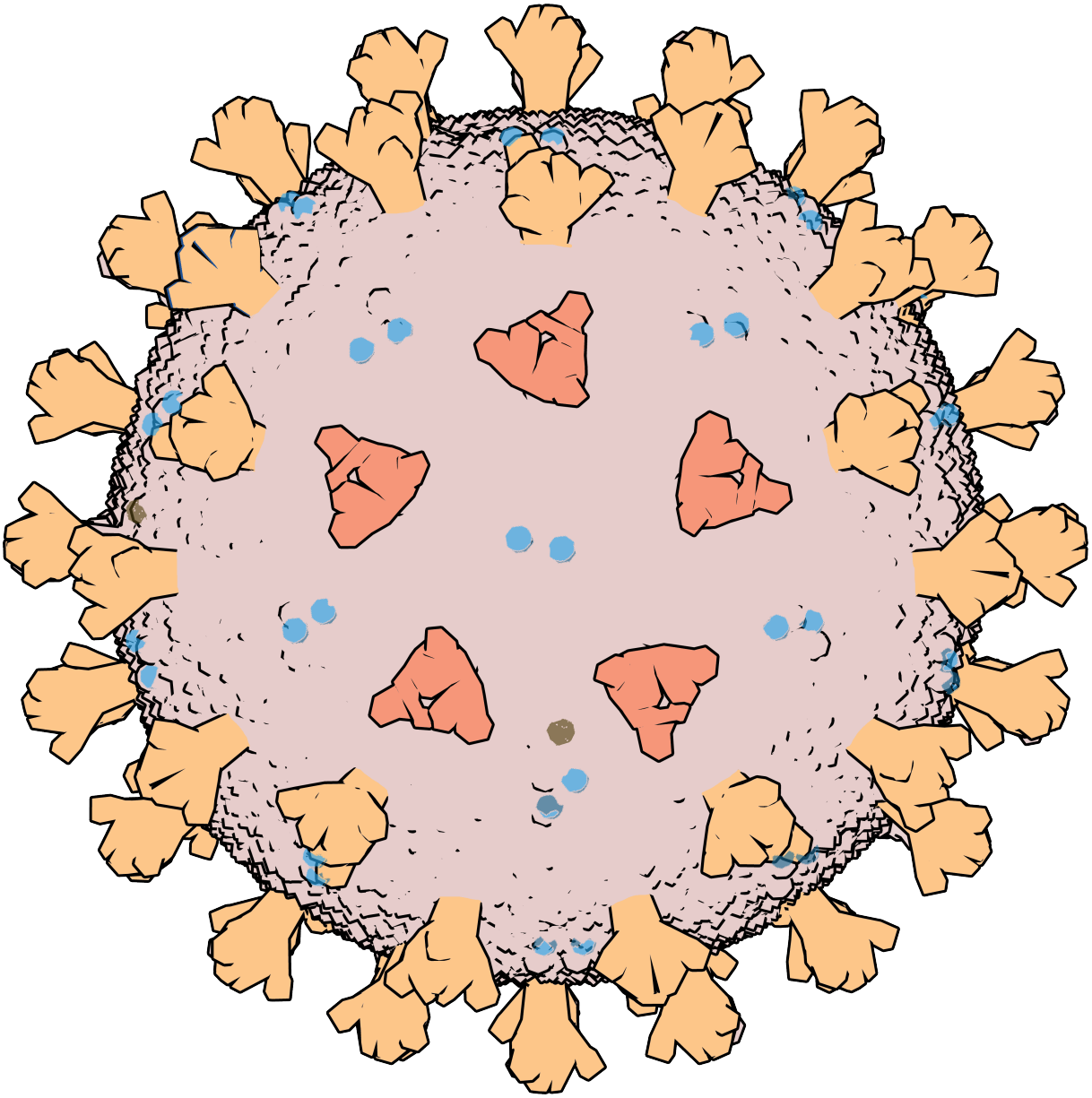
SARS-COV-2 - COVID-19
A Coloring Book

JEAN-YVES SGRO, PH.D.



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Cover: "artistic redering" by JYS from 3D design file by Alejandro León (@alelepd) outlined within ChimeraX software and painted in PhotoShop. See text for more details.

CONTENTS

LIST OF FIGURES

LIST OF TABLES

LISTINGS

ACRONYMS

2019-nCo 2019 Novel Coronavirus

CDC Center for Disease Contol and Prevention

COVID-19 Coronavirus Disease 2019

SARS Severe Acute Respiratory Syndrome

WHO World Health Organization

PREFACE

We are in the midst of the COVID-19 pandemic caused by the SARS-CoV-2 coronavirus and the World is holding on, many humans staying at home. I created this little booklet with the idea that it could help distract our minds, especially young minds that like to do coloring.

While I had been thinking of a molecular coloring book for a long time, there has been 2 recent inspirations:

1. The Protein Data Bank, the repository of most known molecular 3D data, has published 2 coloring book: *Coloring Molecular Machinery* and *Discovering Biology Through Crystallography*.[1] (figure 1.)

2 . Artist and Scripps Professor David Goodsell recently created a coronavirus painting as well as a blank coloring version.[2] (figure 2.)

Scripps Prof. David Goodsell[3] [4], famous for his non-photorealistic illustrations of molecules, has created a beautiful rendering of the coronavirus entering the

1 https://pdb101.rcsb.org/learn/coloring-books
2 https://pdb101.rcsb.org/learn/coloring-books/coloring-coronavirus
3 https://ccsb.scripps.edu/goodsell/
4 Twitter: @dsgoodsell

Coloring Coronavirus *(Coloring Book)*

Coloring Molecular Machinery *(Coloring Book)*

Discovering Biology Through Crystallography *(Coloring Book)*

Figure 1: PDB coloring books.

Figure 2: SARS-CoV-2 painting and key, Pr. David Goodsell.

lung as a painting displayed on the Protein Data Bank web site[5].

This painting (figure 2) depicts a coronavirus just entering the lungs, surrounded by mucus secreted by respiratory cells, secreted antibodies, and several small immune systems proteins. The virus is enclosed by a membrane that includes the S (spike) protein, which will mediate attachment and entry into cells, M (membrane) protein, which is involved in organization of the nucleoprotein inside, and E (envelope) protein, which is a membrane channel involved in budding of the virus and may be incorporated into the virion during that process. The nucleoprotein

5 https://pdb101.rcsb.org/sci-art/goodsell-gallery/coronavirus

inside includes many copies of the N (nucleocapsid) protein bound to the genomic RNA.

The present little booklet was done mostly in two week-end and does not have the pretention to be at the same level as these professionally designed coloring books. However, I hope that its entertainment level will help while we wait for better days. Feel free to share it.

1

SARS-COV-2 CAUSES COVID-19

Information from the World Health Organization (WHO)[1].

who.int

Coronavirus disease (COVID-19) is an infectious disease caused by a new virus: SARS-CoV-2

The disease causes respiratory illness (like the flu) with symptoms such as a cough, fever, and in more severe cases, difficulty breathing. You can protect yourself by washing your hands frequently, avoiding touching your face, and avoiding close contact (1 meter or 3 feet) with people who are unwell.

How it spreads: *Coronavirus disease spreads primarily through contact with an infected person when they cough or sneeze. It also spreads when a person touches a surface or object that has the virus on it, then touches their eyes, nose, or mouth.*

Video: **How to protect yourself against COVID-19**[2]

For information purposes only. Consult your local medical authority for advice. Source: World Health Organization

See also: Center for Disease Contol and Prevention(CDC)[3]

1 https://www.who.int/emergencies/diseases/novel-coronavirus-2019
2 https://youtu.be/1APwq1df6Mw
3 https://www.cdc.gov/

Another good information page is from a scientific animation company.[4] The page covers symptoms, transmission, precautions and healthy habits for coronavirus prevention. A set of slides can also be downloaded free as a PDF file.

The following disclaimer appears on their page: *Disclaimer: The information in no way constitutes, or should be construed as medical advice. Nor is the above article an endorsement of any research findings discussed in the article an endorsement for any of the source publications.*

4 https://www.scientificanimations.com/coronavirus-symptoms-and-prevention-explained-through-medical-animation/

2

3D "ARTISITIC" MODELS

Artisitc renderings have been done by computer artists. The 3D file formats used are different than the format used for scientifically deduced structures found at the Protein Data Bank and these "illustration" files are not readily opened with standard molecular graphics software. Many of these files are for purchase on web sites.

Author Alejandro Le'on [1] [2] created a free version that can be accessed already rendered within a web site[3] and that can be manipulated in 3D (See figure 3.)

A 12 seconds video of what this looks like is available on YouTube[4].

According to the author this 3d model of Coronavirus (SARS-CoV-2) based on the images from CDC/PHIL. The model is available to download for free (MIT License)[5].

1 Twitter: @alelepd
2 https://alejandro.fun/
3 https://spline.design/coronavirus3d/
4 https://youtu.be/K0ORIaAuXb4
5 https://opensource.org/licenses/MIT

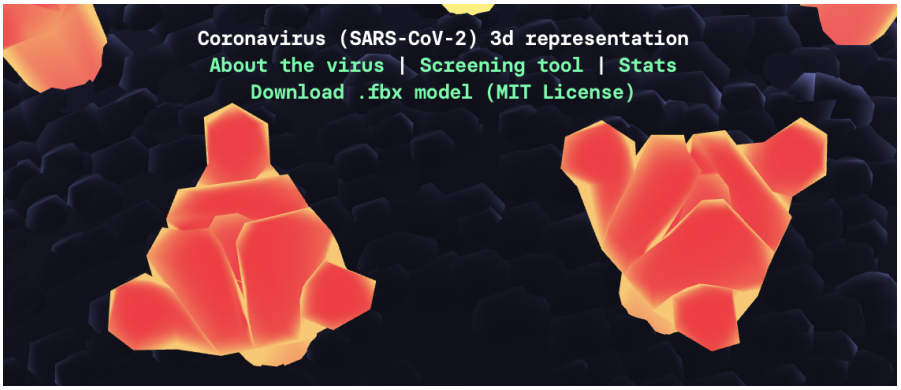


Figure 3: Details of coronavirus3d file shown on spline.design showing artisitic rendering of surface trimeric spike protein.

