I. **Abstract**:

The Center for Disease Control and Prevention estimates as many as 646,000 people die of influenza each year worldwide. Today, there is no cure for influenza, the only option is to prime our immune system to fight the virus.

Our vision is a real time 3D printed vaccine made by printing the shape of the HA and NA molecules in order to present them to the immune system. Artificial Intelligence will analyze information about influenza subtypes circulating around the world. The AI will analyze the virus RNA sequences and predict the shapes of the HA and NA molecules and send this information to the 3D printer. With the current Coronavirus spreading in China and other parts of the world, we hope our vision for influenza could be expanded to 3D print vaccines real time for other viruses.

II. Description:

1. Present Technology

Influenza is an infectious disease that attacks your respiratory system, commonly known as the flu. Type A, Type B, and Type C are the only types that attack humans. The flu comes from the family Orthomyxoviridae. Symptoms include headaches, runny nose, fever, fatigue, sore throat, and muscle aches.

The influenza virion as shown in Figure 1, is an enveloped virus with a lipid membrane outer layer derived from the host cell membrane. The lipid membrane gets these things inserted into it, called protein spikes, which are referred to as (HA) for hemagglutinin and (NA) for neuraminidase. These protein spikes determine the subtype of influenza virus, for example A/H1N1. Proteins called antibodies, made by the immune system to combat infection, recognize HA and NA. This allows the antibodies to mount an immune response against the virus. HA and NA spikes mutate and change their shape from year to year. This helps them escape recognition by the immune system and is the reason we need new flu vaccinations every year.

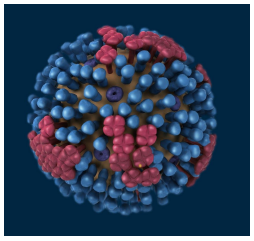
Figure 1: Influenza Virion

The immune system works by using cells and organs, especially white blood cells, also called leukocytes. Some types of white blood cells, called phagocytes can absorb foreign

substances. Other cells, called lymphocytes, help the immune system to remember foreign substances and destroy them. There are several types of lymphocytes including B cells and T cells. Bone marrow makes lymphocytes and some can stay in the bone marrow and mature into B cells, others go to the thymus to mature into T cells. B cells make antibodies that recognize foreign substances while T cells are important to destroy infected cells.

Vaccines use our immune system to recognize foreign substances such as viruses. The recognition creates immune memory so that the same substance can be destroyed quickly when they are encountered again. Today**,** influenza vaccine takes 5 months to plan out and develop that isn't effective if the virus mutates. In figure 2, the 5 month timeline explains the different steps today to make a vaccine for influenza. The limitations with today's vaccine is the effectiveness of the vaccine, the length of time it takes to develop and distribute the vaccine.

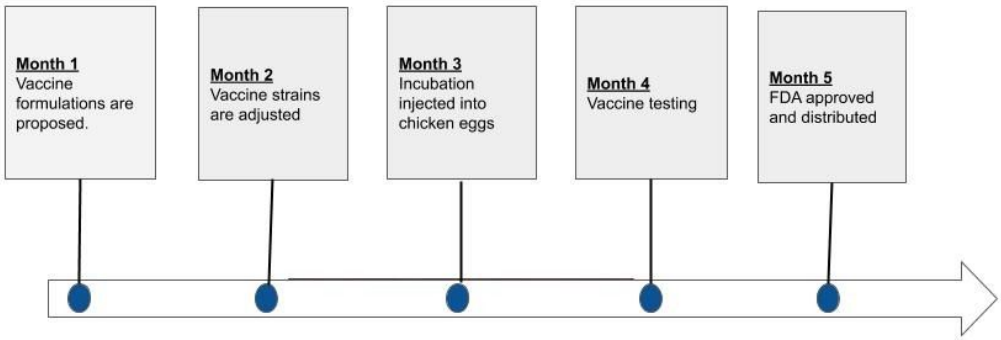

Figure 2: Today's Influenza Vaccine Timeline

2. History

History of Vaccines

The smallpox vaccine was first invented in 1776 by Edward Jenner. He made this possible by taking material from a blister of someone infected with cowpox and putting it into another person's skin. In 1955, many people rejoiced over Jonas Salk's invention of the polio vaccine. In 1885, a groundbreaking discovery of the vaccine for cholera by Louis Plasteur between 1890 to 1950. In 1963 the vaccine for measles and mumps was made, there were also

vaccines made in the 60s for mumps in (1967) and rubella (1969). Then the MMR made in 1971 this vaccine had all three of those vaccines in it.

