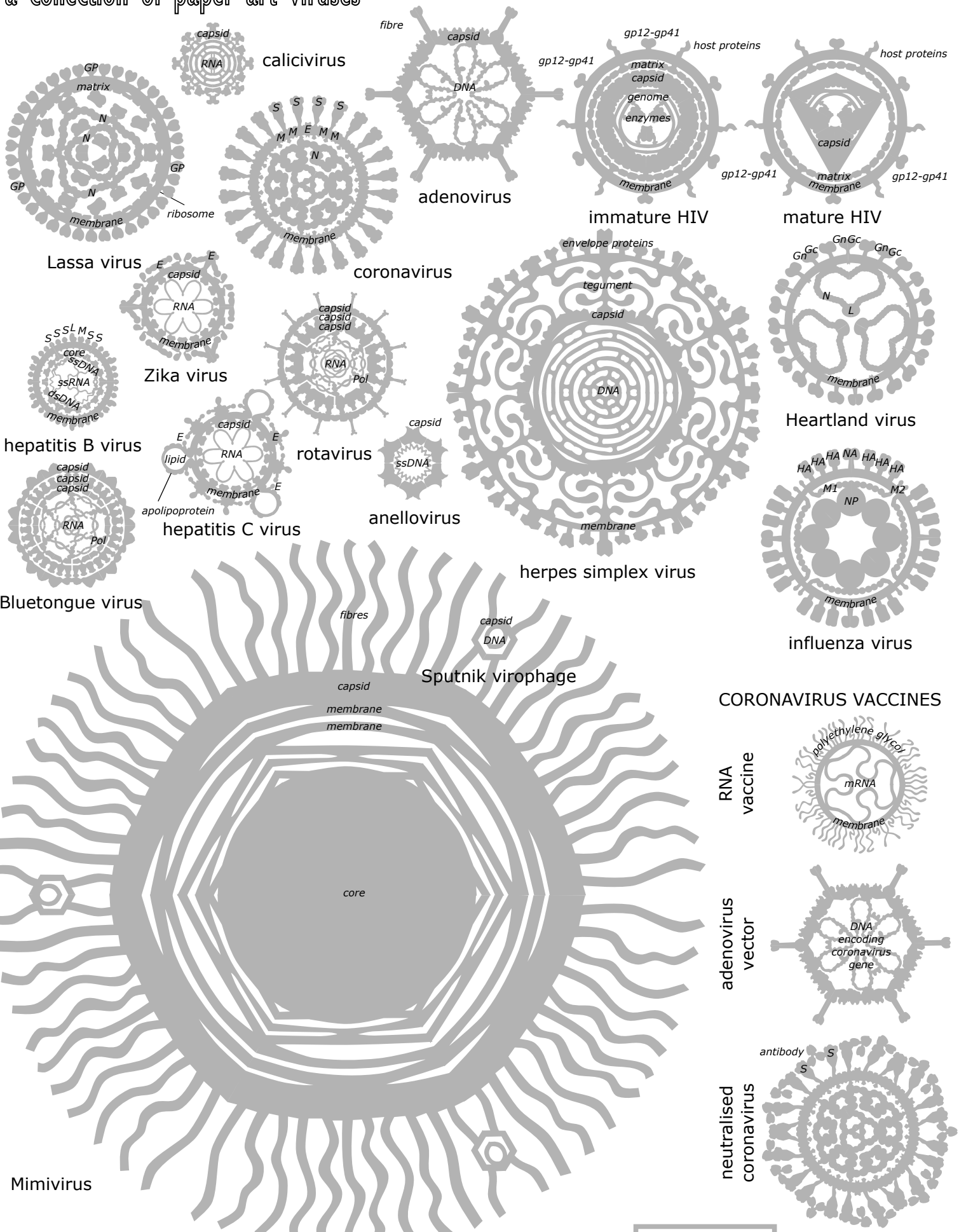
VIRUS SNOWFLAKES

a collection of paper art viruses

Ed Hutchinson

MRC Medical Research Council | University of Glasgow | CVR Centre for Virus Research



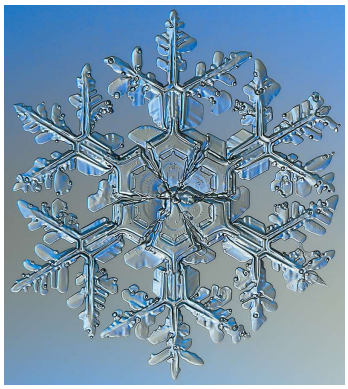
CORONAVIRUS VACCINES

100 nm = 1/10,000th of a mm

VIRUS SNOWFLAKES

Viruses and snowflakes

A traditional Christmas activity, here in Glasgow and in many other parts of the world, is making paper snowflakes. Fold up a circle of paper, cut a design into it, unfold it again and you end up with a symmetrical design that looks like a snowflake. If, like my colleagues at the MRC-University of Glasgow Centre for Virus Research, you spend a lot of time thinking about the microscopic world, these symmetrical decorations can also remind you of something else – viruses.



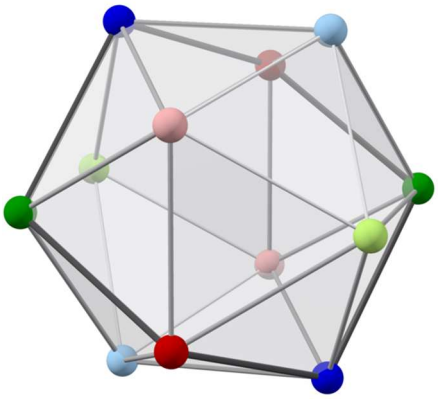
Snowflake (Alexey Kljatov, 2015)

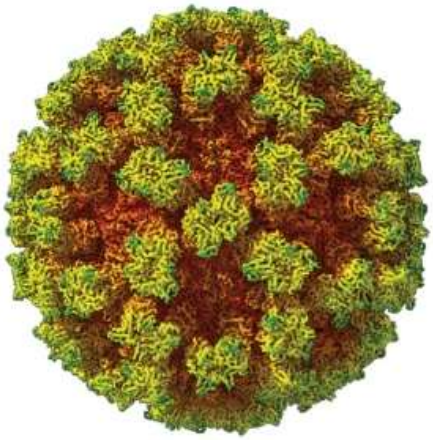
Virus particles and symmetry

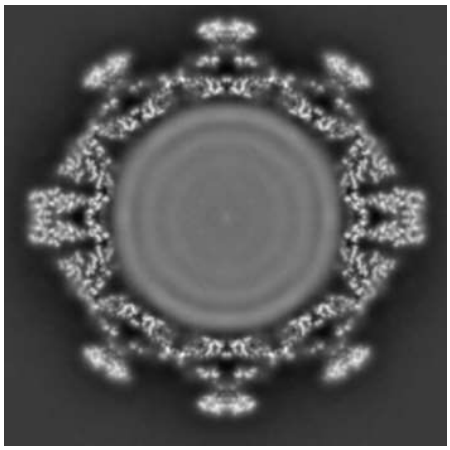
Why would viruses look like snowflakes? After all, we don't expect bacteria to look like snowmen or fungi to look like icicles (although some do; nature is quite varied).

It becomes clear if we think about what a virus is. A virus is a set of genetic instructions that take over a cell and turn it into a factory for making more viruses. Importantly, one of the things the viral genes make the cell do is to produce microscopic particles that can package up new copies of viral genes, in order to transport them to new host cells. These infectious virus particles (or 'virions') are very distinctive, and are usually the first thing we think of when we think 'virus.' They are, if you can leave the associations with disease aside, quite beautiful.

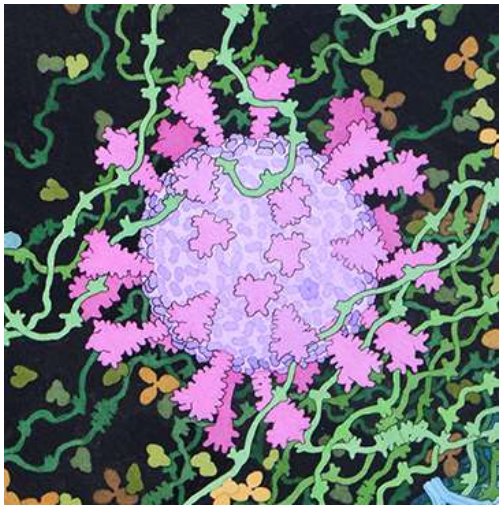
One of the things that makes virus particles beautiful is that they are often symmetrical. Indeed, some virus particles are so regular that, like the water that forms snowflakes, they will assemble into crystals if they are kept under the right conditions in a laboratory – this trick has







An icosahedron (Tilman Piesk, 2015)**, and an icosahedral calcivirus particle, shown in 3D and in cross-section** (Conley *et al.* (2019) *Nature* 565 (7739) 377-381)**.**



Artistic representation of SARS-CoV-2, which is wrapped in an envelope of membrane (David S. Goodsell, RCSB Protein Data Bank; doi: 10.2210/rcsb_pdb/goodsell-gallery-024)**.**

been used by crystallographers to study their invisible small structures in great detail.

Why are virus particles so regular?

Virus particles are symmetrical because, despite the huge impact they have on our world, viruses are very simple. Compared to us, viruses have very few genes, and so they need to make virus particles from an extremely small set of components, which they use repeatedly.

One way to do this is to assemble a regular box of 'capsid' proteins to enclose the viral genes (an icosahedron, which has twenty sides). A 2D projection of an icosahedron is roughly hexagonal, giving it the same symmetry as a snowflake.

Another way to make virus particles is for the virus to steal components from our own cells. Many virus particles are wrapped in a layer of membrane obtained from the cell they grew in – a good way of protecting the viral genes, though it can be disrupted by detergents in soap, or alcohol in hand gels. Surface tension tends to pull membranes into spheres, and proteins that float in them or within them tend to spread out to a roughly even spacing.

Because of this, it turns out that many viruses can be made into paper snowflakes. (A little bit of tweaking was needed to make them fit the symmetry of Christmas decorations exactly, and if you are already interested in viruses you can try and predict where that was needed.)