The 3D model file can be downloaded[6] as a compressed binary in the `.fbx` format that is typically used to allow transfer to and from various 3D illustration software.

A web site[7] can convert this file in other 3D formats[8]. Noteworthy is the fact that the most recent Photoshop version can open the `.obj` format into a 3D layer where the various "layers" can be assigned a color or a texture (figure 4.)

Figure 4 is a stereo version created with this file within Photoshop.

The coronavirus3d (*e.g.* in `.obj` format) can also be rendered with the free 3D software MeshLab[9] available for Windows/Mac/Linux. Within this software

6 https://spline.design/coronavirus3d/_assets/coronavirus3d.fbx
7 https://products.aspose.app/3d/conversion/
8 Available formats: FBX, OBJ, 3DS, DRC, AMF, RVM, DAE, GLTF, GLB, PDF, HTML, PLY, STL, U3D
9 http://www.meshlab.net/

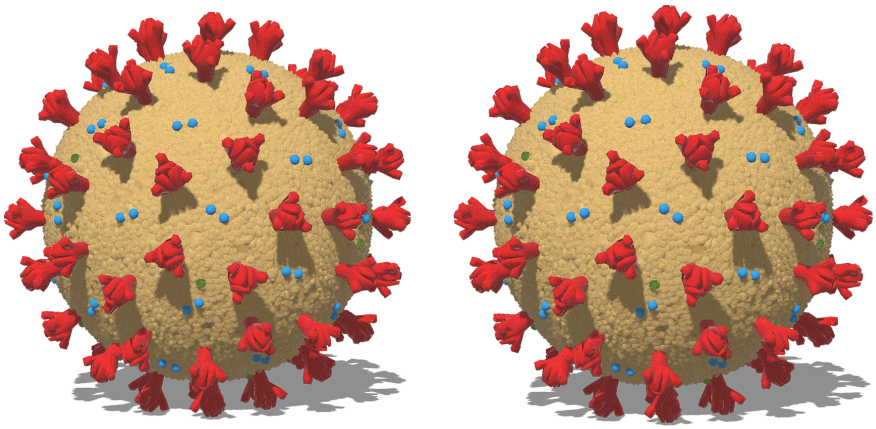


Figure 4: Stereo rendering of coronavirus3d file in Photoshop

all "layers" are given the same color, but vertices can be colored which can create "artistically nice" renderings as well (figure 5.)

2.1 INTERACTIVE 3D MODEL

Another, interactive 3D model describing the viral particle and its proteins was created by Corinth, a Czech educational companies, and Lifeliqe. In collaboration with experts from Charles University, they created a visual 3D model COVID-19 for educational purposes.[10]

2.2 CAVEATS OF MODELS

The actual structure of the virus would not appear as symmetrical as these models which show what is called "icosahedral symmetry." This is mostly due to the techniques to create such models.

10 https://www.lifeliqe.com/blog/3dmodel-of-coronavirus/

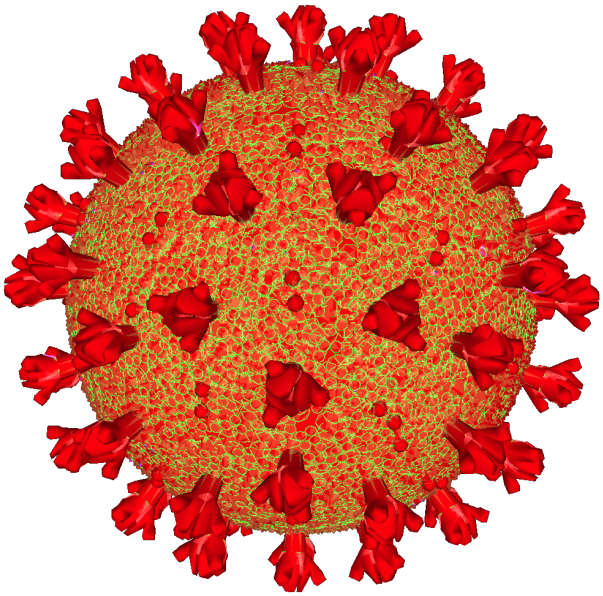


Figure 5: MeshLab rendering of coronavirus3d file.

Therefore, the black and white images to be colored show inherent (icosahedral) symmetry, that could be recognized as two-fold, three-fold, and 5-fold symmetry in the images.

However, since the (mostly artificial) symmetry built-in the model, the coloring pages will be presented by groups of images seen from the same symmetry venture point separated within different chapters labeled 5X, 3X and 2X.?

SARS virus was described by Neuman et al. [4] as *enveloped and pleomorphic and are thus refractory to crystallization and symmetry-assisted reconstruction.*

In that sense it would be more "blobby", less symmetrical, varying in the size and shape as was seen already in 1975 in this coronavirus electron micrograph (figure 6.)

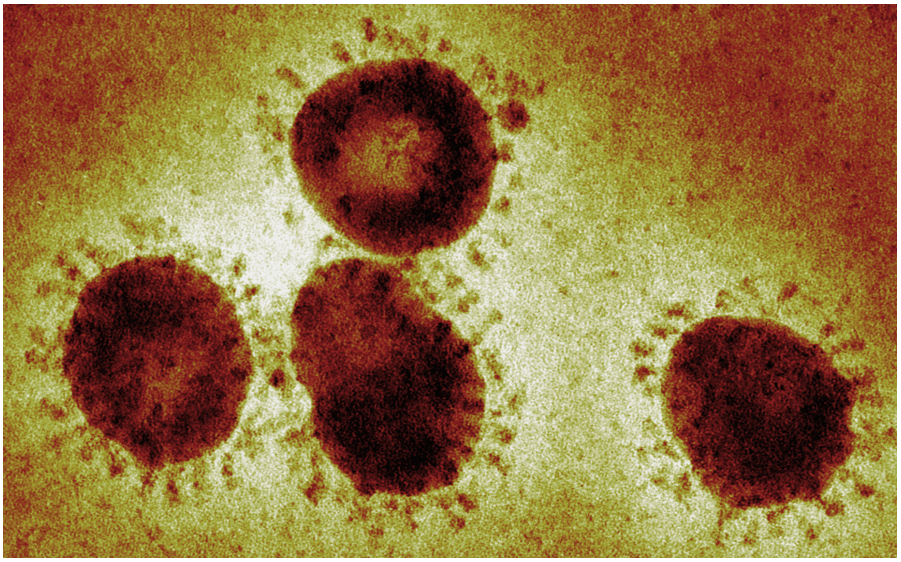


Figure 6: Coronaviruses harbor a halo, or crown-like (corona) appearance when viewed under an electron microscope. Credits: CDC/Dr. Fred Murphy.

2.3 VIRUS STRUCTURE

SARS-CoV-2 virus is a "Positive Strand" virus in the Nidovirales order, Coronaviridae order, beta-coronaviruses family type B.[11]

SARS-CoV-2 virus enter the cell by binding to a protein playing the role of a cellular receptor: the *angiotensin convertase* (ACE2) found on the surface of lung, heart, kidney and intestine cells. ACE2 regulates blood pressure and heart rate. The virus uses its trimeric spike protein, which visually creates the "corona" under the electron microscope, to attach to ACE2.

This may explain how the virus was transferred to the human population, probably through bats, as the

11 https://talk.ictvonline.org/ictv-reports/ictv_9th_report/positive-sense-rna-viruses-2011/w/posrna_viruses/222/coronaviridae

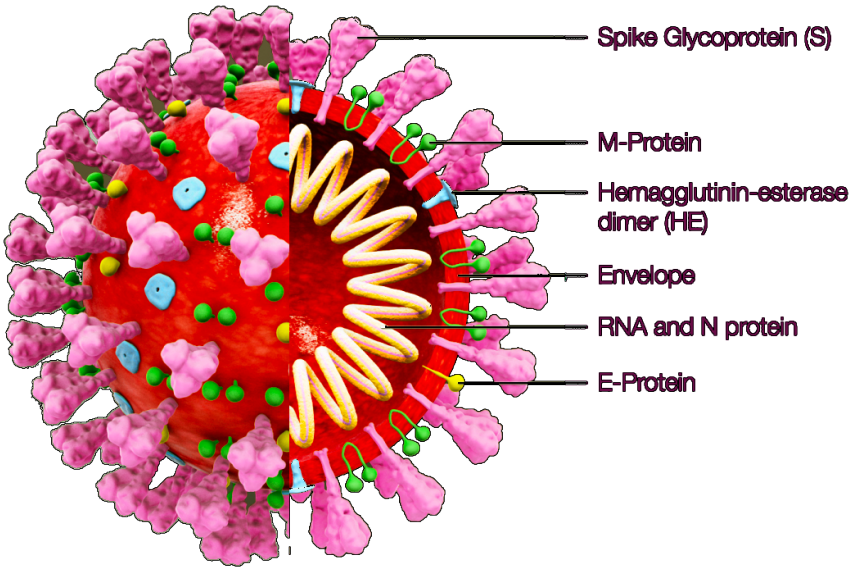


Figure 7: Coronavirus structure organization.