History of 3D printing

Charles Hull invented 3D printing, he called it stereolithography in the early 1980s. 3D printing has been applied in medicine since the early 2000s for prosthetics, dental implants and more. In 1981 Hideo Kodama invented a fast printing system that uses photopolymers and in order to make a model he did it layer-by-layer. In 1999 scientists at the Wake Forest Institute for Regenerative Medicine made the first 3D printed human bladder structure. The first 3D printed blood vessel was made by bioprinting company Organovo. In 2004 a project called RepRap made a 3D printer that can self replicate by 3D printing its own parts.

3. Future Technology

Our vision is a real time 3D printed influenza vaccine. If the virus mutates, you can easily 3D print an update to the vaccine. The 3D printer would be able to be bought/received at places like supermarkets, pharmacies, and doctor offices similar to the access we have today but our vision would one day have a printer in your own home.

The vaccine will be made by printing the shape of the HA and NA molecules using cellulose (formula: $(C_6H_{10}O_5)_n$) so that the protein spike on the flu virus will be recognized by the immune system. We are using cellulose because cellulose is an abundant organic polymer similar to other biological organic polymers like proteins and carbohydrates.

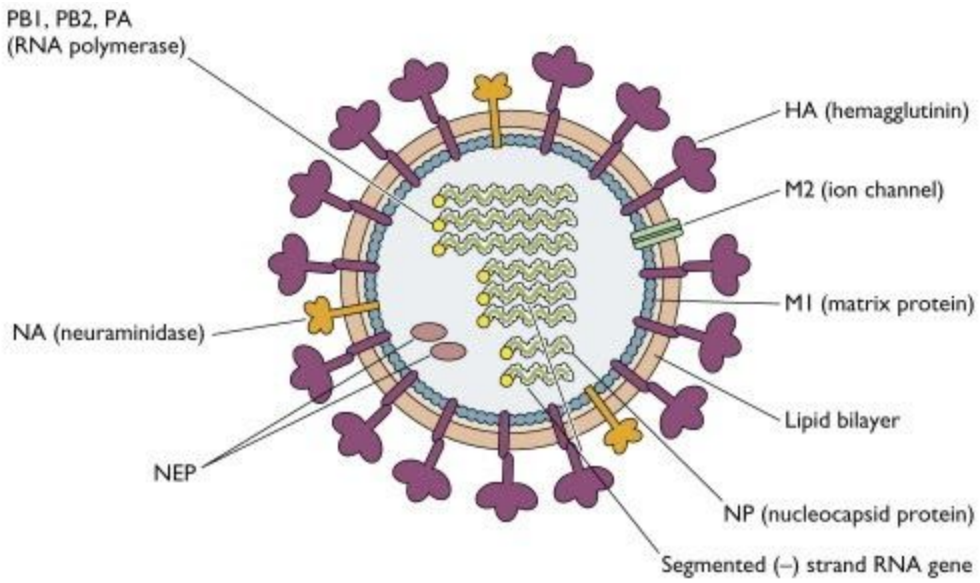

Figure 3: Influenza Virion

As an alternative to an injection we decided on using a lollipop/lozenge so that people with Trypanophobia (fear of injections) do not have to get injected. We are using lollipops for an oral mucosa approach. The immune system cells in the oral mucosa will be effective because the flu infects the mucosal surfaces. The lollipop or lozenge will be in a mixed solution containing the 3D printed HA and NA cellulose shapes with added adjuvants that help increase the immune response.

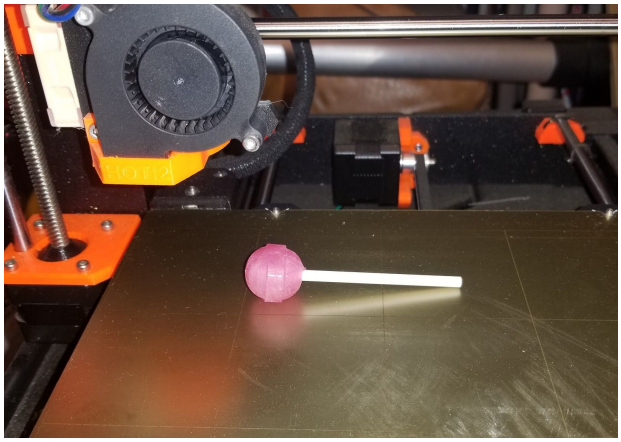

Figure 4: VacciPrint Influenza Vaccine

We would like to put a structure in place where influenza data can be collected real time around the world and be analyzed. We would like to use an artificial intelligence program to help analyze and determine the HA/NA shape and how it might need to be updated based on the virus mutating.