Virus Snowflakes

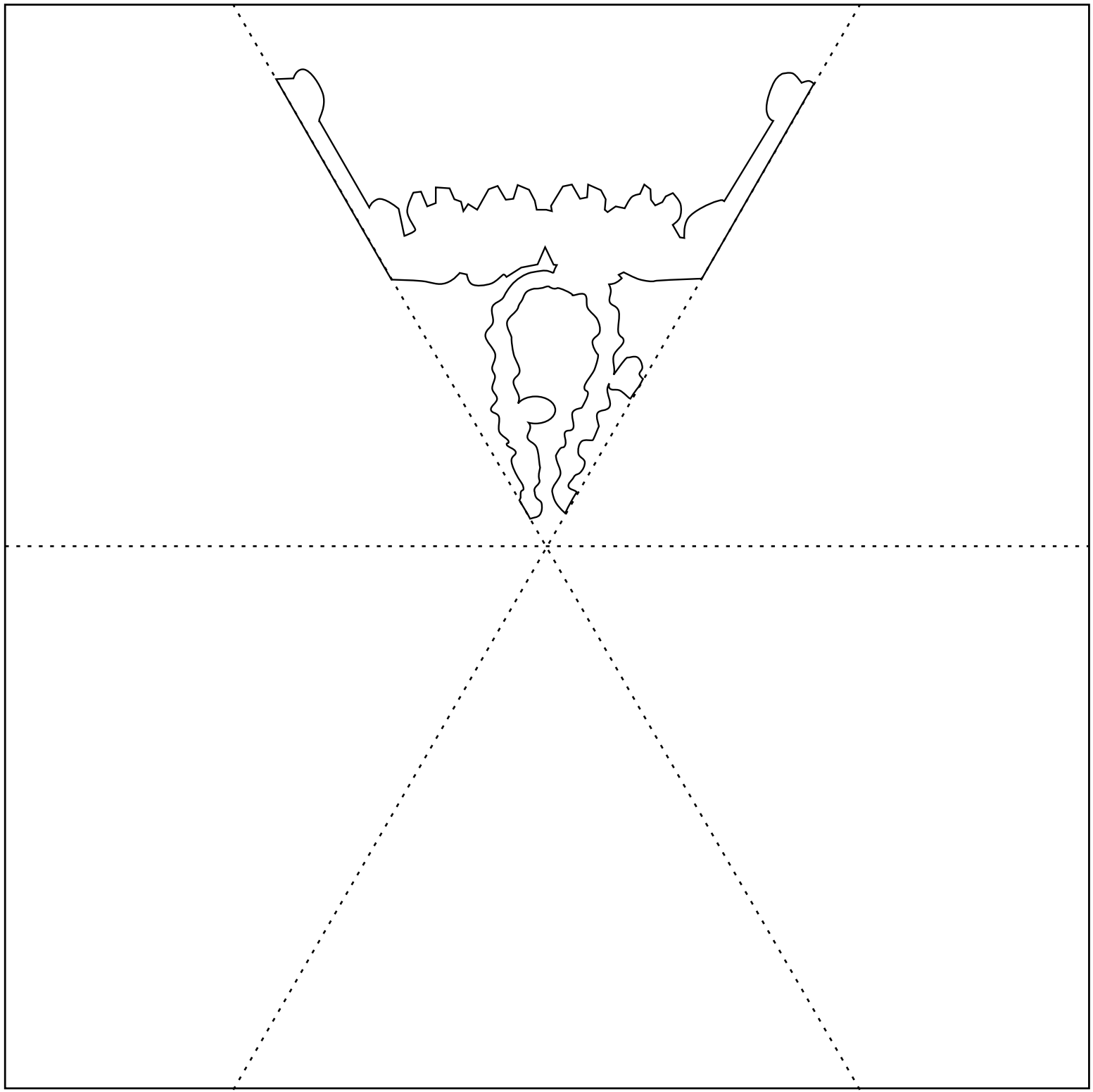
In this collection you'll find viruses that we care about because they make people sick, and viruses that we care about because they make animals sick. You will find viruses that don't do either of these things but are just really cool – the enormous Mimivirus and the tiny satellite virus that infects it (a virus infecting a virus!); the unobtrusive anellovirus, which you are likely to be infected with right now without noticing it or having any ill-effects.

You will not find some viruses, either because they are not symmetrical enough (the tailed bacteriophage, or bacteria-infecting viruses, that resemble lunar landing modules are among the most beautiful viruses but they only have one copy of their long tail) or because they have the wrong sort of symmetry (this includes viruses that stack their capsid proteins into a helix, like the filament-shaped Ebola virus, and certain viruses that have distinctive shapes like the bullet-shaped rabies virus, the brick-shaped smallpox virus or the lemon-shaped viruses that infect some single-celled archaea).

Finally, this collection was put together in a year dominated by one particular virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) the cause of coronavirus disease 2019 (COVID-19) and the resulting pandemic. Happily, by understanding the structure of virus particles we now have some tools to fight it, and this collection ends with two SARS-CoV-2 vaccines inspired by virus structures, as well as a final snowflake showing how vaccination can protect us against SARS-CoV-2 – perhaps the best Christmas gift any of us could have this year.

Other Resources

* More free resources for learning about viruses, including a colouring book, 3D paper art models (including of helical viruses) and an augmented reality app, can be found with the files for these snowflakes at the website of the MRC-University of Glasgow Centre for Virus Research (https://tinyurl.com/yc8edw7a).
* These virus snowflakes were based on a wide variety of research papers but I was also grateful, as many virologists are, for the excellent virus summaries at ViralZone (https://viralzone.expasy.org). Any errors are mine, though some of them, due to the unforgiving symmetry relationships of Christmas decorations, were deliberate.



ADENOVIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Adenoviruses cause a variety of illnesses, particularly cold-like symptoms and conjunctivitis. They can be genetically modified to deliver genes. These finds uses in gene therapy and in vaccines for viruses including SARS-CoV-2.

About the Virus Particle:

An adenovirus particle's 12 corners are decorated with long, spike-like fibres, which it uses to attach to new cells. Inside the particle are core and minor/cement proteins, which help to package the virus' DNA genome.

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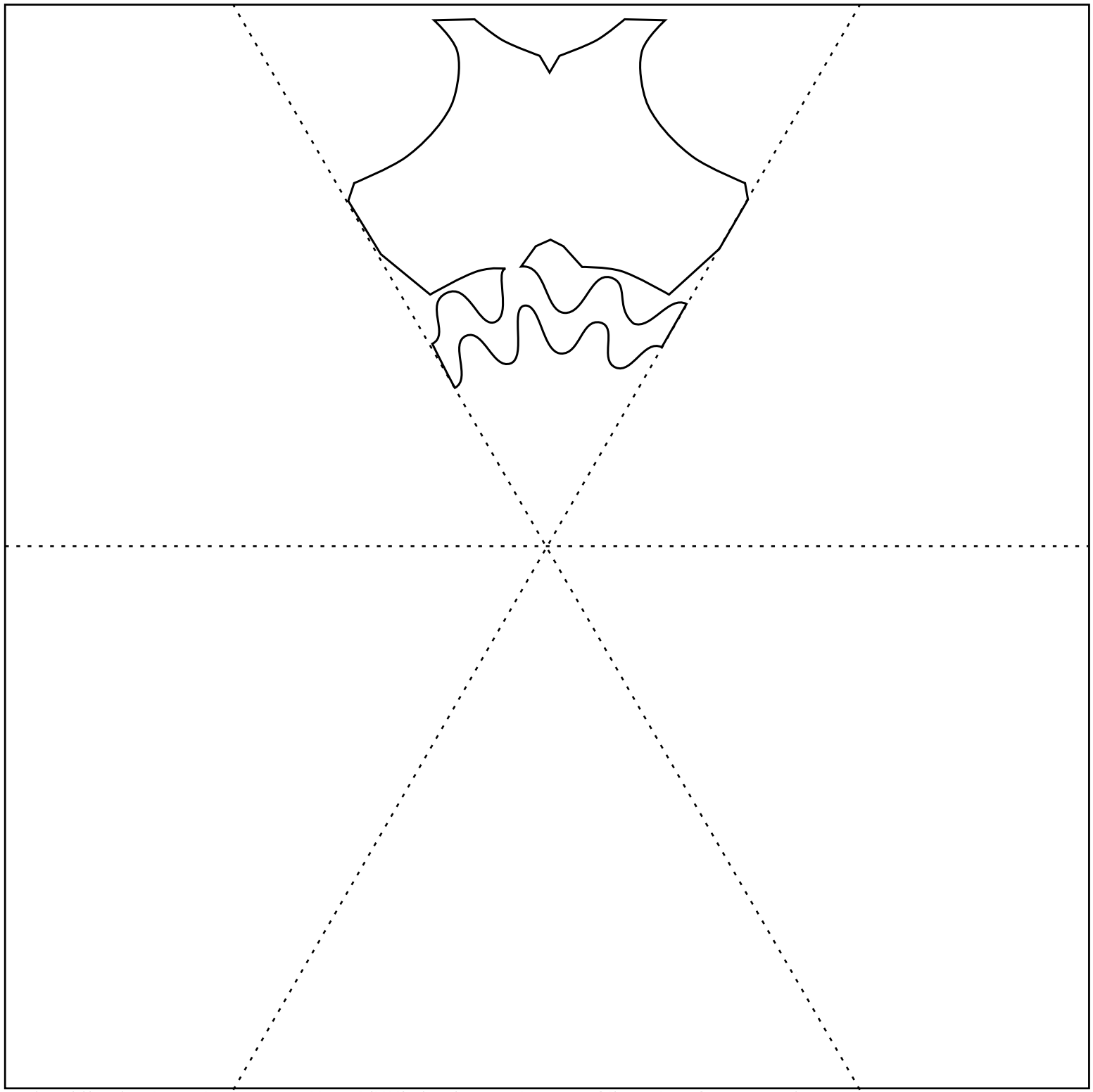


ANELLOVIRUS

Difficulty: Easy

Instructions:

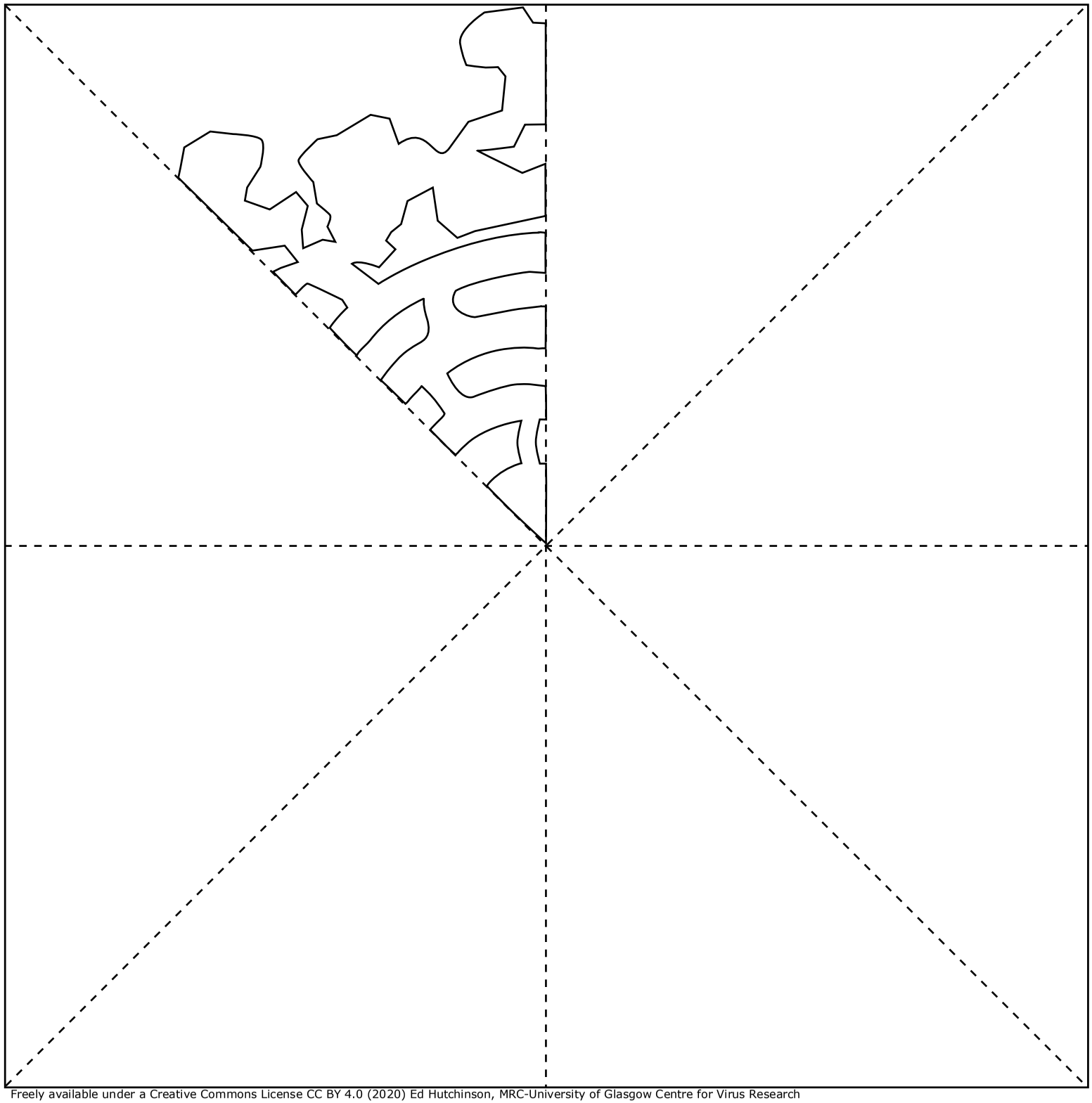
(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Members of this virus family are not known to cause disease, but they are extremely common - it is likely that anelloviruses are replicating inside your body at the moment without you even noticing.

About the Virus Particle:

Anelloviruses form simple particles: an icosahedral box of capsid proteins surround a circle of single-stranded DNA, which gives the virus its name (from anello, 'ring'). The virus relies on our own enzymes to make more copies of its genome.



CALICIVIRUS

Difficulty: Easy

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Caliciviruses are a family of viruses that cause diseases including one of the most common infectious forms of vomiting and diarrhoea, winter vomiting disease. Other caliciviruses infect pets, notably feline calicivirus, which causes a respiratory infection in cats.

About the Virus Particle:

Caliciviruses are transmitted by a 20 sided (icosahedral) particle, which contains the viral genome. Once it is inside a cell, the particle rearranges itself. A pore opens in its surface, allowing the viral genome to escape and take control of the cell's functions.

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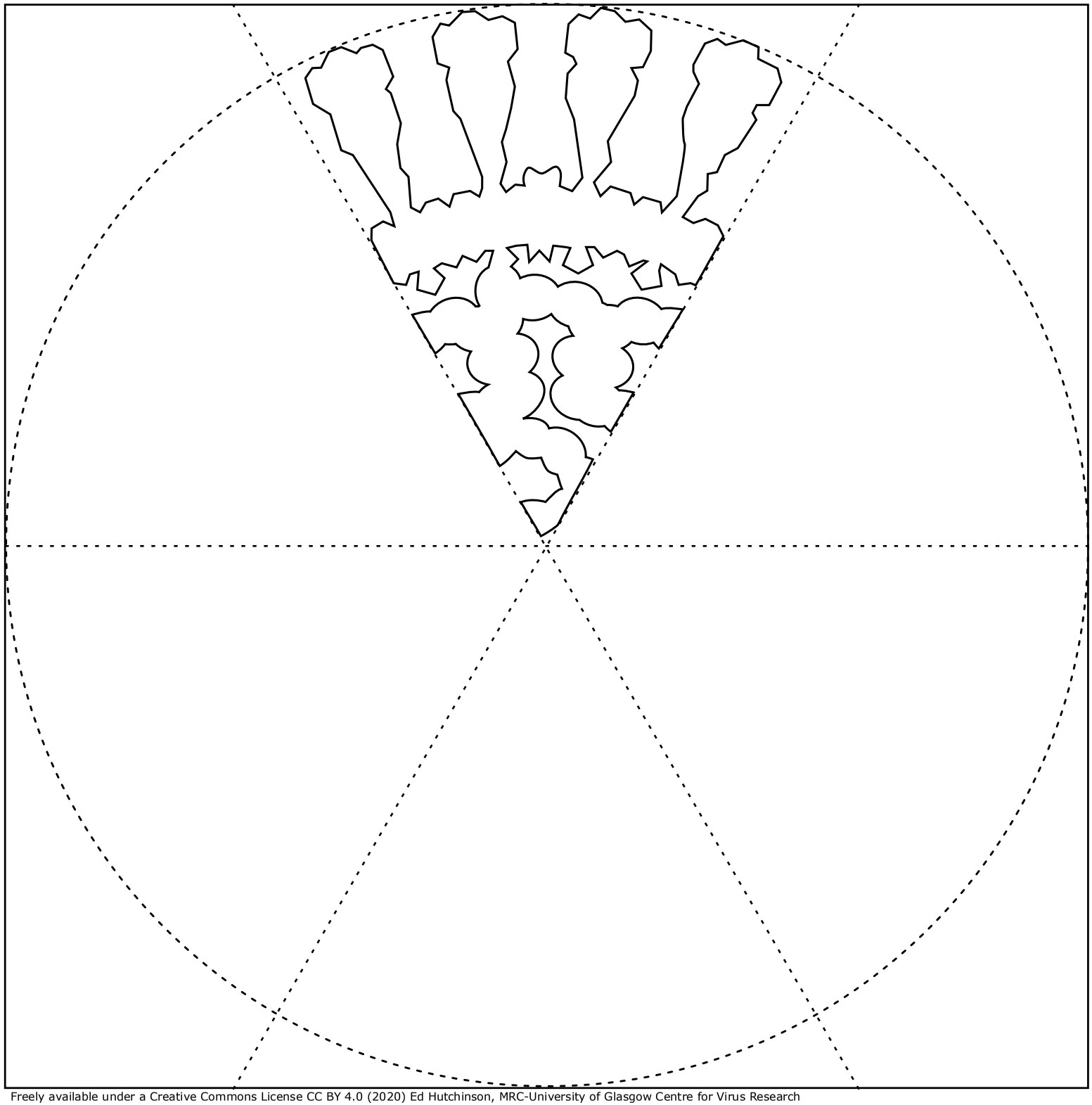

CORONAVIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Different coronaviruses can infect many species of mammals and birds. In humans, coronaviruses are one of the causes of the common cold. Some coronaviruses are more serious: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which causes Coronavirus disease 2019 (COVID-19) has caused a world-changing pandemic.

About the Virus Particle:

The long spikes of S protein, which resemble a solar corona (or 'crown') give the virus its name. S binds to new host cells, which can be blocked by antibodies. The virus has a membrane which can be destroyed by soap or alcohol, and inside this the RNA genome is wrapped in many copies of N protein.

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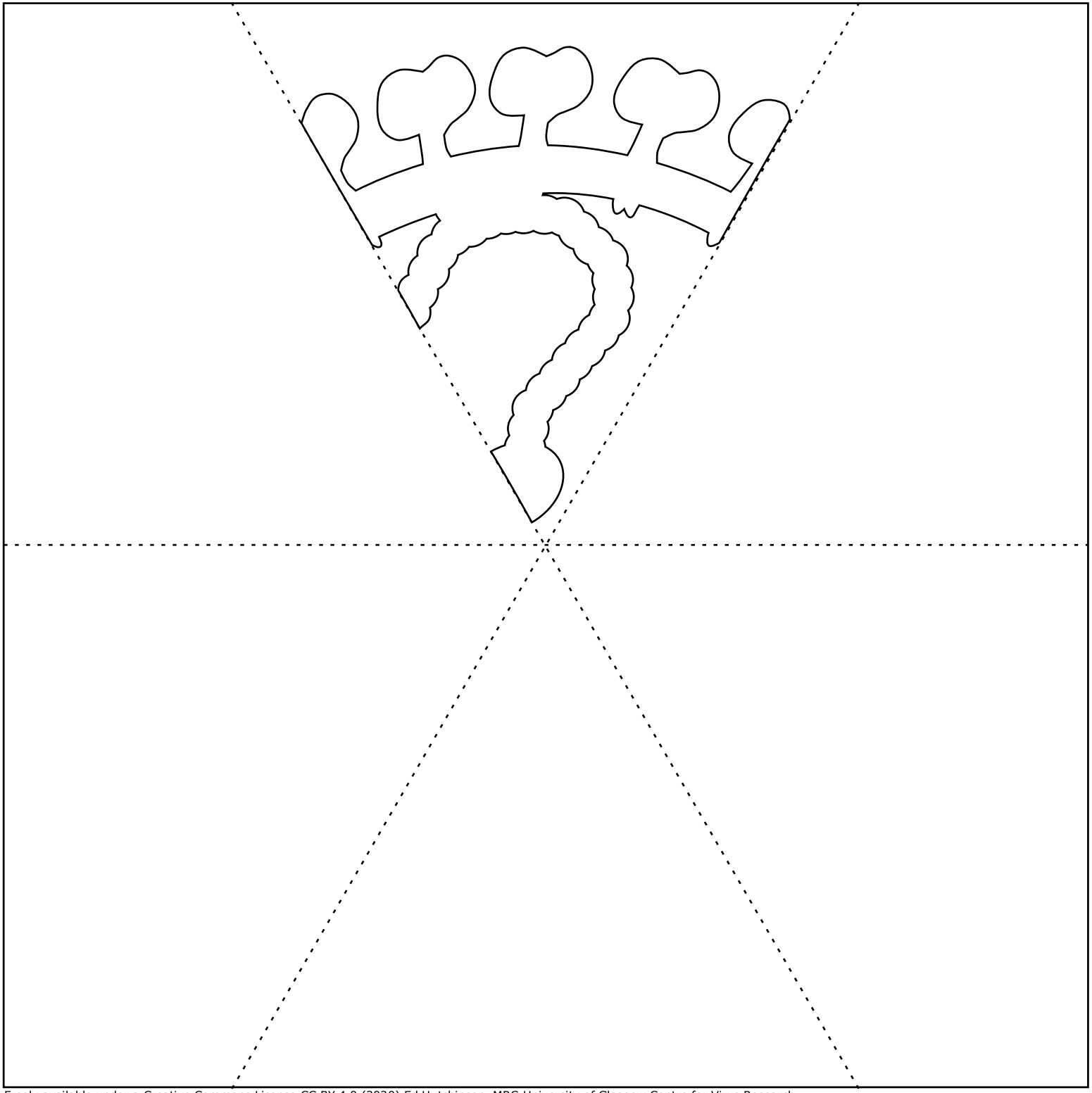

HEARTLAND VIRUS

Difficulty: Easy

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Heartland virus, discovered in 2009 and named after Heartland Regional Medical Center in Missouri, is an example of a bunyavirus. Bunyaviruses are a diverse order of animal and plant viruses, most of them transmitted by biting arthropods - in the case of Heartland virus, by ticks.