ACE2 surface protein is common to the natural reservoir of suspected intermediate hosts (civets, camels and possibly pangolins.)

SARS-CoV-2 virus genome is a "positive strand RNA" of about 30,000 nucleotides, some of the longest genomes in this category. This means that the genome is immediately ready to be decoded into proteins as it enters the cell, using the cell machinery called *ribosome*.

These viral proteins will form the viral particle (trimeric spike glycoprotein (S), envelope (E), membrane (M)) and other proteins necessary for the virus replication (polymerase and protease) that are not part of the final viral particle.

3

COLORING FUN

As described in section 2.2 the *models* are artificially symmetrical. The images are presented as viewed from a symmetry axis and shown with less and less details to better allow imaginative drawing and coloring.

Some of the views also show a "split" version of the particle to see the "inside" even though there is no genomic representation within the model (see 7 for example.)

Each coloring chapter will open with a figure showing all the pages dedicated to the chapter target view angle.

Later chapters will illustrate molecular structures known experimentally at the atomic level. These are more complex and an colored example on the opposite page is included as a guide to see the structures better.

These structures will represent the spike protein, with and without its attached receptor (ACE2) (see section 2.3.) The last structure is a very small segment of the SARS virus genome with a special structure.

4

SARS-COV-2 MODEL - 5X

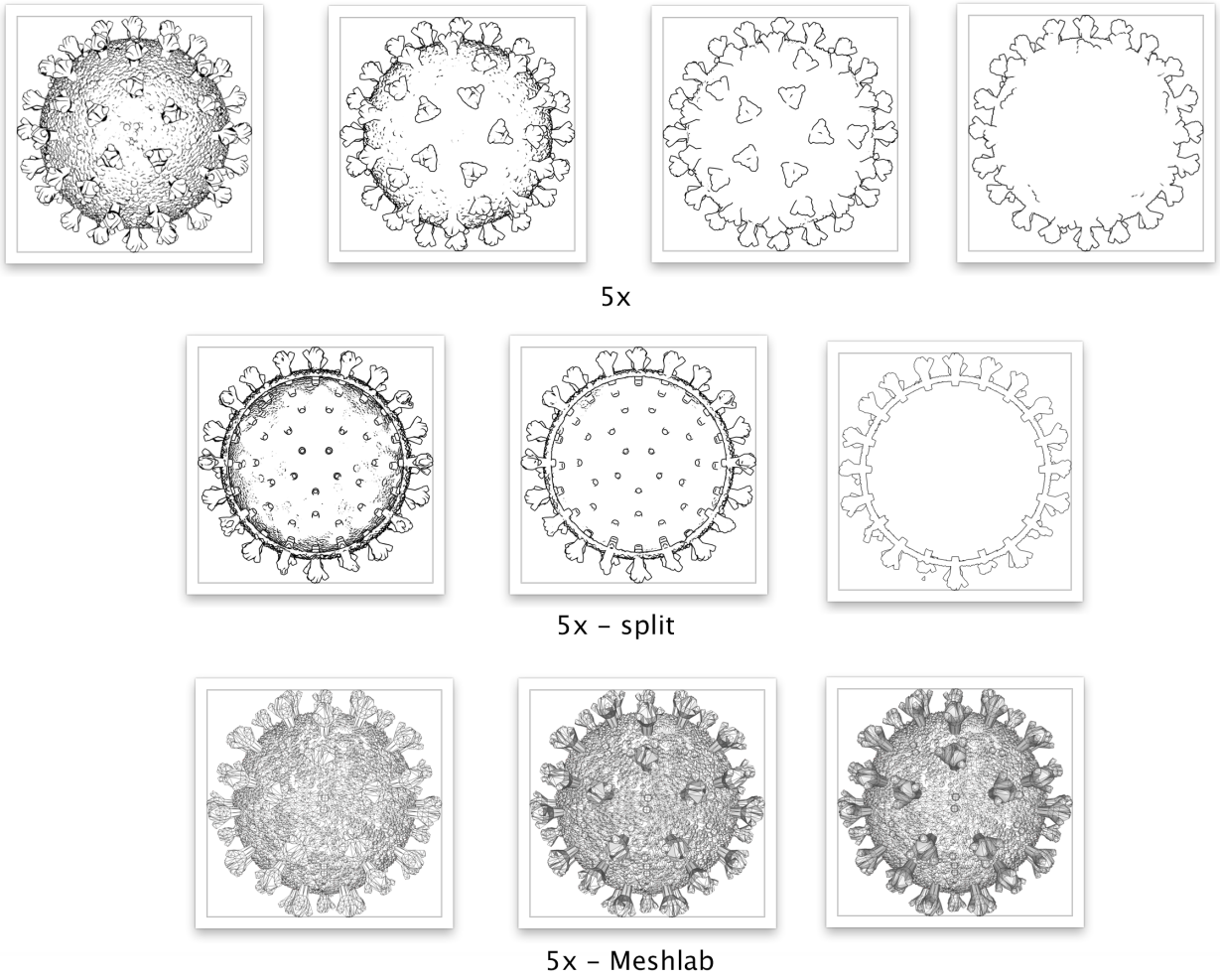
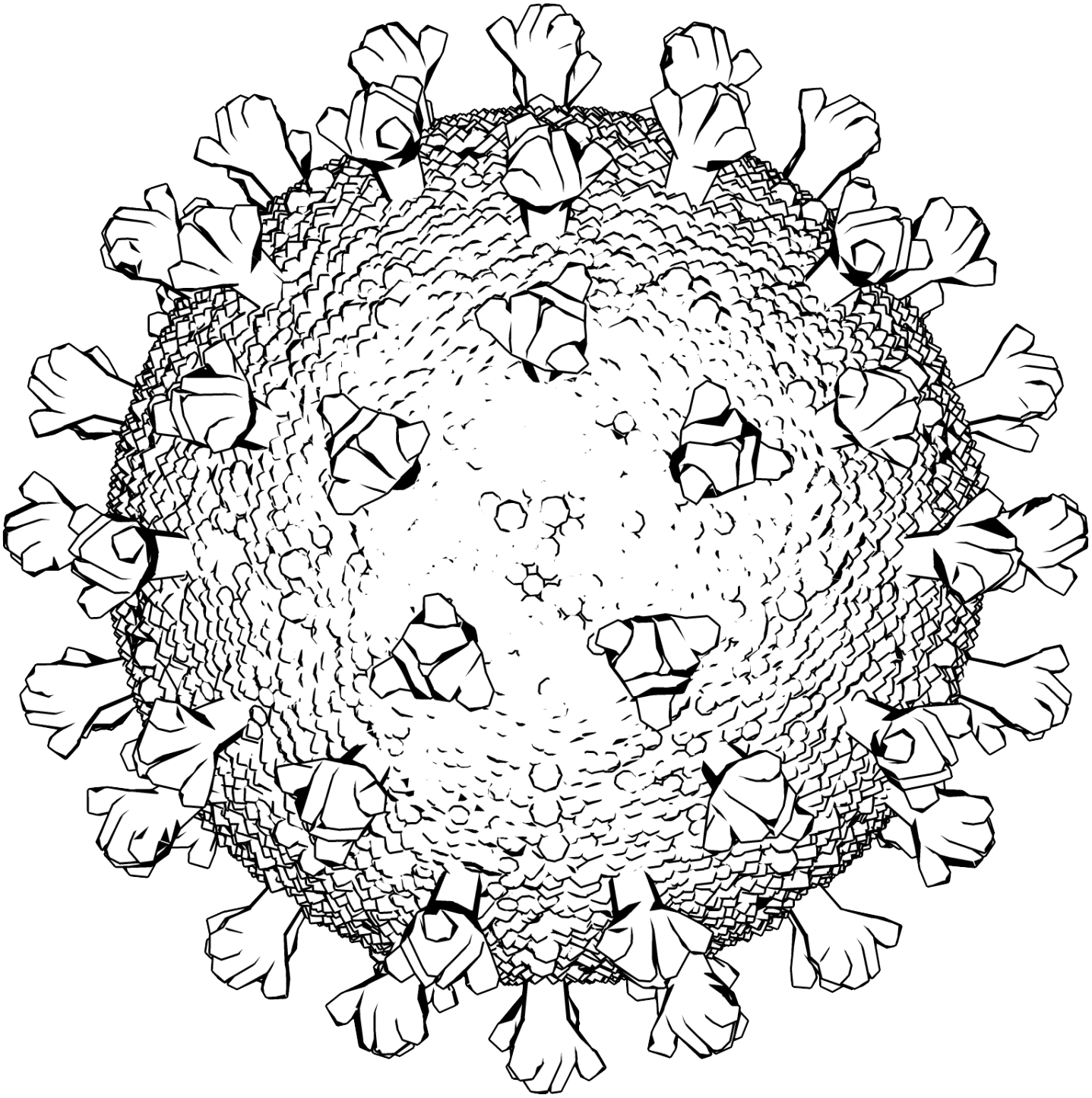
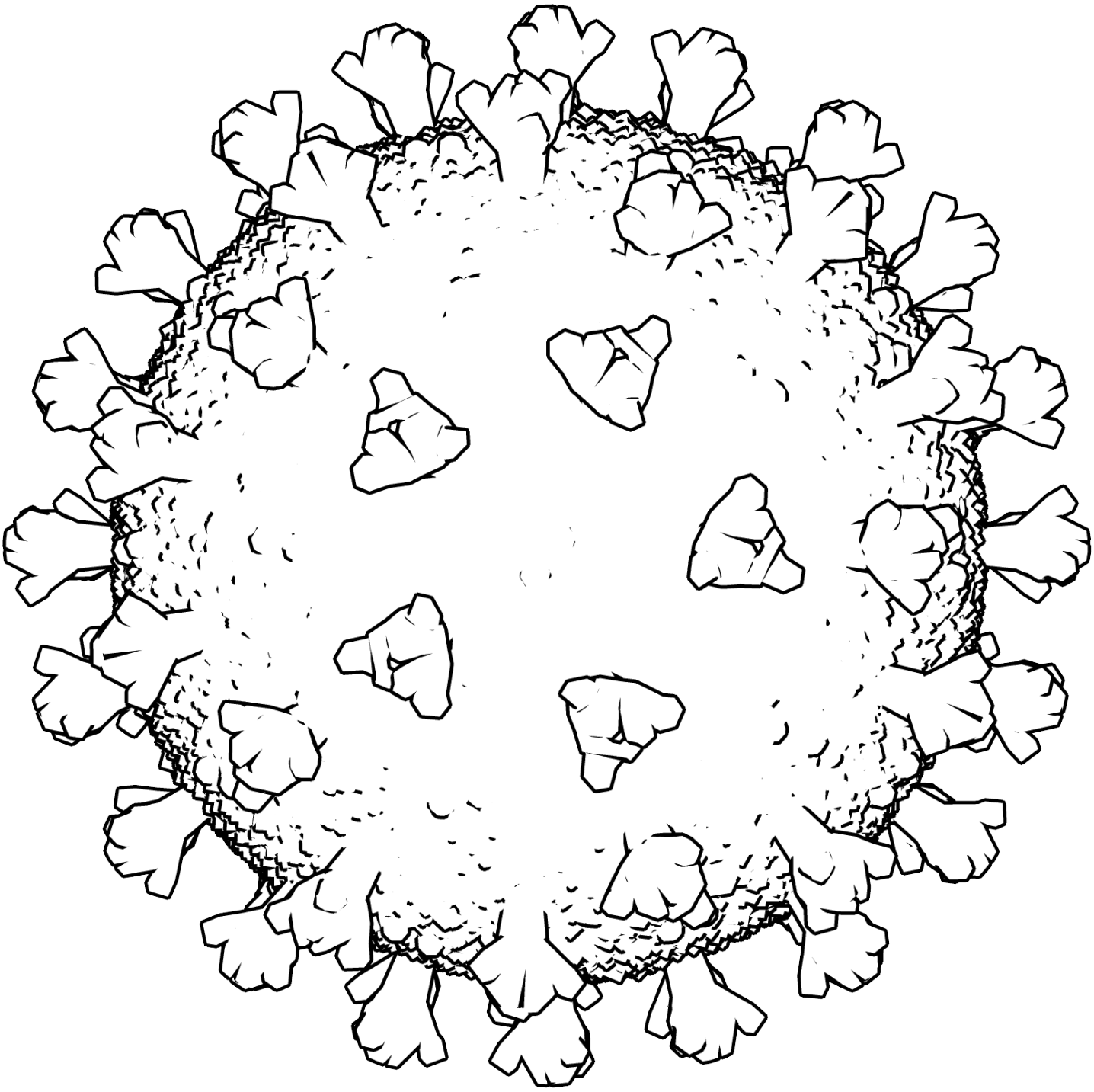
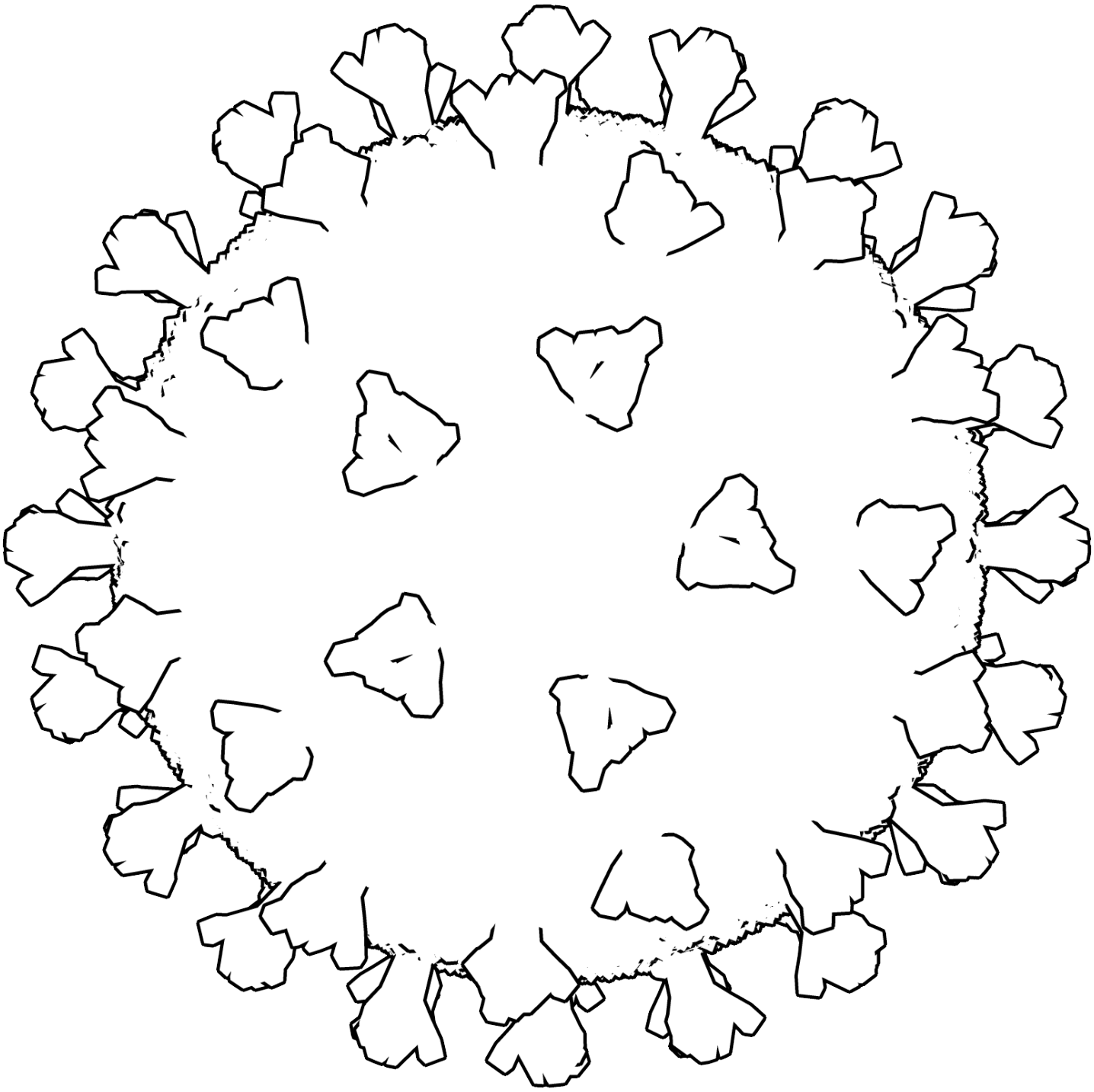
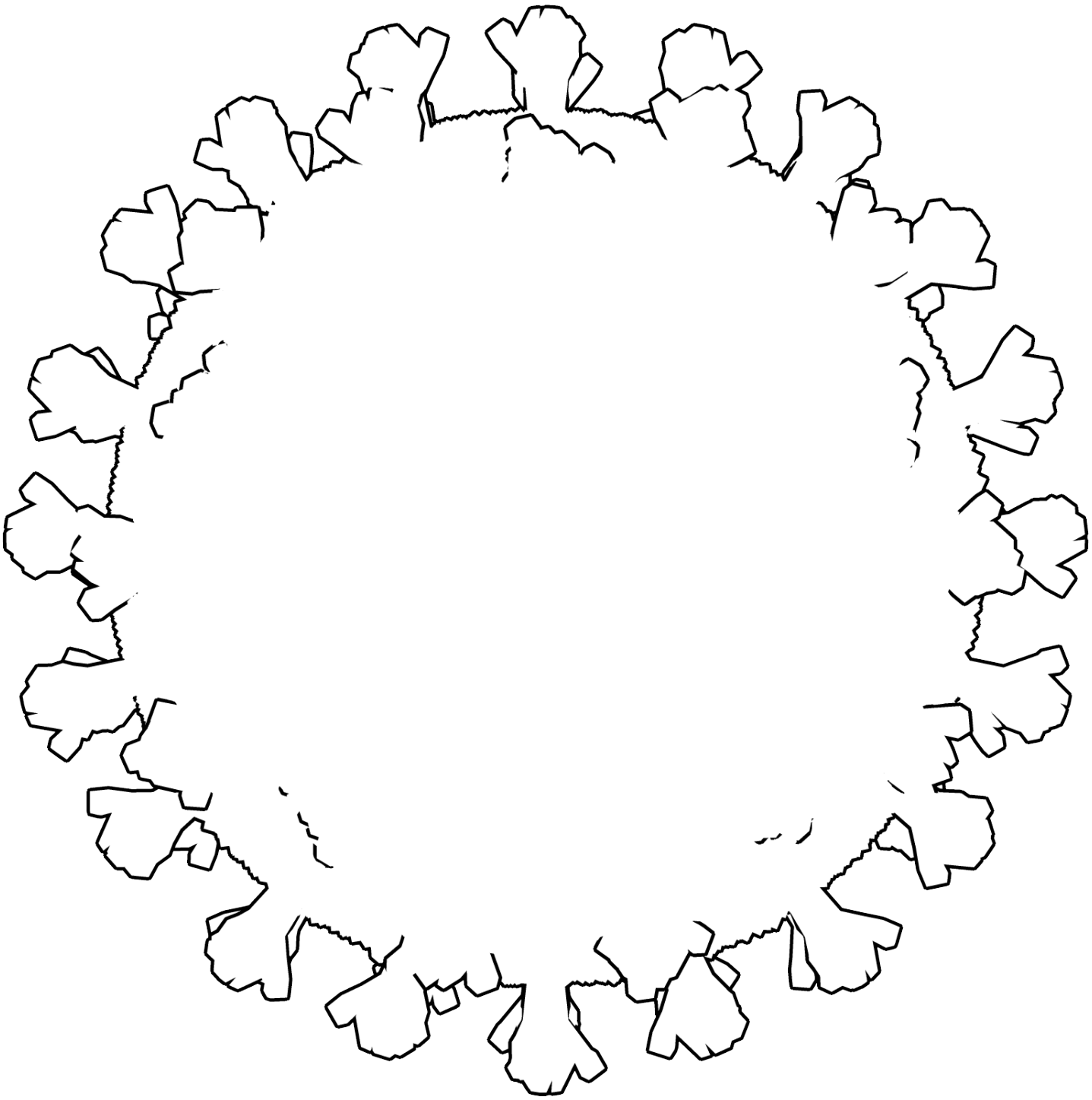


