, which disappeared around 1770—has no obvious surrogate of any kind.

But creating a wolf was feasible. Over 1,500 dogs had been cloned, primarily by one company in South Korea. Researchers in Asia had even used dog eggs and dog mothers to produce both coyote and wolf clones. That's not surprising, since all these species are closely enough related to interbreed. "Just thinking about surrogacy for the dire wolf … it was like 'Oh, yeah,'" recalls Shapiro. "Surrogacy there would be really straightforward."

Dire wolves did present some new problems. One was the lack of any clear ecological purpose in reviving animals that disappeared during the Pleistocene epoch and are usually portrayed as ferocious predators with slavering jaws. "People have weird feelings about things that, you know, may or may not eat people or livestock," Shapiro says. The technical challenge was there was still no accurate DNA sequence of a dire wolf. A 2021 effort to obtain DNA from old bones had yielded only a tiny amount, not enough to accurately decode the genome in detail. And without a detailed gene map, Colossal wouldn't be able see what genetic differences they would need to install in gray wolves, the species they intended to alter.

Shapiro says she went back to museums, including the Idaho Museum of Natural History, and eventually got permission to cut off more bone from a 72,0000-year-old skull that's on display there. She also got a tooth from a 13,000-year-old skull held in another museum. which she drilled into herself. This time the bones yielded far more DNA and a much more complete gene map. A paper describing the detailed sequence is being submitted for publication; its authors include George R.R. Martin, the fantasy author whose books were turned into the HBO series *Game of Thrones*, and in which dire wolves appear as the characters' magical companions.

In addition to placing dire wolves more firmly in the *Canidae* family tree (they're slightly closer to gray wolves than to jackals, but more than 99.9% identical to both at a genetic level) and determining when dire wolves split from the pack (about 4 to 5 million years ago), the team also located around 80 genes where dire wolves seemed to be most different. If you wanted to turn a gray wolf into a dire wolf, this would be the obvious list to start from.

Crying wolf

Colossal then began the process of using base editing, an updated form of the CRISPR gene-modification technique, to introduce some of those exact DNA variations into blood cells of a gray wolf kept in its labs. Each additional edit, the company hoped, would make the eventual animal a little more dire-wolf-like, even it involved changing just a single letter of a gene.

Shapiro says all the edits using information from the ancient dire wolf were made to "genetic enhancers," bits of DNA that help control how strongly certain genes are expressed. These can influence how big animals grow, as well as affecting the shape of their ears, faces, and skulls. This tactic was not as dramatic as intervening right in the middle of a gene, which would change what protein is made. But it was less risky—more like turning knobs on an unfamiliar radio than cutting wires and replacing circuits.

That left the scientists to engineer into the animals what would become their showstopper trait—the dramatic white fur. Shapiro says the genome code indicated that dire wolves might have had light coats. But the specific pigment genes involved are linked to a risk of albinism, deafness, and blindness, and they didn't want sick wolves. That's when Colossal opted for a shortcut. Instead of reproducing precise DNA variants seen in dire wolves, they disabled two genes entirely. In dogs and other species, the absence of those genes is known to produce light fur.

The decision to make the wolves white did result in dramatic photos of the animals. "It's the most striking thing about them," says Mairin Balisi, a paleontologist who studies dire wolf fossils. But she doubts it reflects what the animals actually looked like: "A white coat might make sense if you are in a snowy landscape, but one of the places where dire wolves were most abundant was around Los Angeles and the tar pits, and it was not a snowy landscape even in the Ice Age. If you look at mammals in this region today, they are not white. I am just confused by the declaration that dire wolves are back."

Bergström also says he doesn't think the edits add up to a dire wolf. "I doubt that 20 changes are enough to turn a gray wolf to a dire wolf. You'd probably need hundreds or thousands of changes—no one really knows," he says. "This is one of those unsolved questions in biology. People argue [about] the extent to which many small differences make a species distinct, versus a small number of big-effect differences. Nobody knows, but I lean to the 'many small differences' view."

Some genes have big, visible effects—changing a single gene can make a dog hairless, for instance. But it might be many more small changes that account for the difference in size and appearance between, say, a Great Dane and a Chihuahua. And that is just looks. Bergström says science has much less idea which changes would account for behavior—even if we could tell from a genome how an extinct animal acted, which we can't.

Report

You are a journalist for a scientific magazine, and you have been asked to write a report outlining the merits of, and issues with, cloning and bioprinting. State your stance and support by citing from the studies you have read. Then, include a section in which you advocate one biotechnical advancement over the other, and discuss whether there are moral/ethical differences or similarities.

Your report structure must include the following

- Introduction, thesis statement and stance
- Findings
- Preferred technology
- Conclusion

You will have 120 minutes to study the research materials provided and to write your report. This section of the test covers 25% of the overall exam grade.

Title: _____

UNIVERSITY OF HOHENHEIM

Akademisches Auslandsamt | Referat Sprachenzentrum (AA4)

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English for Natural Sciences, UNIcert III, C1 **Date**

Topic

Cloning and 3D Bioprinting

Situation or scenario

You are a journalist for a scientific magazine, which is looking into advancements in cloning and bioprinting. You have been assigned to research the merits of and issues surrounding these technologies and to compile both a written report and a presentation of your findings. Your editor-in-chief is interested in your informed stance, advocating one biotechnical advancement over the other, and in their applications, and ethical considerations. You will then present your findings at Harvard University's Annual Bioethics Conference.

Tasks and goals

Your task is to give a presentation of your findings in the area of cloning and bioprinting and take part in a question and answer session at the Annual Bioethics Conference. It should include your informed stance, an exploration of the technological applications, and ethical considerations.

			SPEAKING	
			Case study - presentation *30 min* **25 points**	

Examiners´ signatures:

1st Examiner

2nd Examiner

SPEAKING

Case study - Presentation

Prepare a presentation based on your report for the Annual Bioethics Conference, summarizing your key research findings and recommendations. Outline your informed stance be prepared to answer questions

Your presentation should be in PowerPoint format and include references. You will have 10 minutes present your findings and 15 minutes to answer questions from the panel. This section of the test covers 25% of the overall exam grade.

LISTENING

- *What is Human Cloning? How to Clone a Human* [00:06:38]
  David Bird Science, https://www.youtube.com/watch?v=VL8lw4i5qkM

READING

- *Medical Applications for 3D Printing: Current and Projected Uses*
  Ventola CL. Medical Applications for 3D Printing: Current and Projected Uses. P T. 2014 Oct;39 (10):704-11. PMID: 25336867; PMCID: PMC4189697.

WRITING

- Seeker 24.12.2020, The first full-size 3D print of a human heart is here: https://www.youtube.com/watch?v=_rfeCSQxDBg
- Colossal Biosciences 07.04.2025, The Making of the Colossal Dire Wolves - World's First De-Extinction https://www.youtube.com/watch?v=F5uCuOwK_VE
- MIT Technology Review, 08.04.2025, Game of Clones: Colossal´s new wolves are cute, but are they dire?

For Examiner's Use Only

1st examiner's notes

1st examiner's questions

For Examiner's Use Only

2nd examiner's notes

2nd examiner's questions