About the Virus Particle:

The genome of Heartland virus consists of three segments of RNA, each wrapped in nucleoproteins and bound to a polymerase protein. The virus particle's membrane is coated in a lattice of viral proteins.

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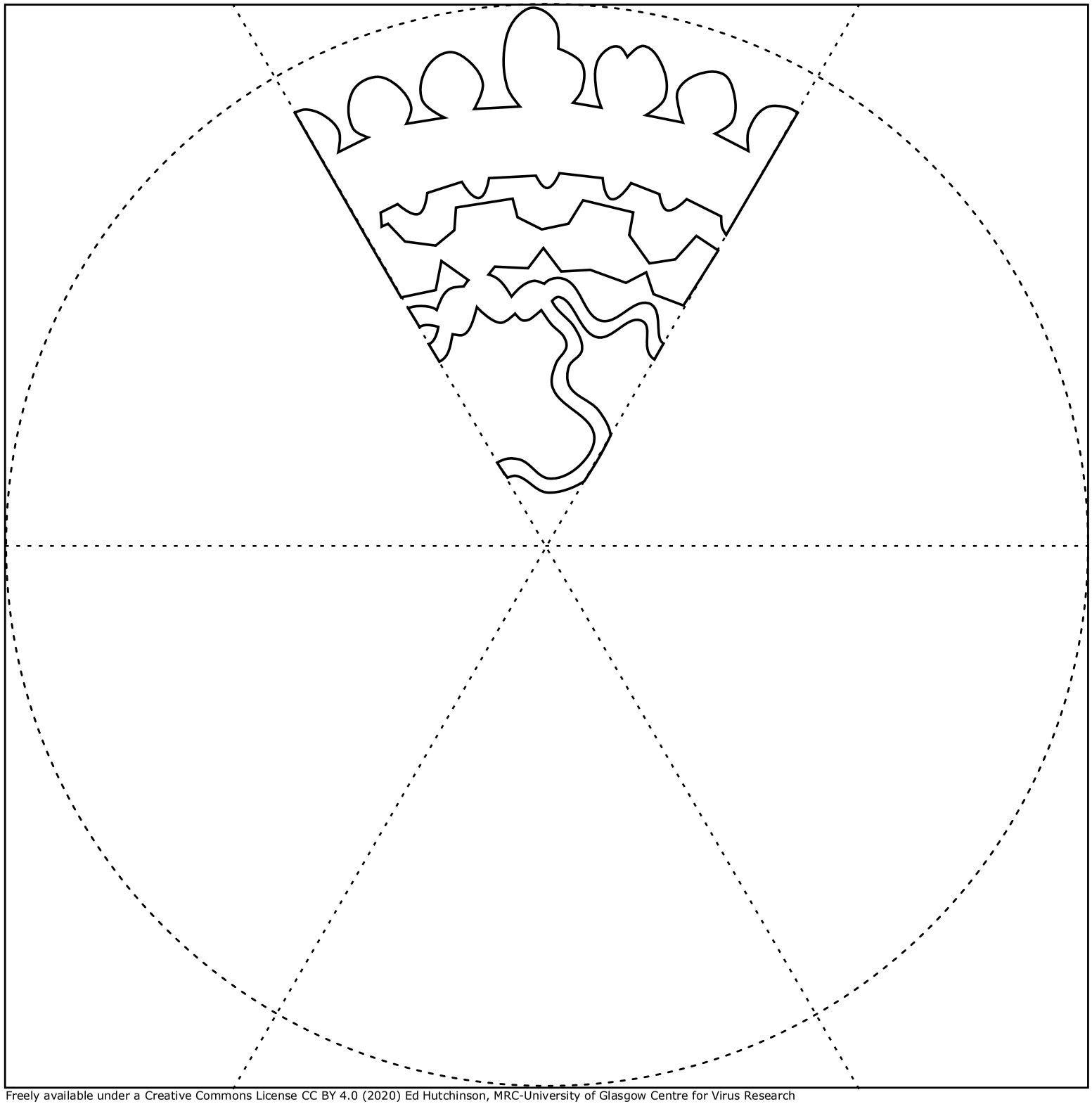

HEPATITIS B VIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

There are many viral diseases that can cause inflammation of the liver (hepatitis), which can lead to liver failure and cancer. Hepatitis B virus (HBV) is a global health problem, though infection can be prevented by vaccination.

About the Virus Particle:

HBV has an unusual genome, formed partly from double-stranded DNA, partly from single-stranded DNA, and partly from single-stranded RNA. This is wrapped in a small particle of membrane and viral proteins.

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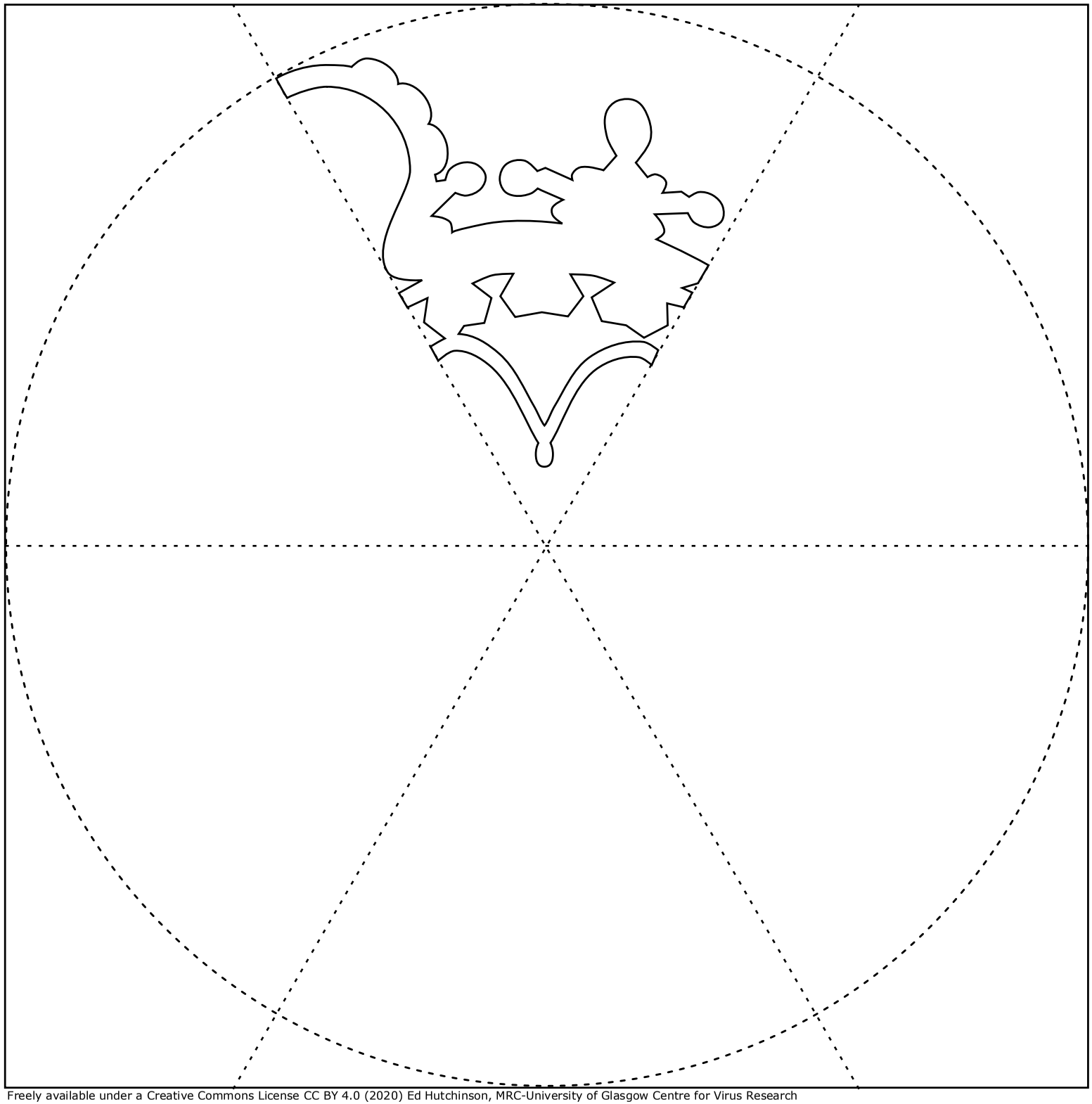

HEPATITIS C VIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

There are many viral diseases that can cause inflammation of the liver (hepatitis). Hepatitis C virus (HCV) is a major cause of viral hepatitis, which causes chronic illness, liver failure and cancer. Recently, improved drugs have made HCV much easier to treat and cure.

About the Virus Particle:

The single-stranded RNA of the HCV genome is surrounded by a layer of matrix protein and wrapped in membrane. HCV particles can fuse with the lipoprotein particles that transport lipids around the body.