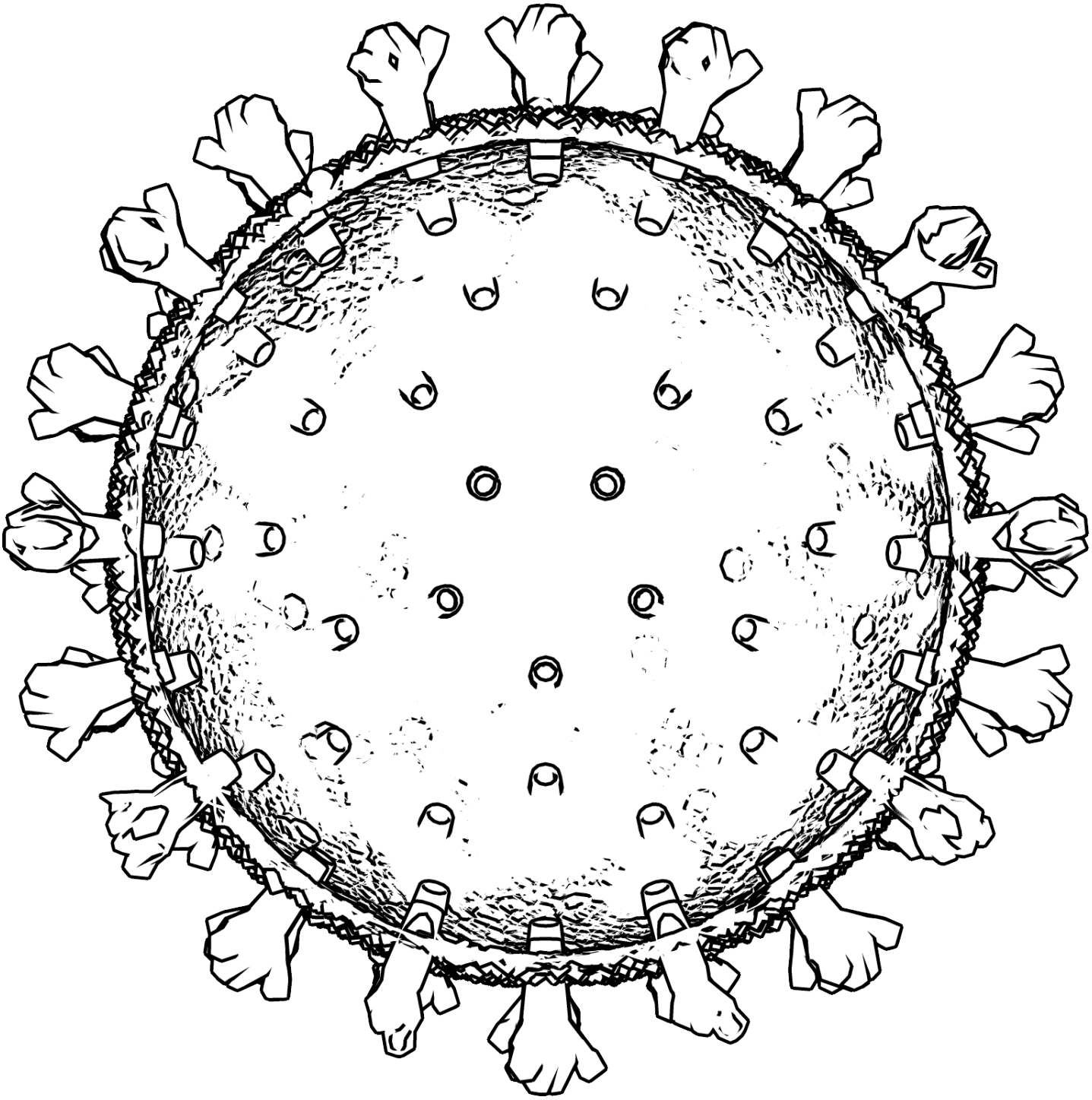
Figure 8: View down 5x axis. From outside. Split particle. Meshlab