4. Breakthroughs:

Our first breakthrough will be the ability to print with cellulose on a molecular scale. Our second breakthrough is the use of AI to predict the shapes of HA and NA protein spikes. We need to print the molecular shapes that require nano machines to print, this is possible but not commonly available.

Artificial intelligence is an emerging technology, we will need it to connect the influenza information from around the world and be able to quickly analyze and send the relevant virus strain sequence and structure information to the 3D printer. Our focus is on influenza, but a breakthrough would be able to print any shape to use as a vaccine to prevent viral infection at any time.

For our future technology vision we would need to conduct several tests to prove that the vaccine will be effective. We would test adults by giving them the lollipop with the 3D printed vaccine with the vaccine and then testing their blood for the presence of antibodies. We would test by gathering subjects and then give them the lollipop vaccination, we would do blood tests every day for 10-14 days because that is how long it usually takes for the immune system to respond, in these blood tests we would be searching for the presence of antibodies in the subjects blood because that is the immune response. After 14 days we would test again if the immune system was still producing antibodies against the flu virus. The conducted tests would consist of 7 steps in chronological order.

1. Question: will the immune system respond with antibodies to the foreign virus?
2. Conduct research on the subjects immune status through the course of the test.
3. Hypothesis: the immune system will respond to the lollipop vaccine by producing flu virus antibodies.
4. Experiment: conduct the test by giving the subject a lollipop vaccine.
5. Observation: detect antibodies specific for the flu in the subjects blood sample.
6. Conclude test and see results if the antibodies were present throughout the test.
7. Conclusion: the antibodies to the flu either are or are not present in the blood samples of vaccinated subjects.

5. Design Process:

When we started with this idea we discussed several options on what we were actually going to print for a vaccine to fight against influenza. The first option was to print a whole influenza virus using biological materials. We rejected this idea because it would be hard to have the virus locally and ready to print. The second was to focus on printing the HA and NA molecules using plant based materials. We researched and decided to use plant based material called cellulose. This because we decided using cellulose instead of biological materials and on printing the protein shape was most compatible with our vision to easily print realtime.

Another major design decision was the printing of the shape of the HA/NA molecules. Immune cells in the mucosal surfaces of the mouth interact with lollipop or lozenge and the immune system detects and reacts. We rejected the option of having a lollipop with spikes/bristles that inject the vaccine through and into the cheek because we wanted to have a pain free approach to the vaccine.

We didn't have a good solution for when the virus mutated, so we researched artificial intelligence. We thought this would be a good way to collect data and analyze influenza data from around the world to determine whether the protein HA/NA shape needs to be updated. We added this part of our vision to ensure that our printer information is always accurate.

6. Consequences

The positive effect on society is that the flu lollipop/lozenge will be more accessible. Since it's a machine, it could have a bug or problem in the programming specifically in the

making of the vaccine. Since this is a vaccine, there are always possible side effects. These are normal side effects and actual life-threatening side effects are very rare.

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Figure 1:

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Figure 2:

Made by the VacciPrint team.

Figure 3:

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Figure 4:

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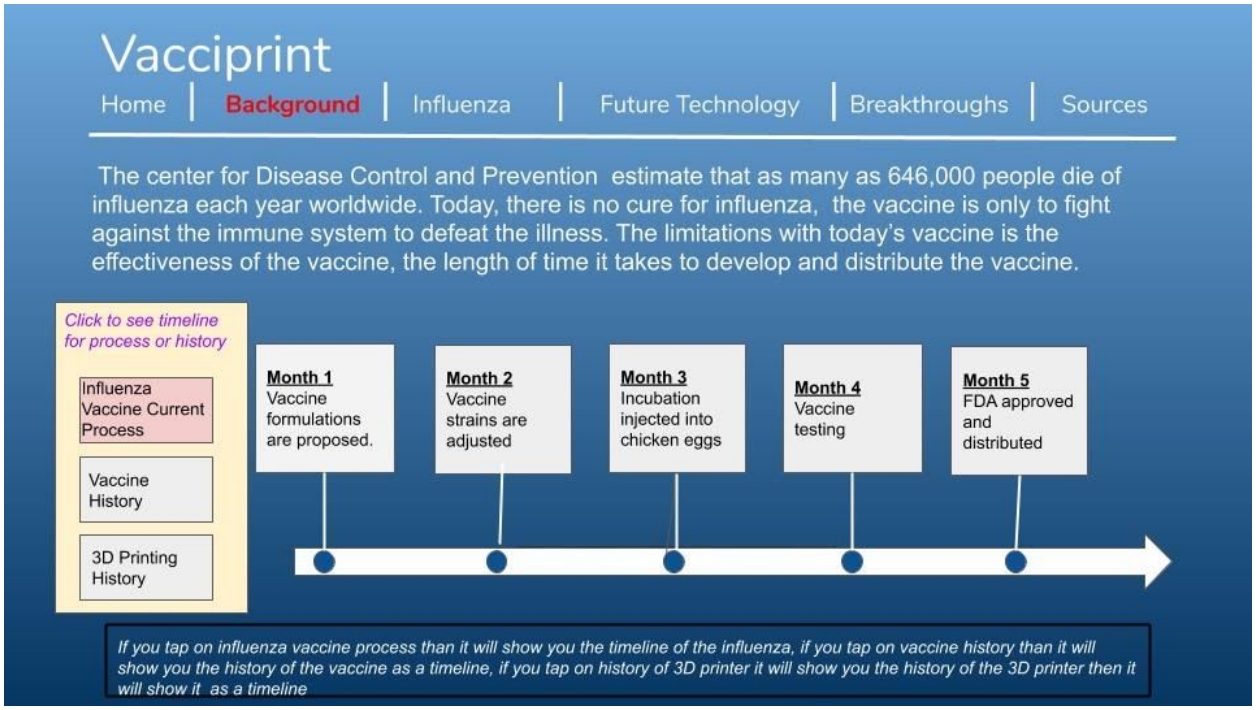
IV. Web Design

Page 1.

Page 2.


Vacciprint
Home | Background | Influenza | Future Technology | Breakthroughs | Sources
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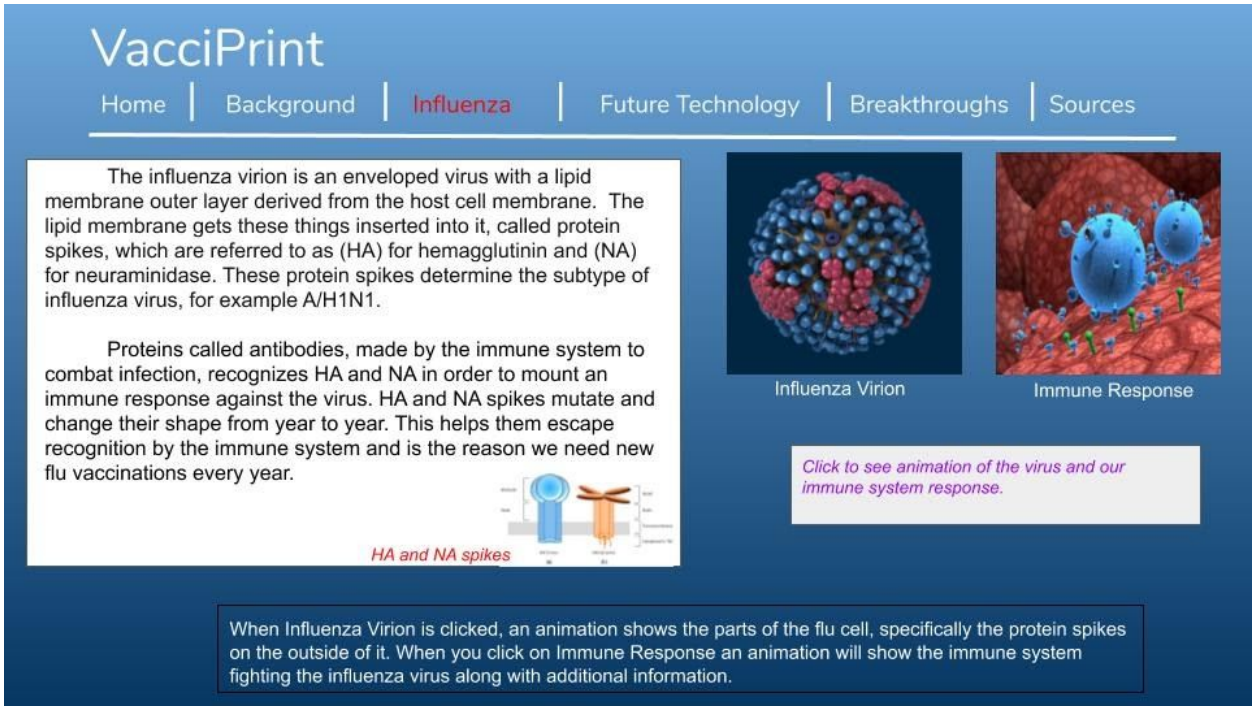
Click to see timeline for process or history
Influenza Vaccine Current Process
Vaccine History
3D Printing History
Month 1 Vaccine formulations are proposed.
Month 2 Vaccine strains are adjusted
Month 3 Incubation injected into chicken eggs
Month 4 Vaccine testing
Month 5 FDA approved and distributed
If you tap on influenza vaccine process than it will show you the timeline of the influenza, if you tap on vaccine history than it will show you the history of the vaccine as a timeline, if you tap on history of 3D printer it will show you the history of the 3D printer then it will show it as a timeline