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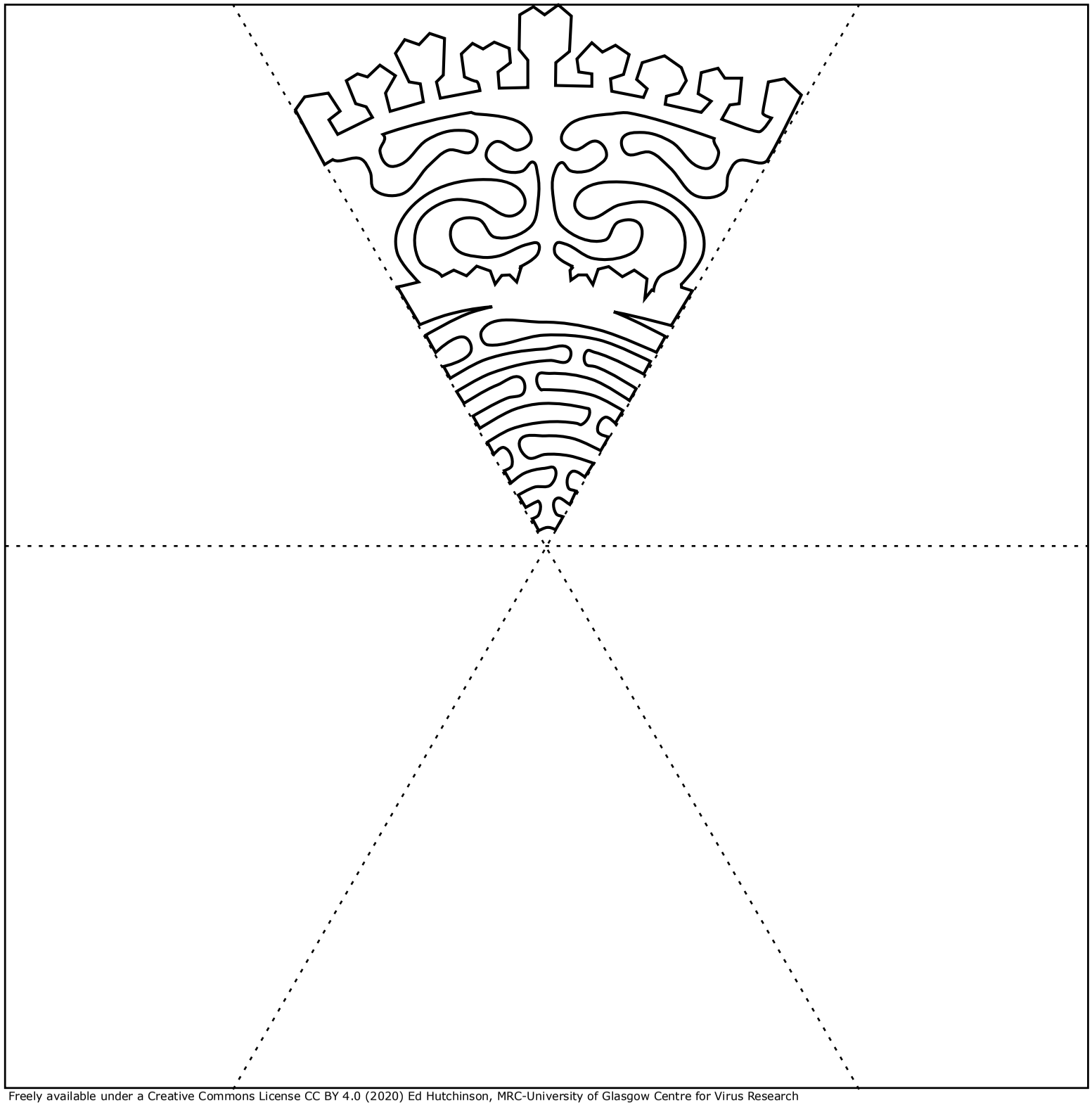

HERPES SIMPLEX VIRUS

Difficulty: Hard

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Herpes viruses are a family of very common viruses that cause lifelong infections. They can lie hidden for long periods but occasionally re-emerge to cause disease. Herpes simplex virus 1, which hides in nerve cells, emerges to cause cold sores.

About the Virus Particle:

A herpes virus particle is complex. It is surrounded by a membrane that is studded with viral proteins. Inside this is a thick protein coat, called the tegument. Within this is a 20-sided (icosahedral) shell or capsid, which contains the viral genome - a long strand of DNA, wrapped into a tight ball to fit into this tiny space.

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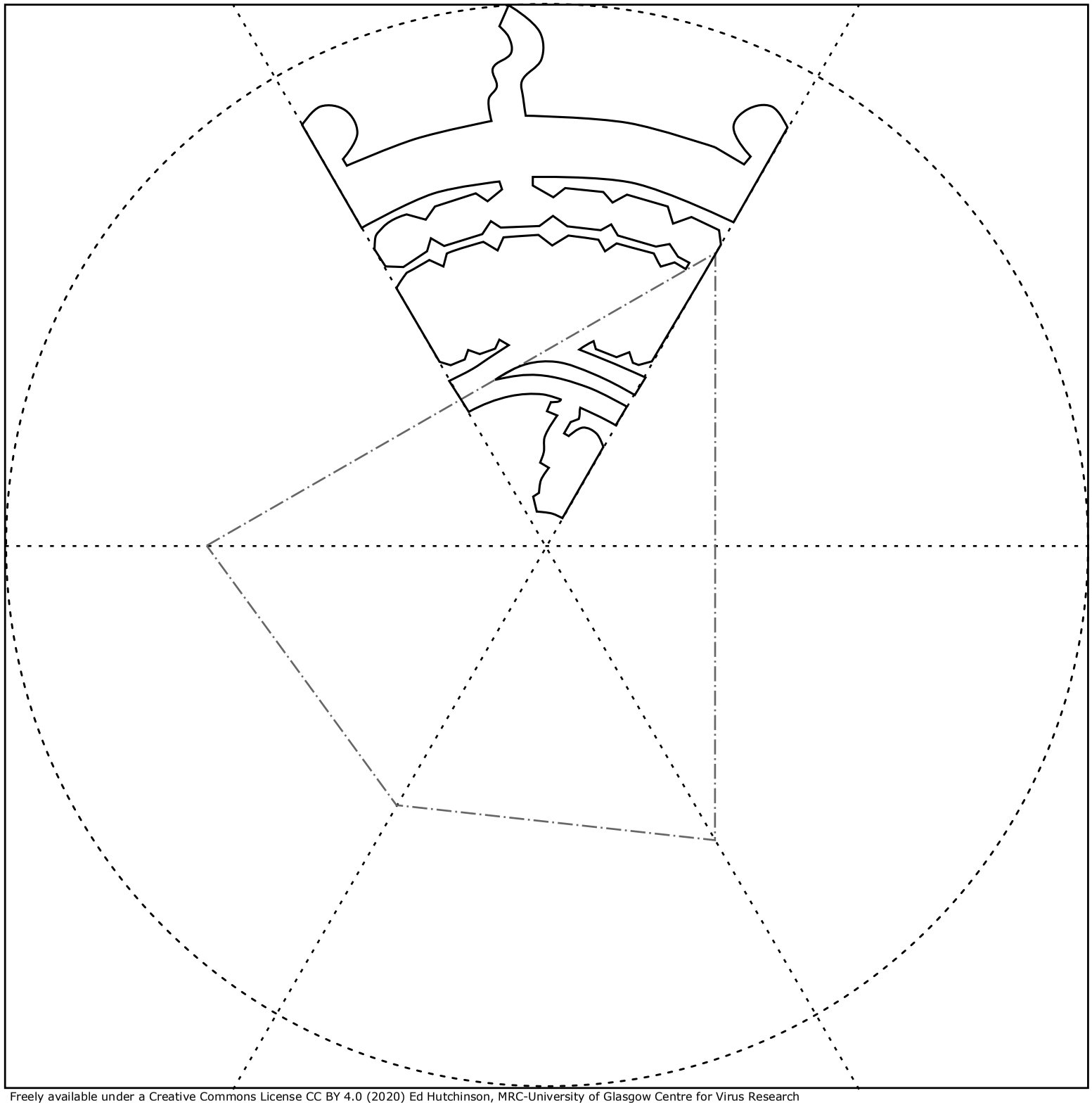

HUMAN IMMUNODEFICIENCY VIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.
(5) To mature the virus particle: refold along the dashed lines.

About the Virus:

HIV is a retrovirus. Our cells copy RNA messages from a DNA genome, but HIV makes a DNA copy of its RNA genome (hence 'retro') which it permanently inserts into the genome of the white blood cells it infects. If untreated, this severly weakens the immune system, causing Acquired Immunodeficiency Syndrome (AIDS).

About the Virus Particle:

Two copies of the viral genome are surrounded by a membrane and viral proteins. After the virus particle has formed, viral enzymes cut the proteins, allowing the particle to rearrange into its mature form.

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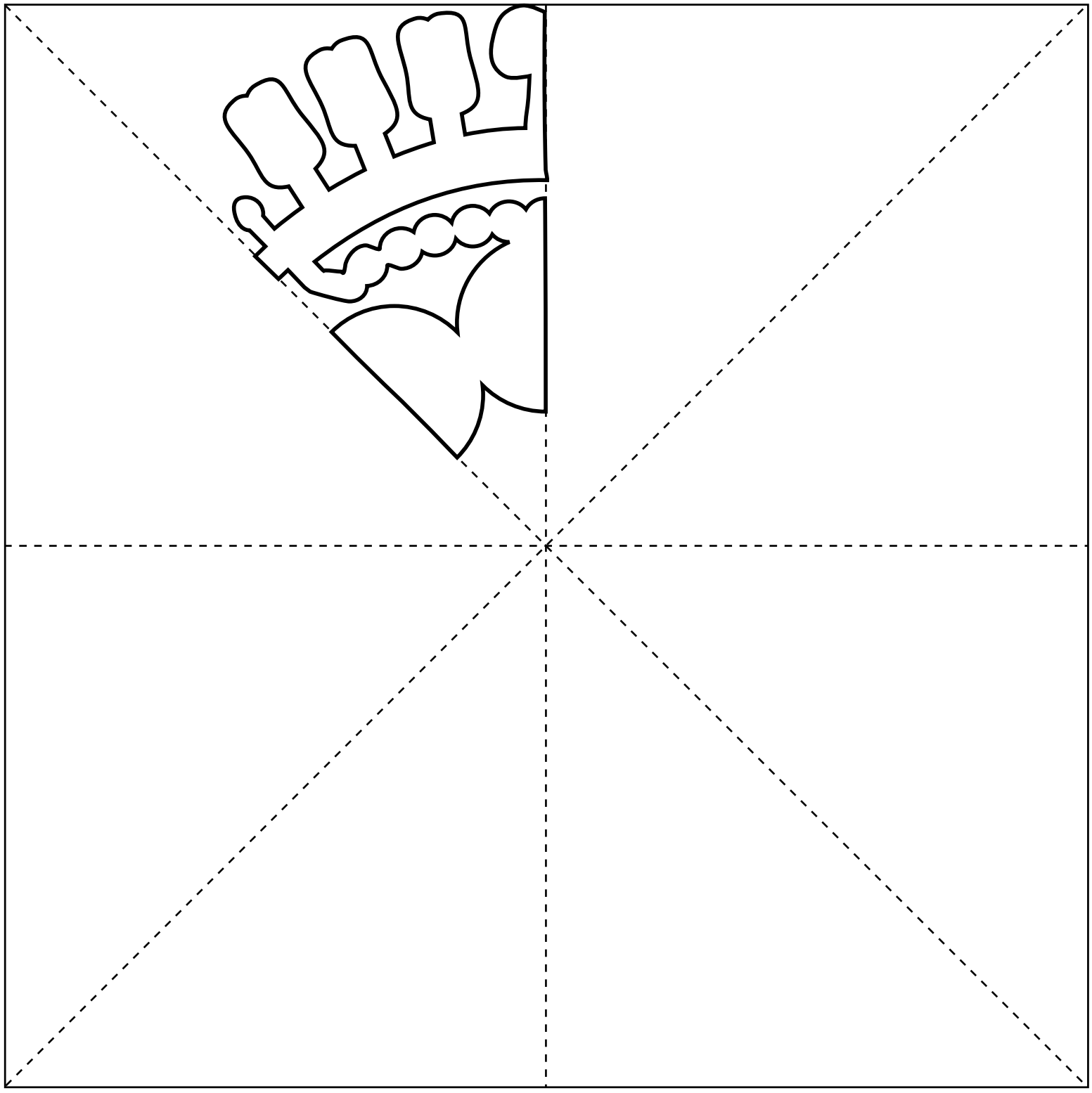

INFLUENZA VIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Influenza viruses cause influenza, a common winter respiratory illness that causes fever and exhaustion. Spikes on their surface, HA and NA, can be blocked by antibodies if they are of the right sort (H1N1, H3N2, etc). However, the spikes change rapidly, and the vaccines which provide immunity to them have to be updated often. Occasionally, human influenza viruses pick up completely new spikes from an animal influenza virus, allowing them to escape all immune protection - this creates an influenza pandemic.