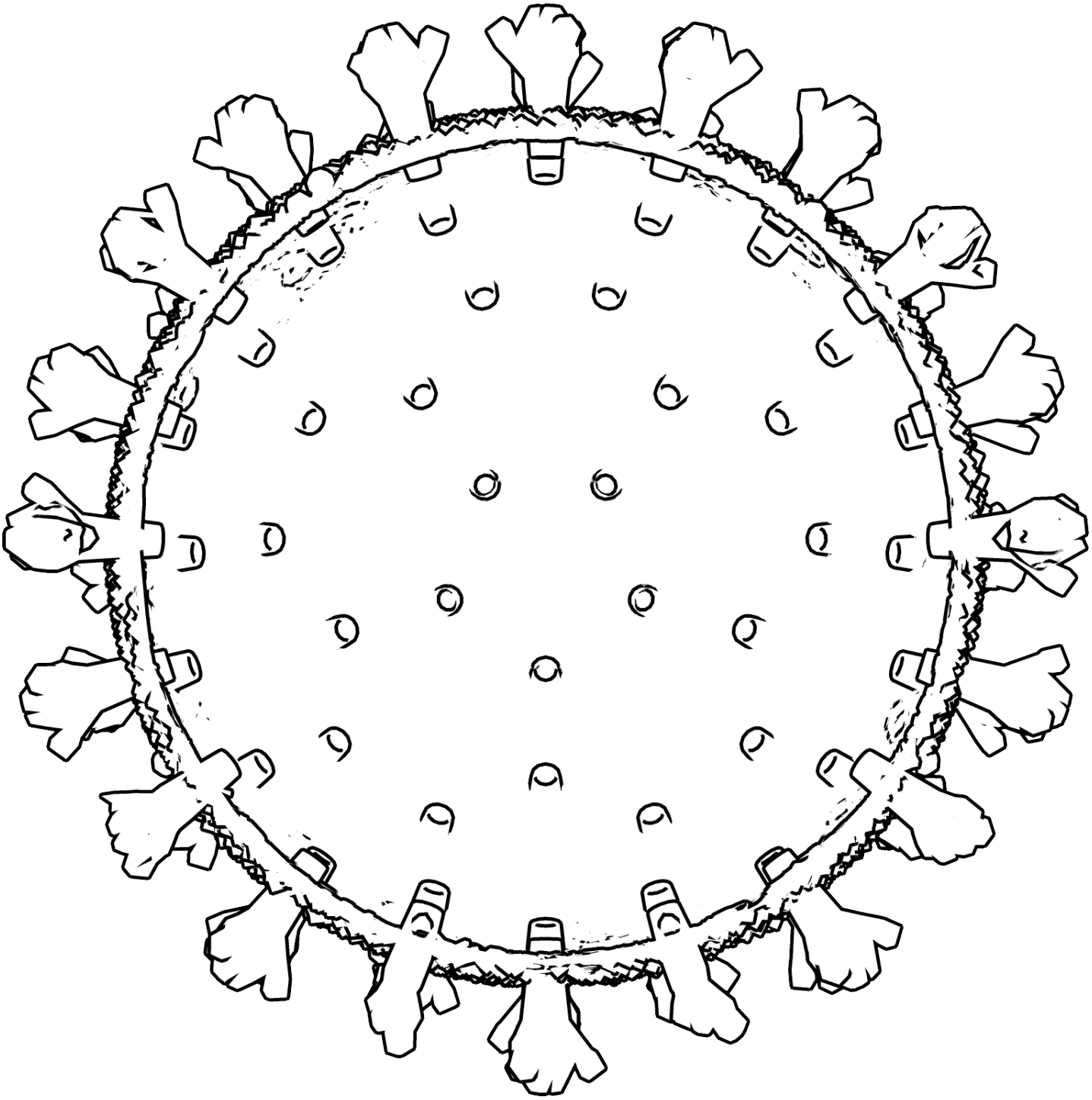


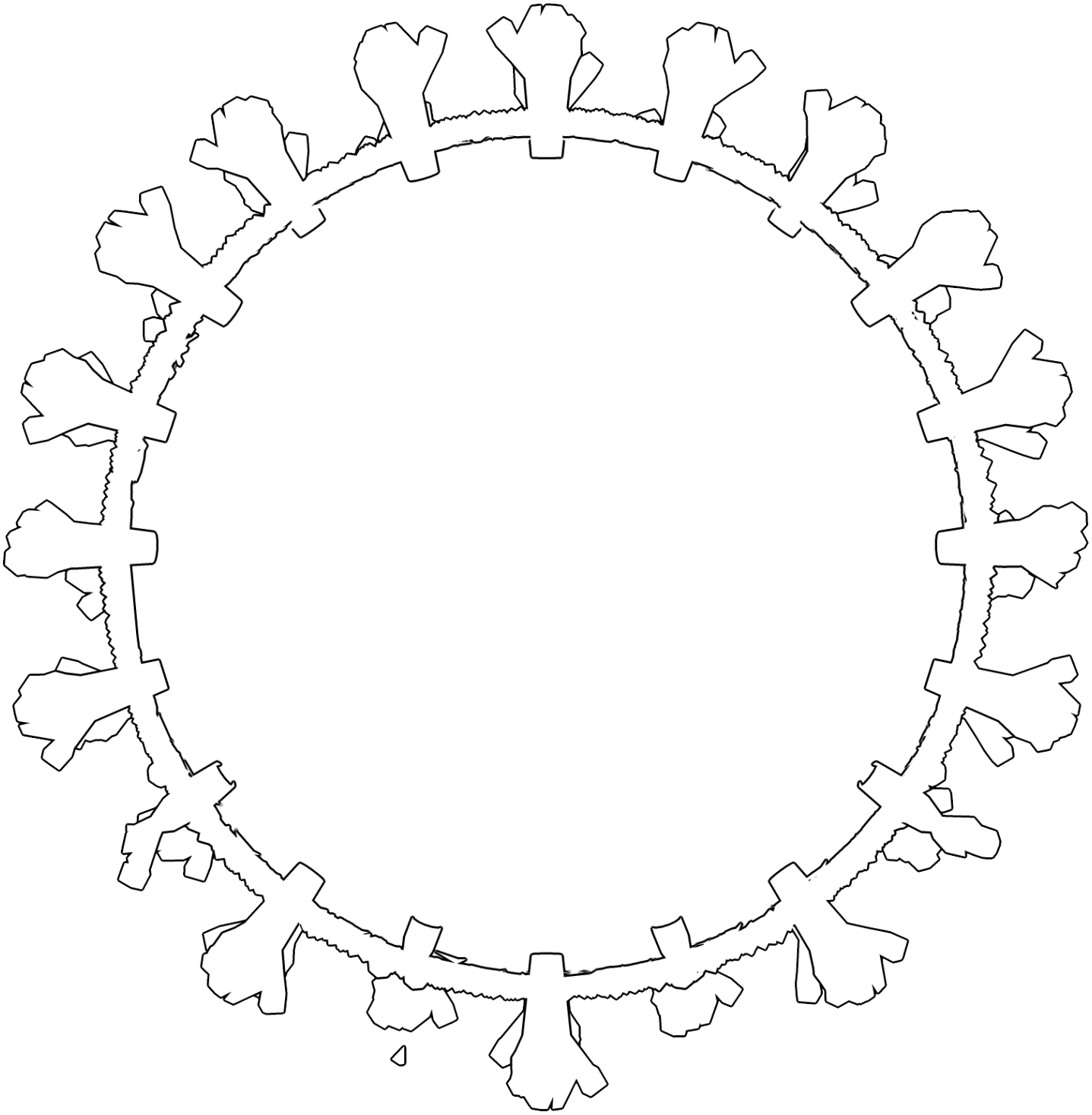




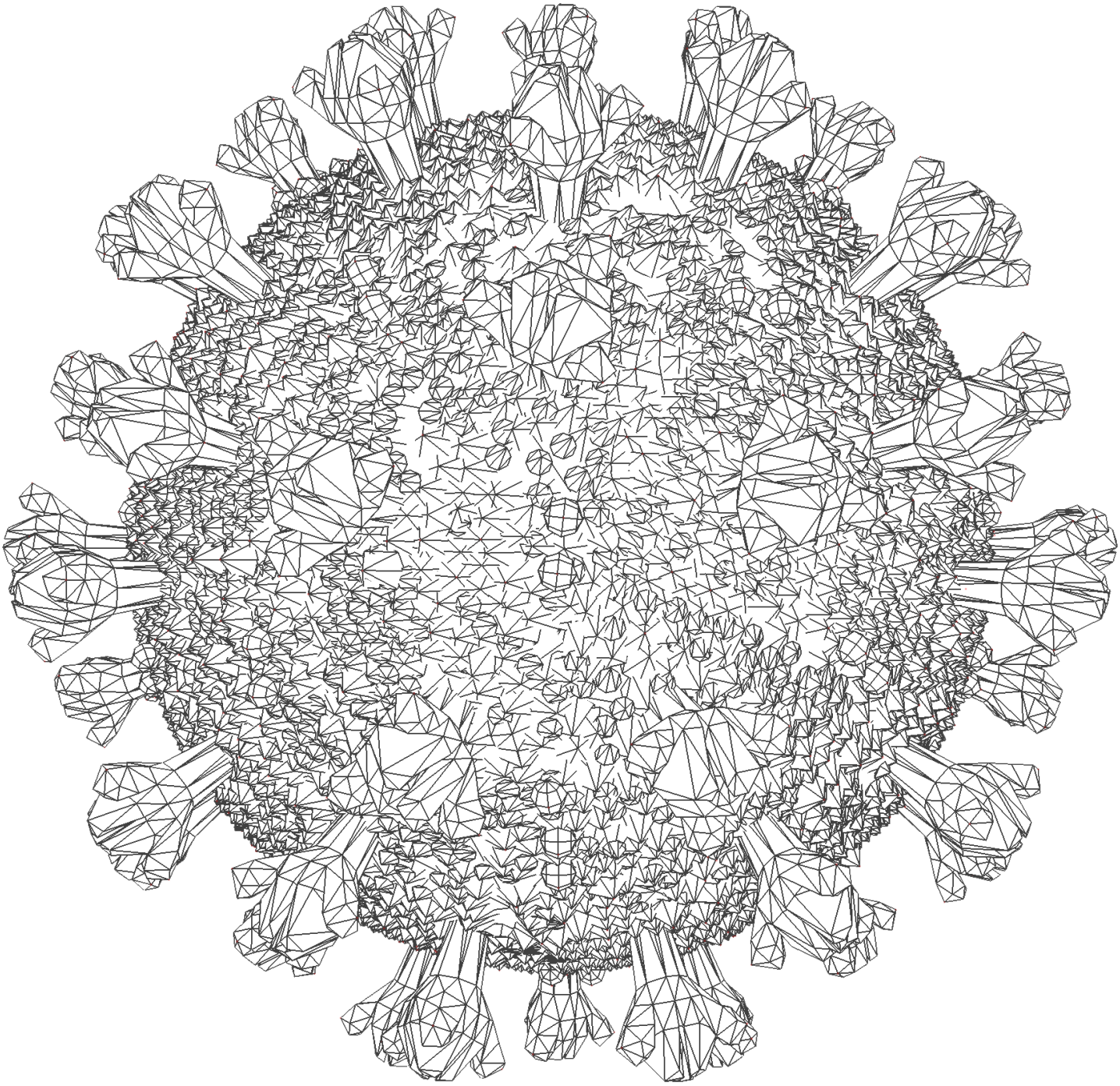




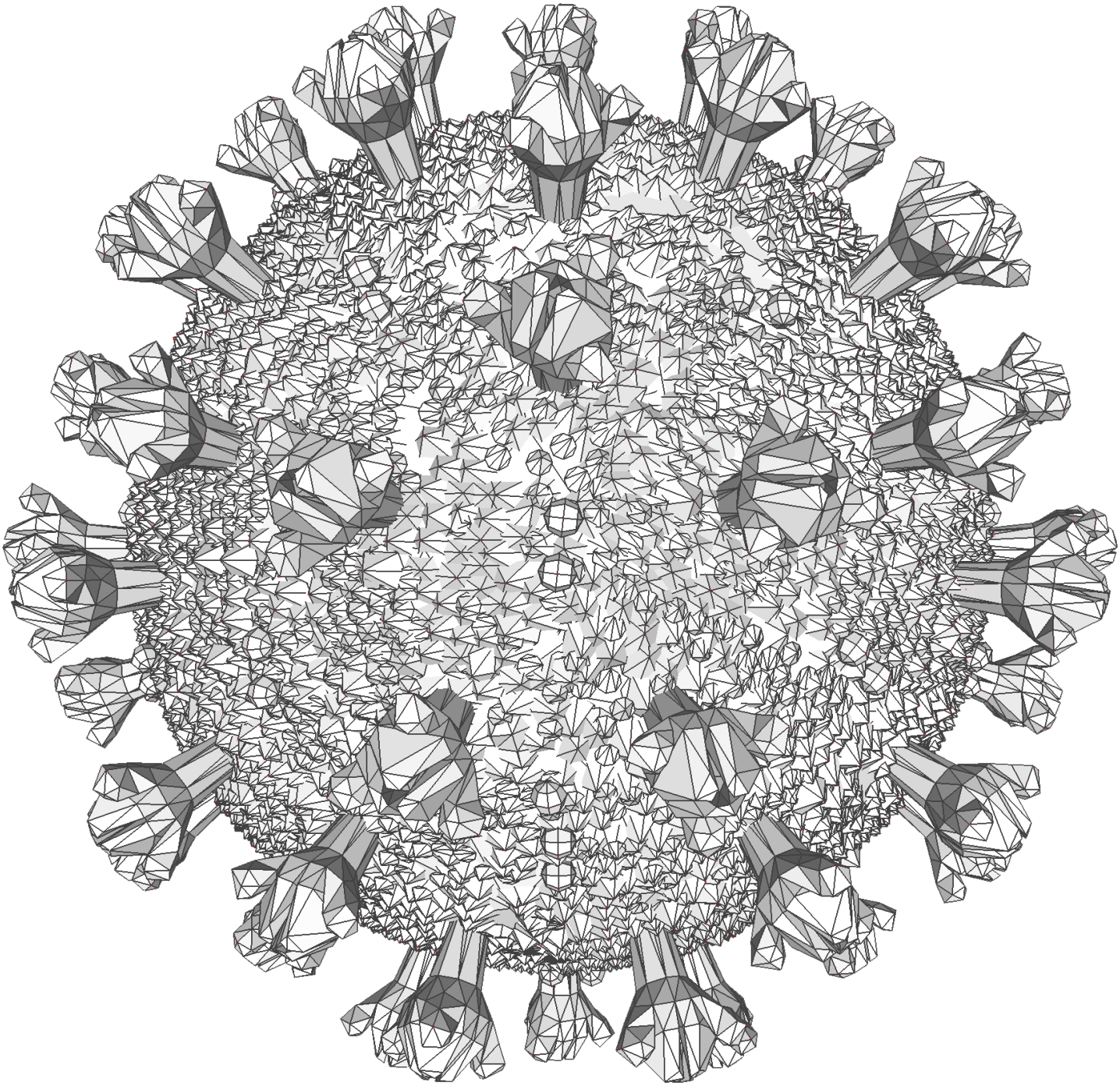




SARS-COV-2 MODEL - 5X