Page 3.


VacciPrint
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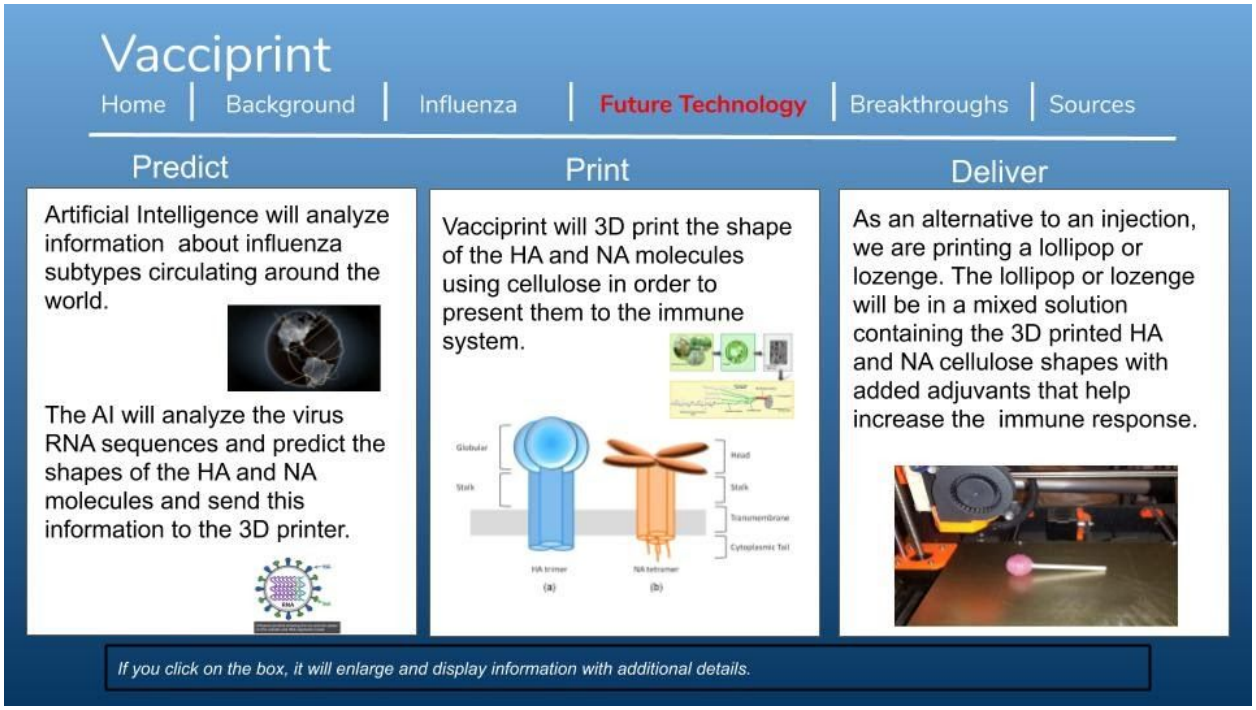
HA and NA spikes
Influenza Virion
Immune Response
Click to see animation of the virus and our immune system response.
When Influenza Virion is clicked, an animation shows the parts of the flu cell, specifically the protein spikes on the outside of it. When you click on Immune Response an animation will show the immune system fighting the influenza virus along with additional information.