About the Virus Particle:

The influenza virus particle is wrapped in a membrane, which is coated with the two spike proteins and penetrated by a pore. Inside is a layer of matrix protein and the eight segments of the viral genome.

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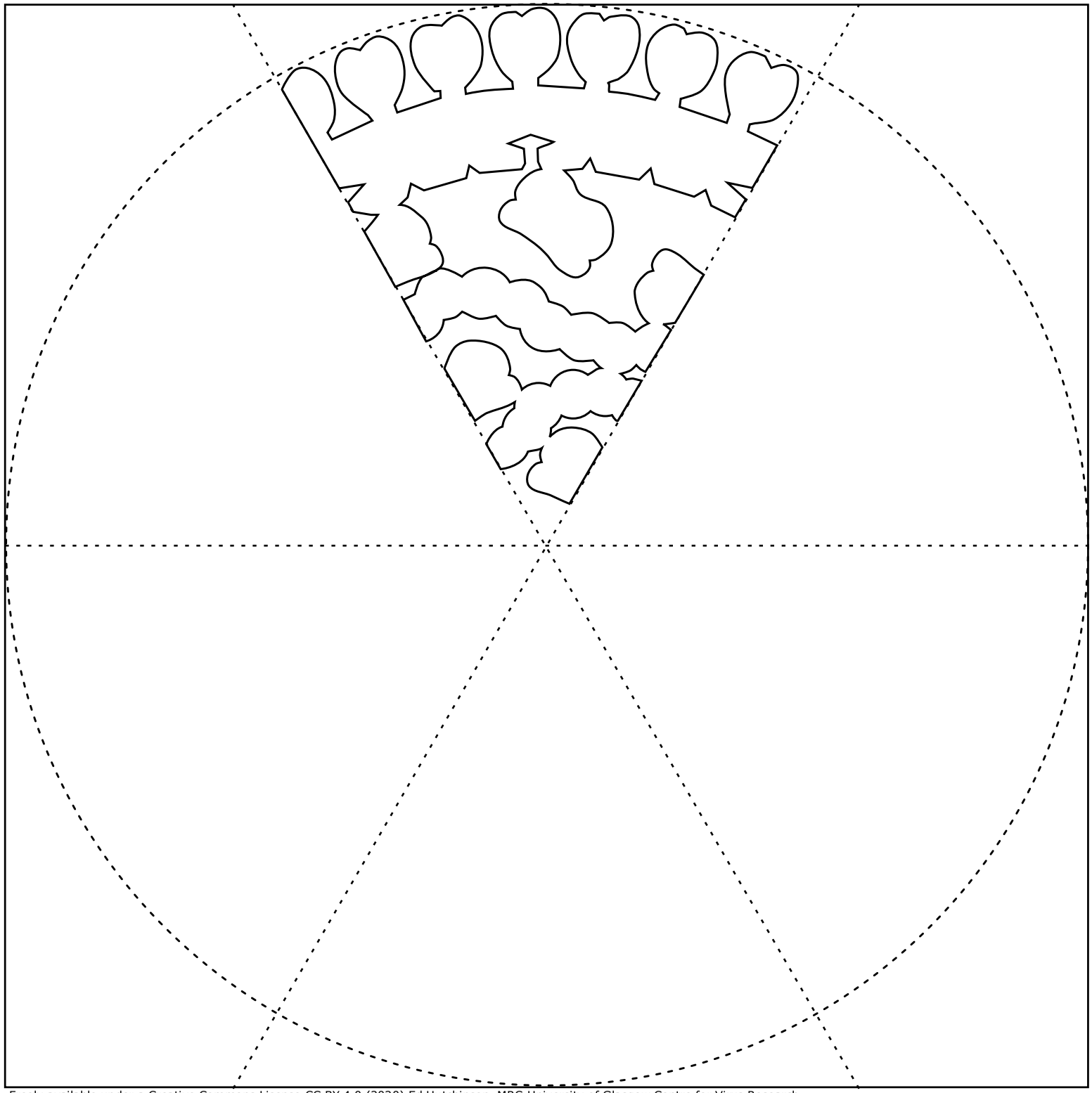


LASSA VIRUS

Difficulty: Medium

Instructions:

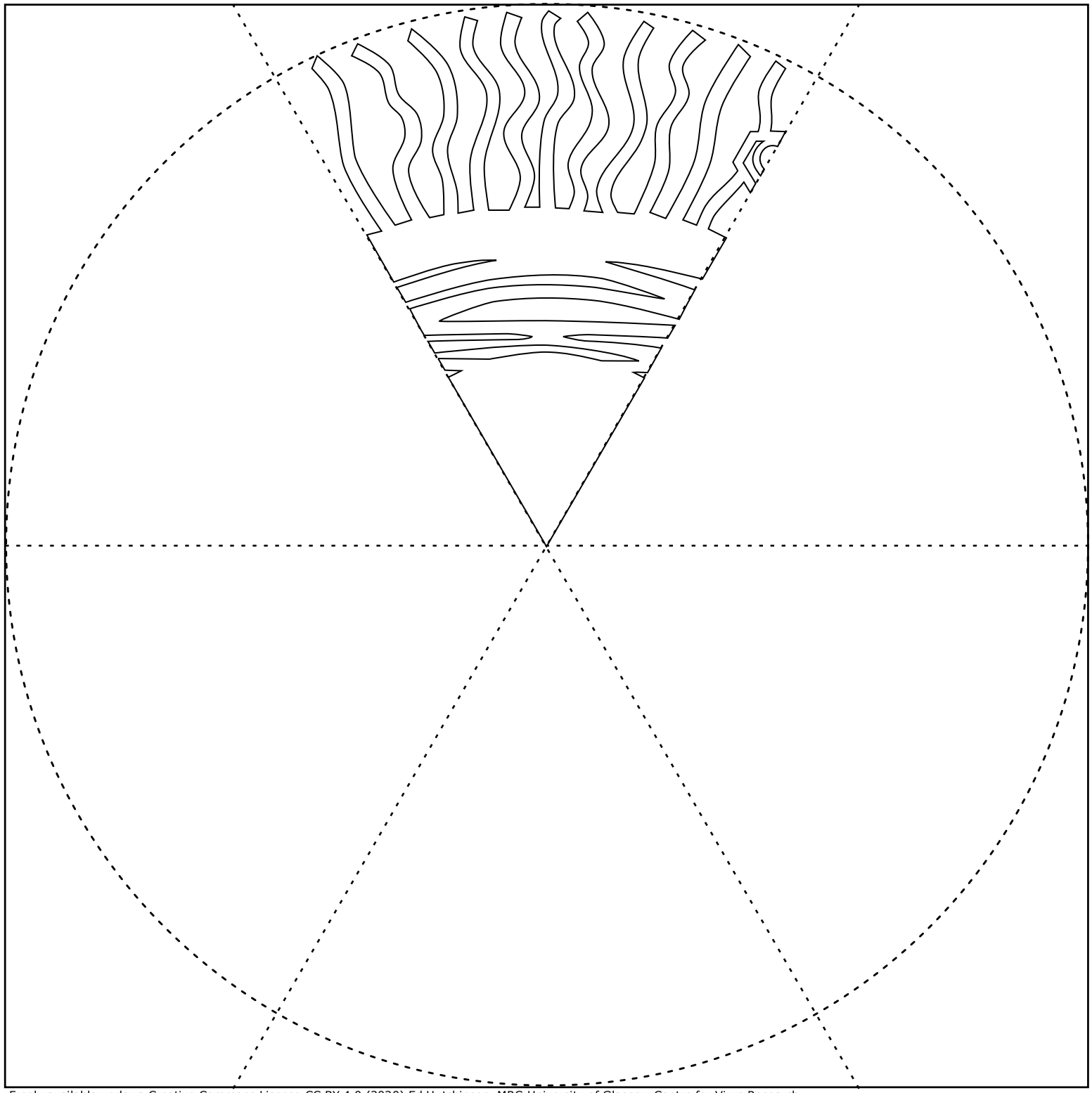
(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Lassa haemorrhagic fever is a severe illness that can be caught from rodents in parts of West Africa. It is caused by an emerging virus (one that is becoming more common), called Lassa mammarenavirus.

About the Virus Particle:

The Lassa virus genome consists of two segments of single-stranded RNA, bound to viral proteins and surrounded by matrix protein and a membrane. Receptor-binding proteins in the membrane allow the virus to enter new cells.



MIMIVIRUS
and Sputnik virophage

Difficulty: Hard

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Viruses:

Viruses were originally identified as microbes that were smaller than bacteria, but recently giant viruses have been discovered, such as this Mimivirus which infects amoebae. Not only are they bigger than some bacteria, giant viruses are even exploited by smaller 'satellite' viruses, or 'virophages,' that require the giant virus for their own replication.

About the Virus Particles:

The Mimivirus particle is icosahedral and decorated with long fibres. Inside, membranes and proteins wrap around a core containing the DNA genome. The Sputnik virophage particle is small, icosahedral and contains a circular DNA genome.