SARS-COV-2 MODEL - 5X



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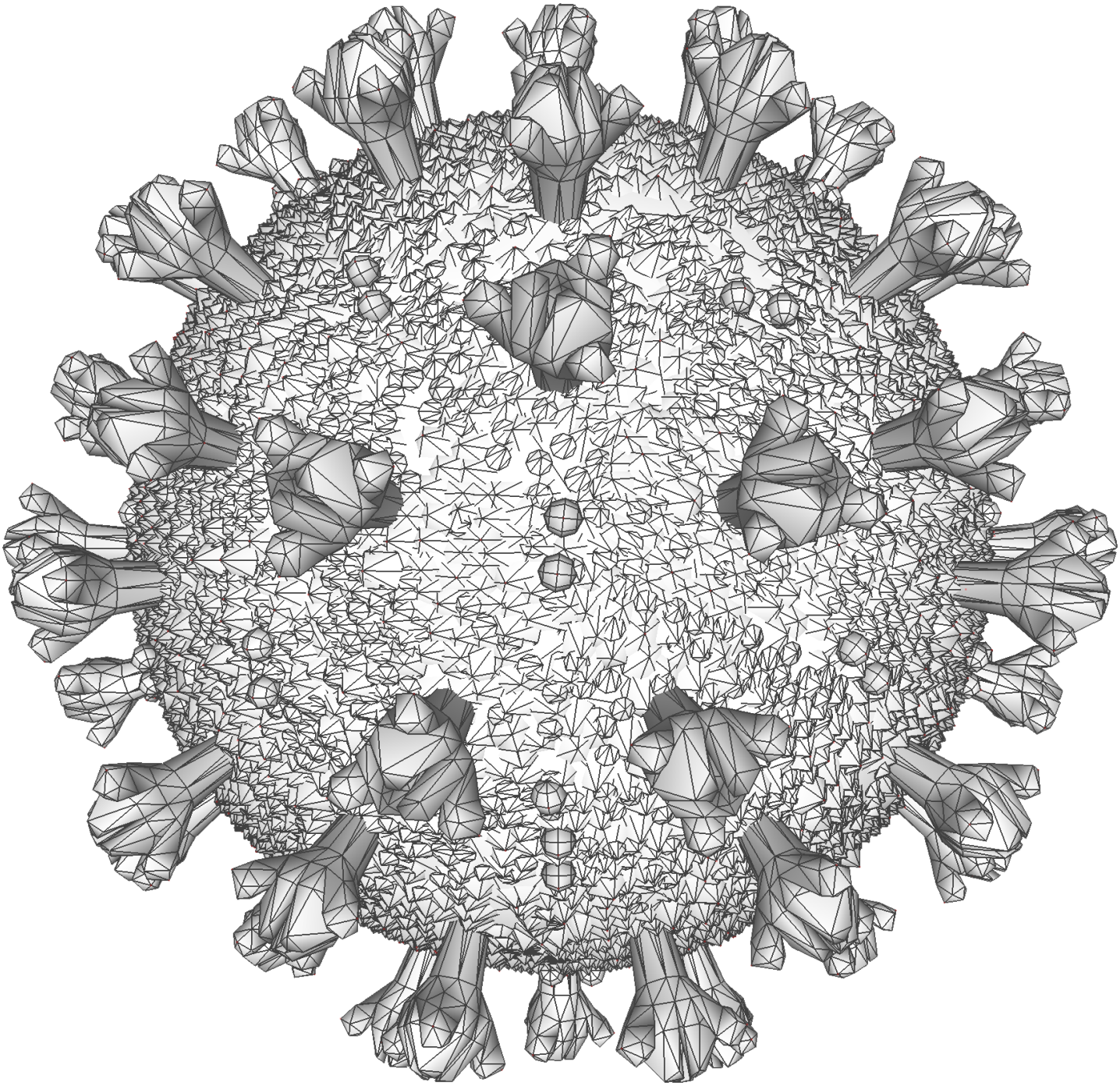
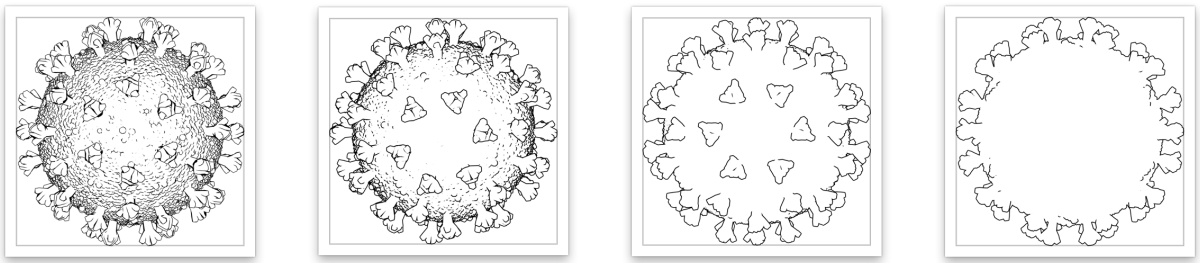
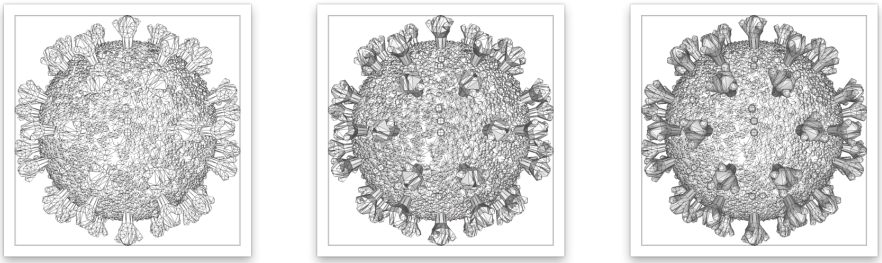