Page 4.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Predict
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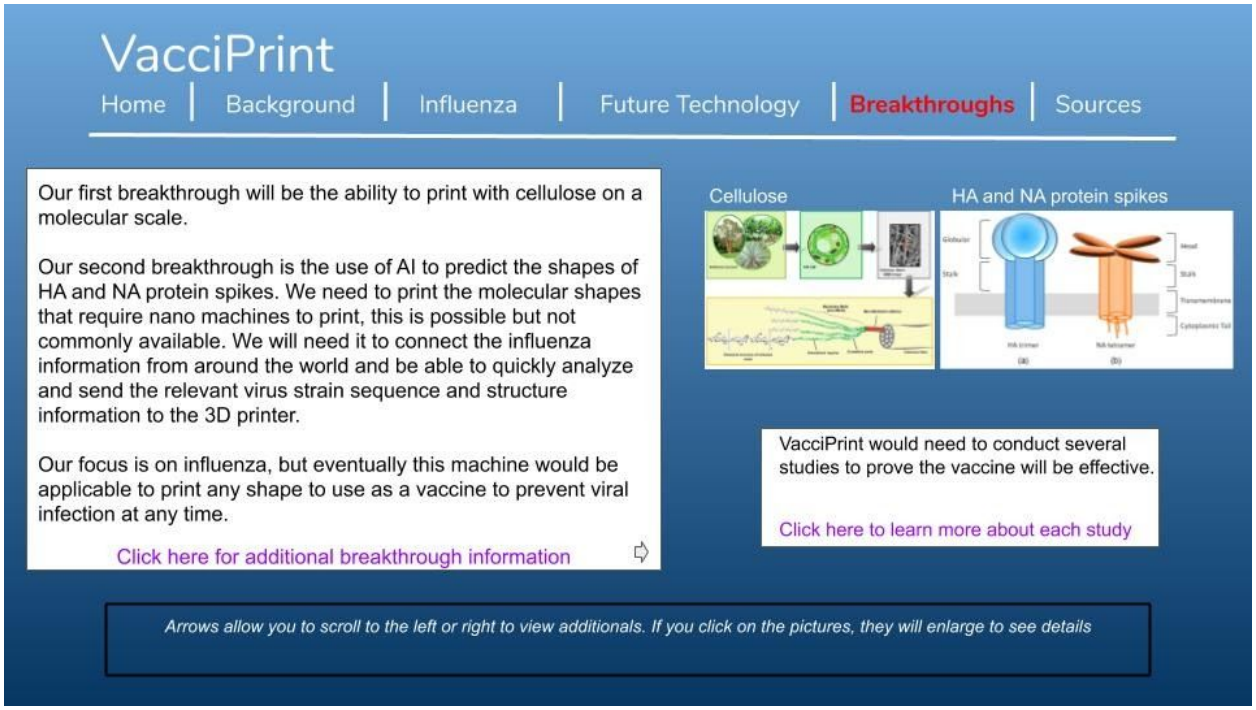
The AI will analyze the virus RNA sequences and predict the shapes of the HA and NA molecules and send this information to the 3D printer.
Print
Vacciprint will 3D print the shape of the HA and NA molecules using cellulose in order to present them to the immune system.
Globular
Stalk
Head
Stalk
Transmembrane
Cytoplasmic Tail
HA trimer
NA tetramer
(a)
(b)
Deliver
As an alternative to an injection, we are printing a lollipop or lozenge. The lollipop or lozenge will be in a mixed solution containing the 3D printed HA and NA cellulose shapes with added adjuvants that help increase the immune response.
If you click on the box, it will enlarge and display information with additional details.

Page 5.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Our focus is on influenza, but eventually this machine would be applicable to print any shape to use as a vaccine to prevent viral infection at any time.
Click here for additional breakthrough information
Cellulose
HA and NA protein spikes
VacciPrint would need to conduct several studies to prove the vaccine will be effective.
Click here to learn more about each study
Arrows allow you to scroll to the left or right to view additionals. If you click on the pictures, they will enlarge to see details