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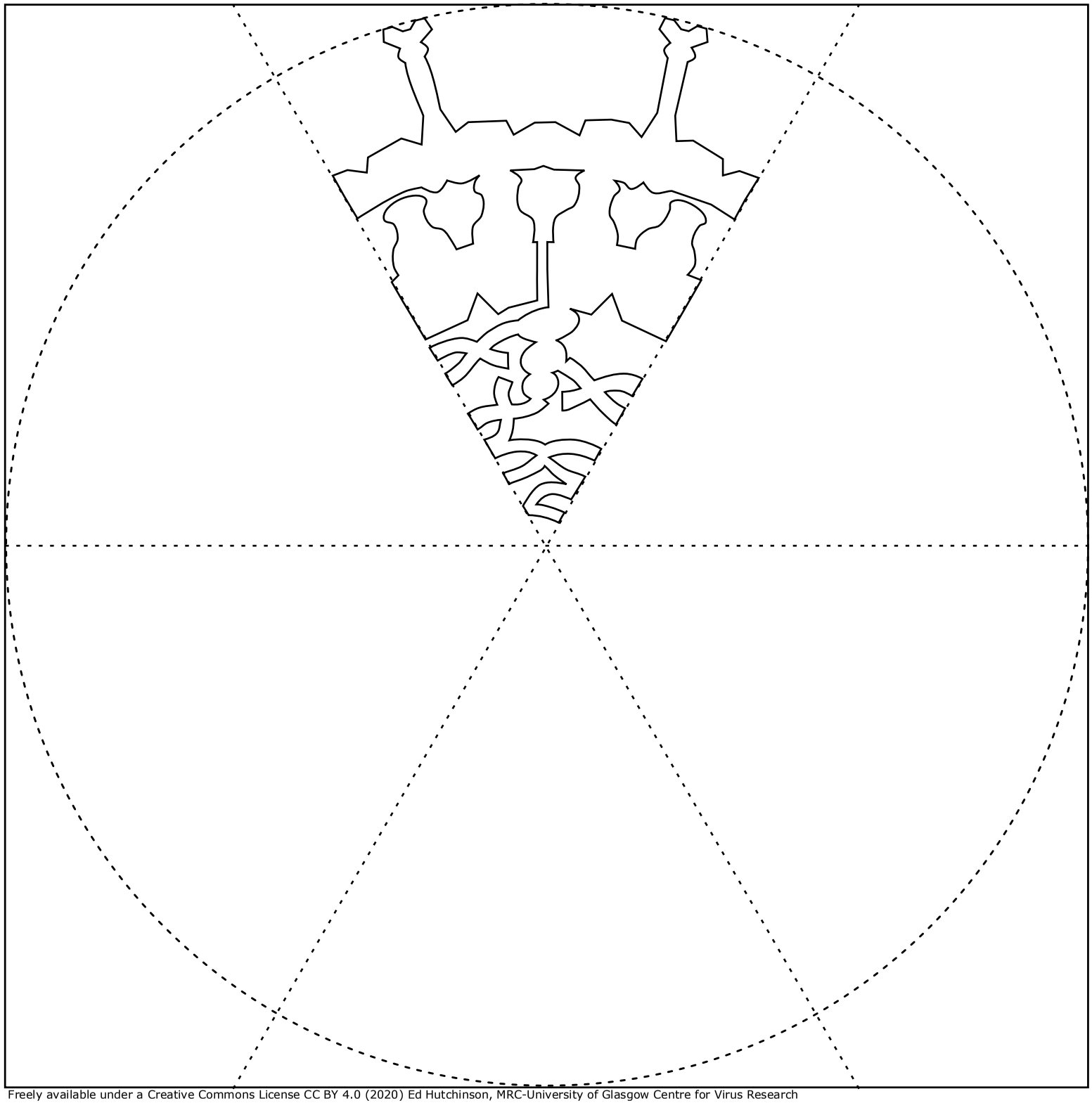

ROTAVIRUS

Difficulty: Hard

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Rotaviruses are an extremely common cause of diarrhoea, particularly in young children. Most people are infected at least once by the age of five.

About the Virus Particle:

The rotavirus particle has a wheel-like appearance (rota means 'wheel') and is formed from three layers of capsid proteins. The inner two layers form a core that contains the genome, as 11 segments of double-stranded RNA, and the enzymes that copy it. Prominent spikes help the particle to enter cells.

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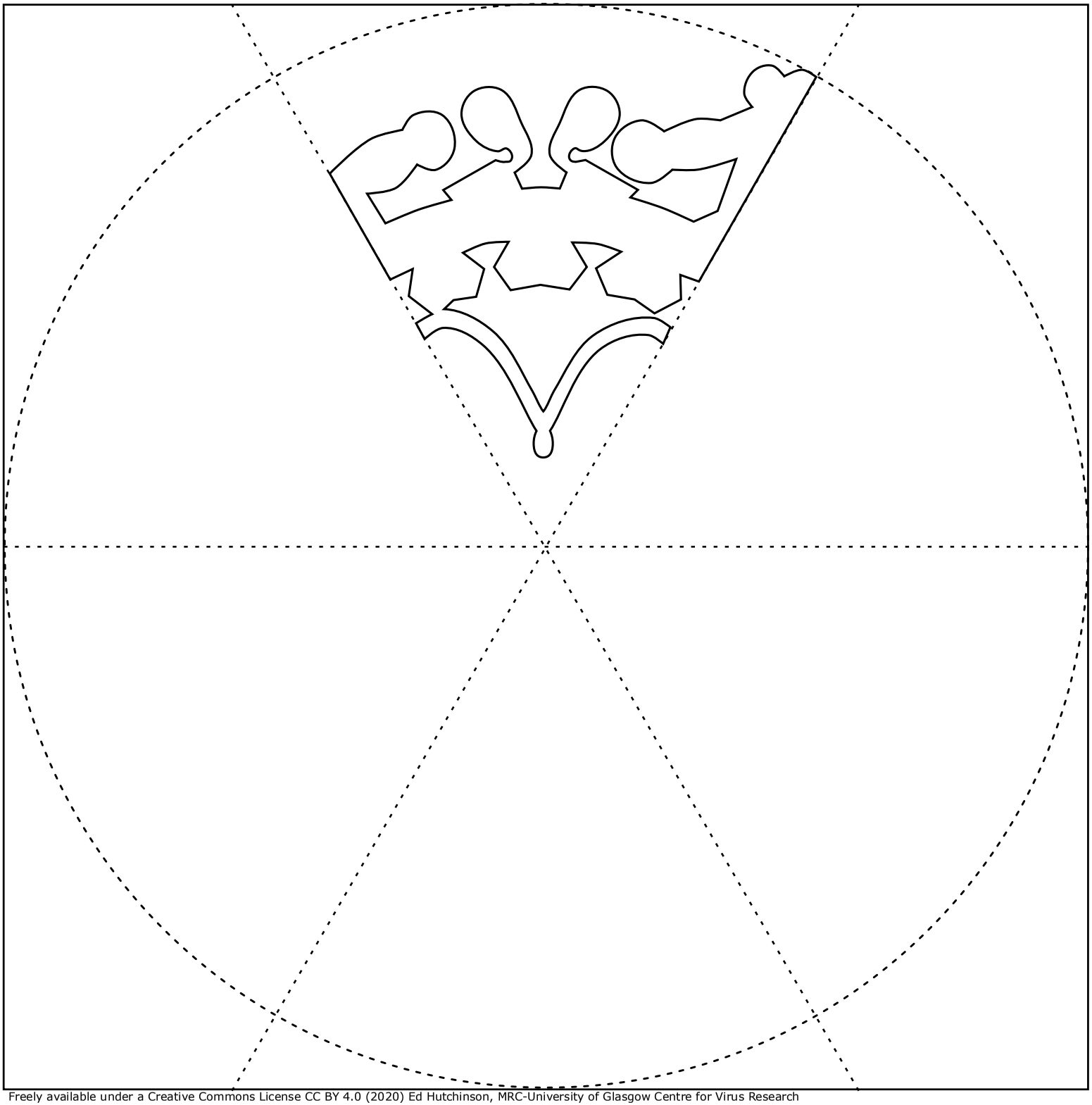

ZIKA VIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Zika virus is spread mainly by mosquito bites. It was first identified in Uganda, but its range is increasing. In 2015 it reached the Americas and caused a major epidemic. Zika fever is typically a mild illness, but infections during pregnancy can cause microcephaly (a shortened head) in babies.

About the Virus Particle:

The Zika virus genome is single-stranded RNA, surrounded by matrix protein and a membrane, which is enclosed in more proteins. The outer proteins are initially raised up in spikes but flatten against the membrane as the particle matures.

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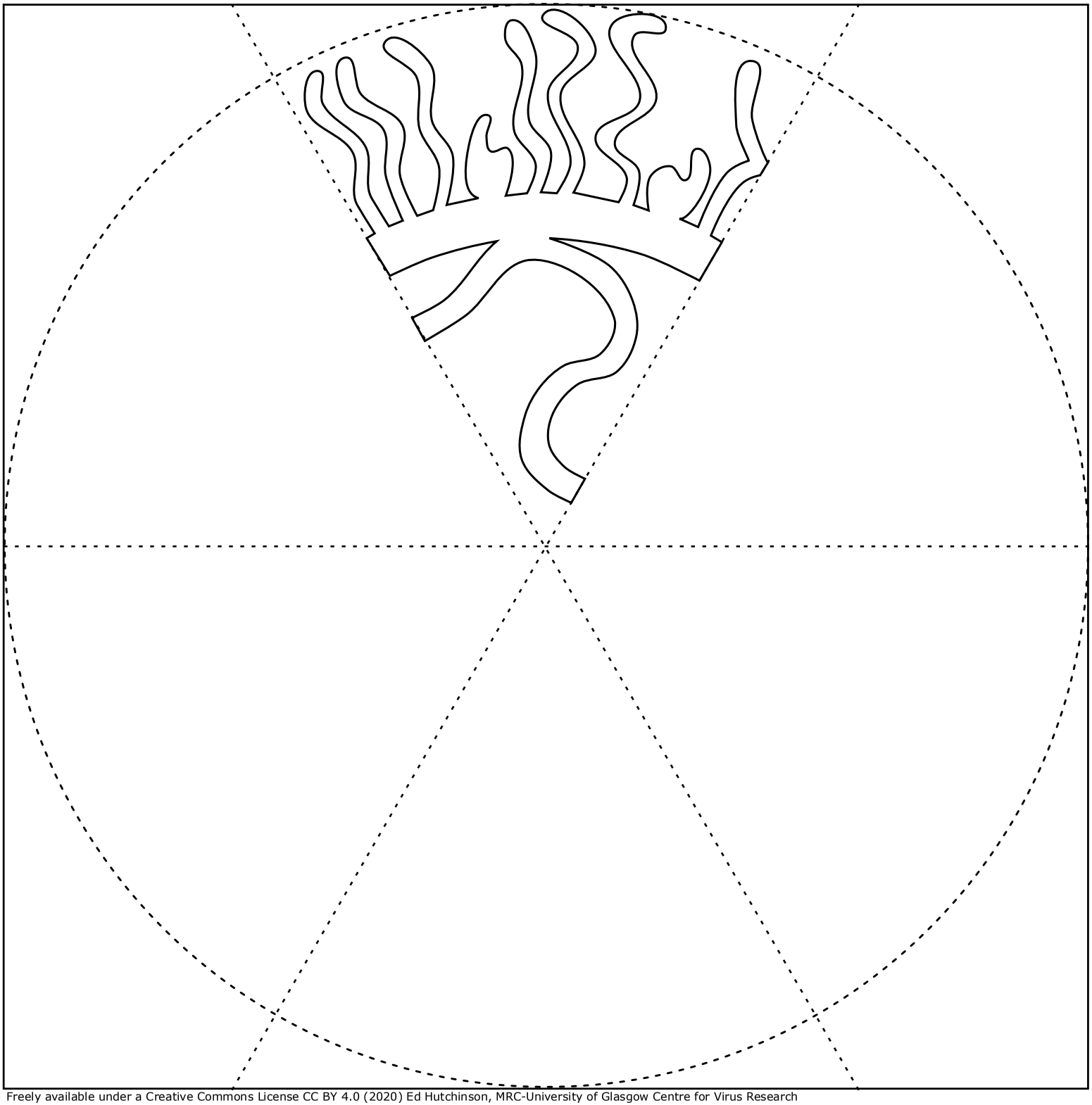

RNA vaccine

Difficulty: Easy

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Vaccine:

This is not a virus, but in many ways it behaves like one. It is an artificial particle, designed to deliver the instructions for making all or part of the SARS-CoV-2 S protein to a cell. When the cell makes this harmless protein, the immune system learns to recognise it and can then attack real SARS-CoV-2 particles effectively.

About the Particle:

Like many viruses, this vaccine is a set of RNA instructions for making protein (mRNA, messenger RNA) wrapped in a membrane. The membrane is stabilised with strands of polyethylene glycol (PEG) but the RNA itself is unstable and so the vaccine needs to be kept very cold.

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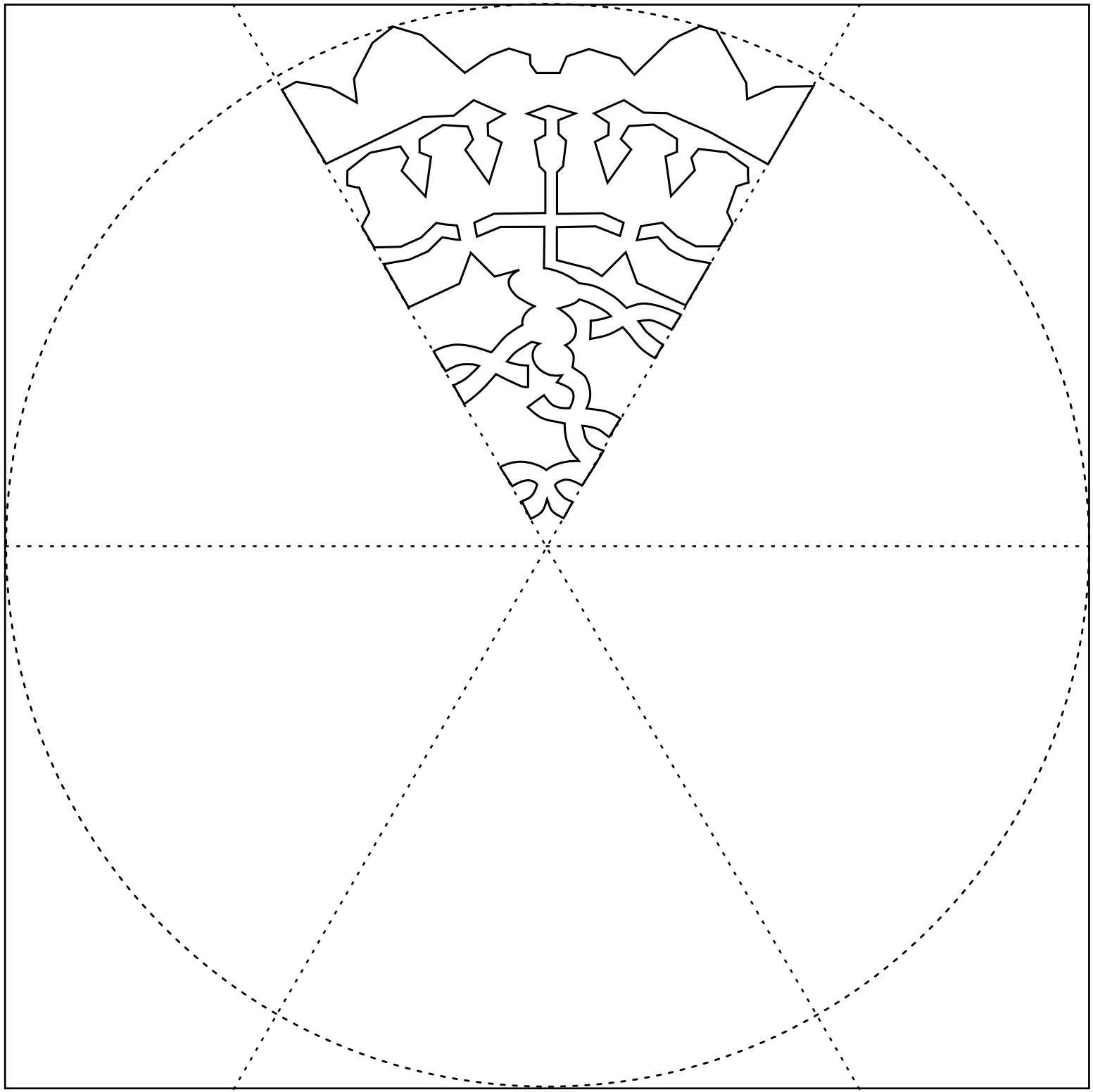

BLUETONGUE VIRUS

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus:

Bluetongue disease affects ruminants, including cattle, goats and particularly sheep. It can cause serious disease, including the swollen, blueish tongue that gives it its name. The virus that causes bluetongue disease is spread by midge bites.

About the Virus Particle:

The bluetongue virus particle is formed from three layers of capsid proteins. The inner two layers form a core that contains 10 segments of double-stranded RNA genome, and the enzymes that copy it.

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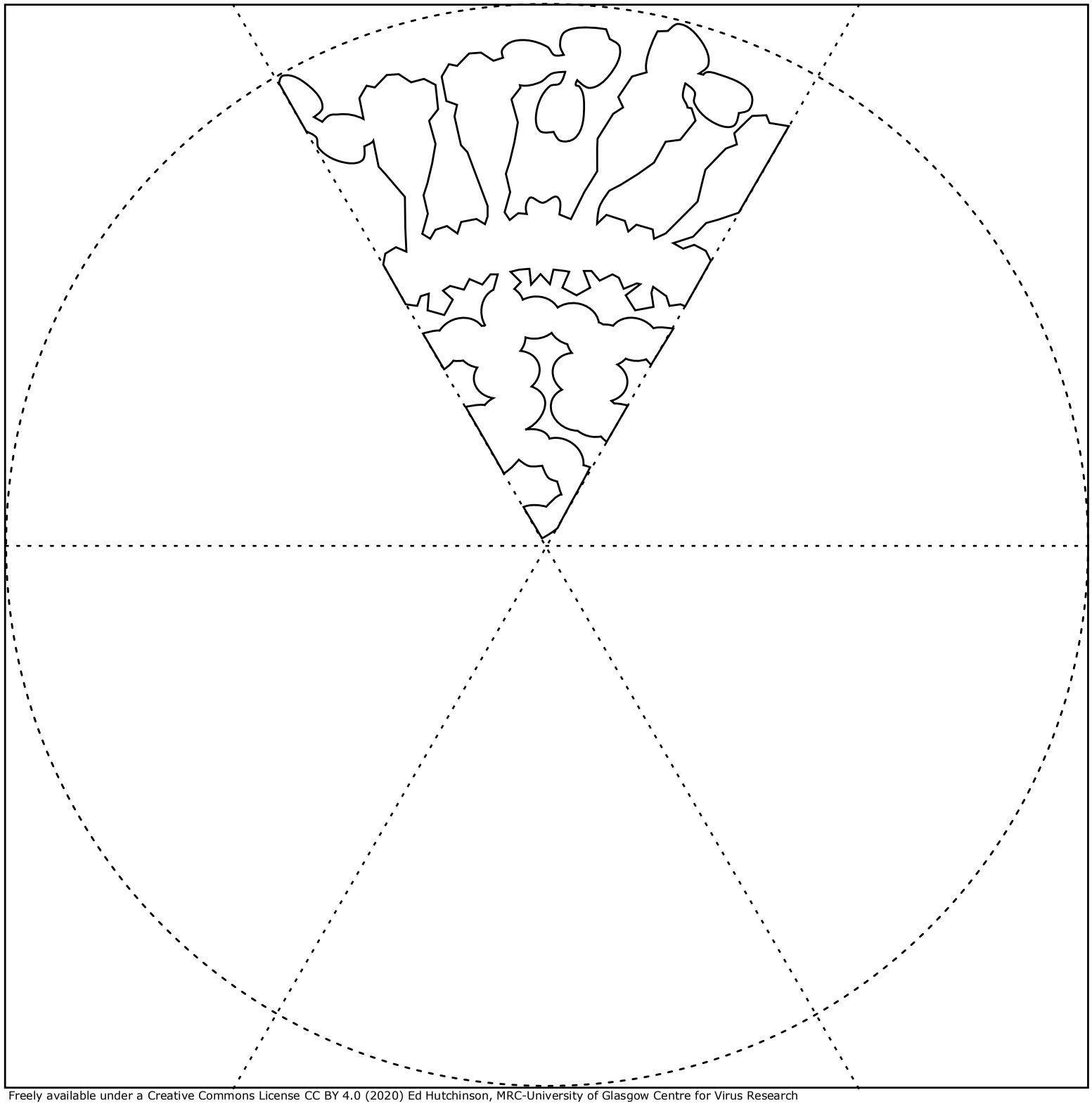

CORONAVIRUS AND ANTIBODIES

Difficulty: Medium

Instructions:

(1) Cut out the square.
(2) Fold dotted lines to form a triangle, with the design on top.
(3) Cut out the design, cutting through the entire stack.
(4) Unfold.

About the Virus Particle:

This is what the end of a pandemic looks like.

Coronavirus particles enter cells by binding to them with the spikes of S protein on their surface. Here, the coronavirus has infected someone whose immune system can recognise S – either from a previous infection, or due to vaccination. Now, the mucus in their airways contains antibodies that lock on to specific sites on S.

Once the S proteins are bound to antibodies the virus is 'neutralised' – it can no longer bind to our cells and infect us. It is no longer a threat.

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