5

SARS-COV-2 MODEL - 3X

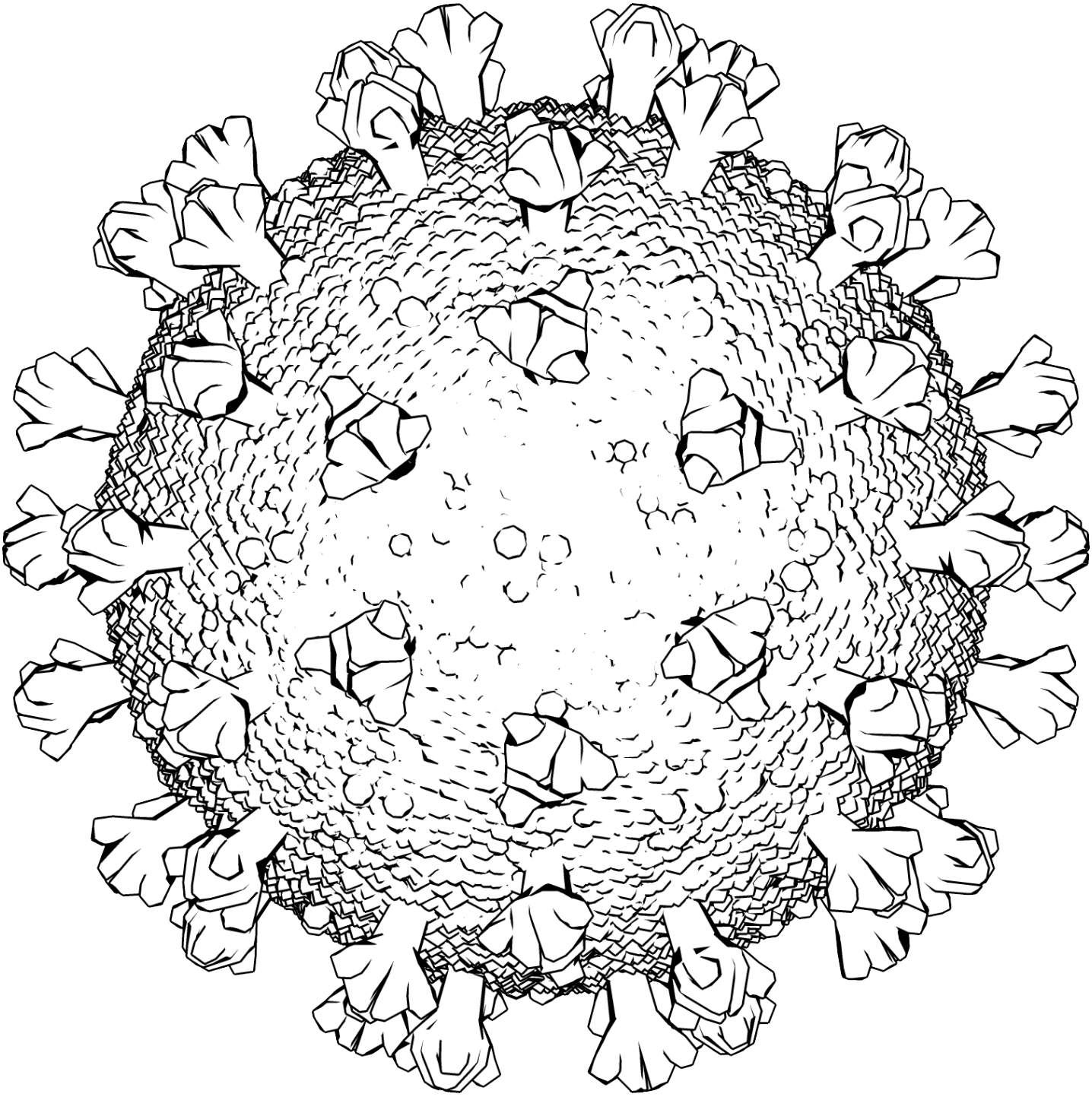


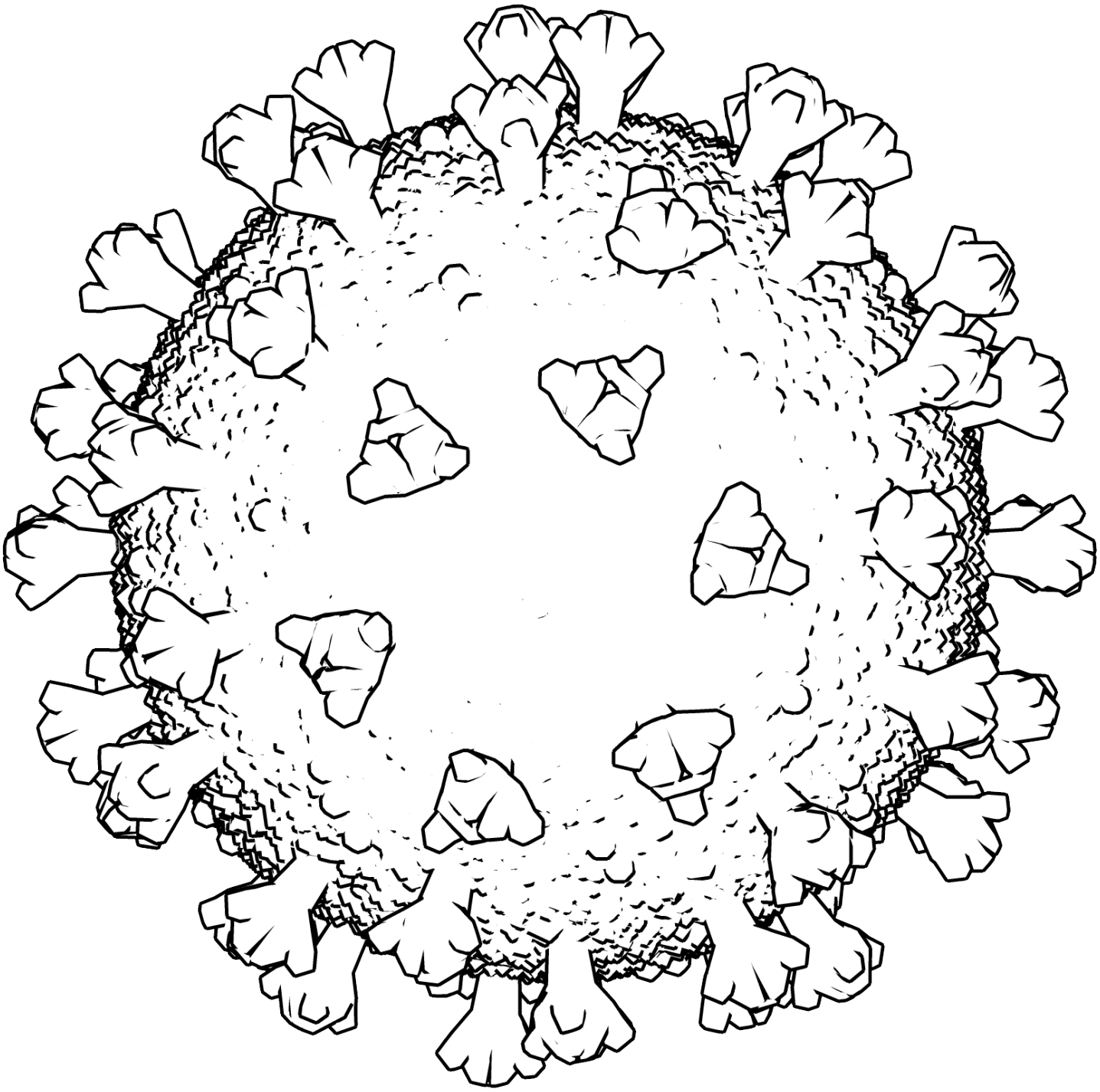
3x

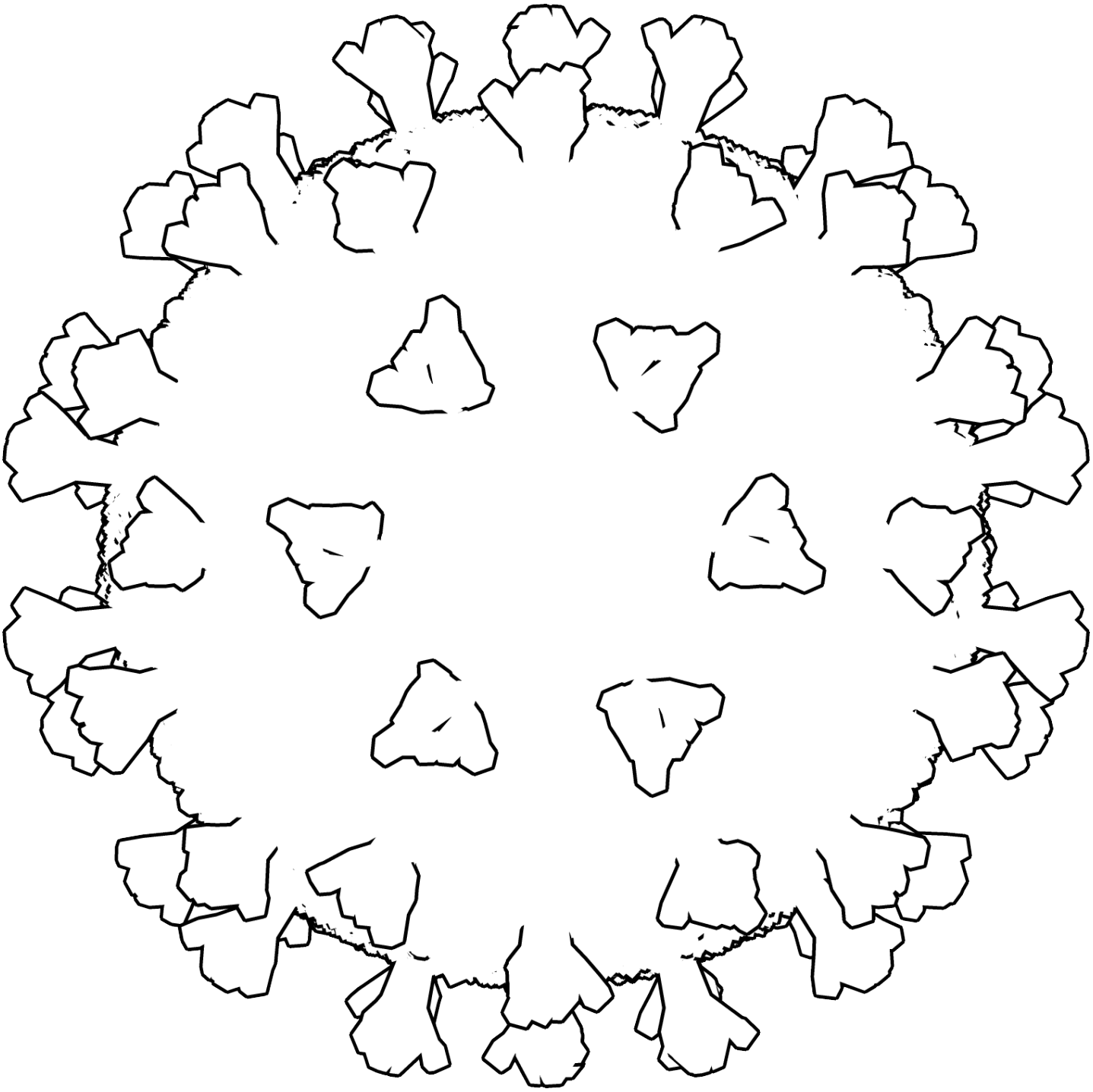


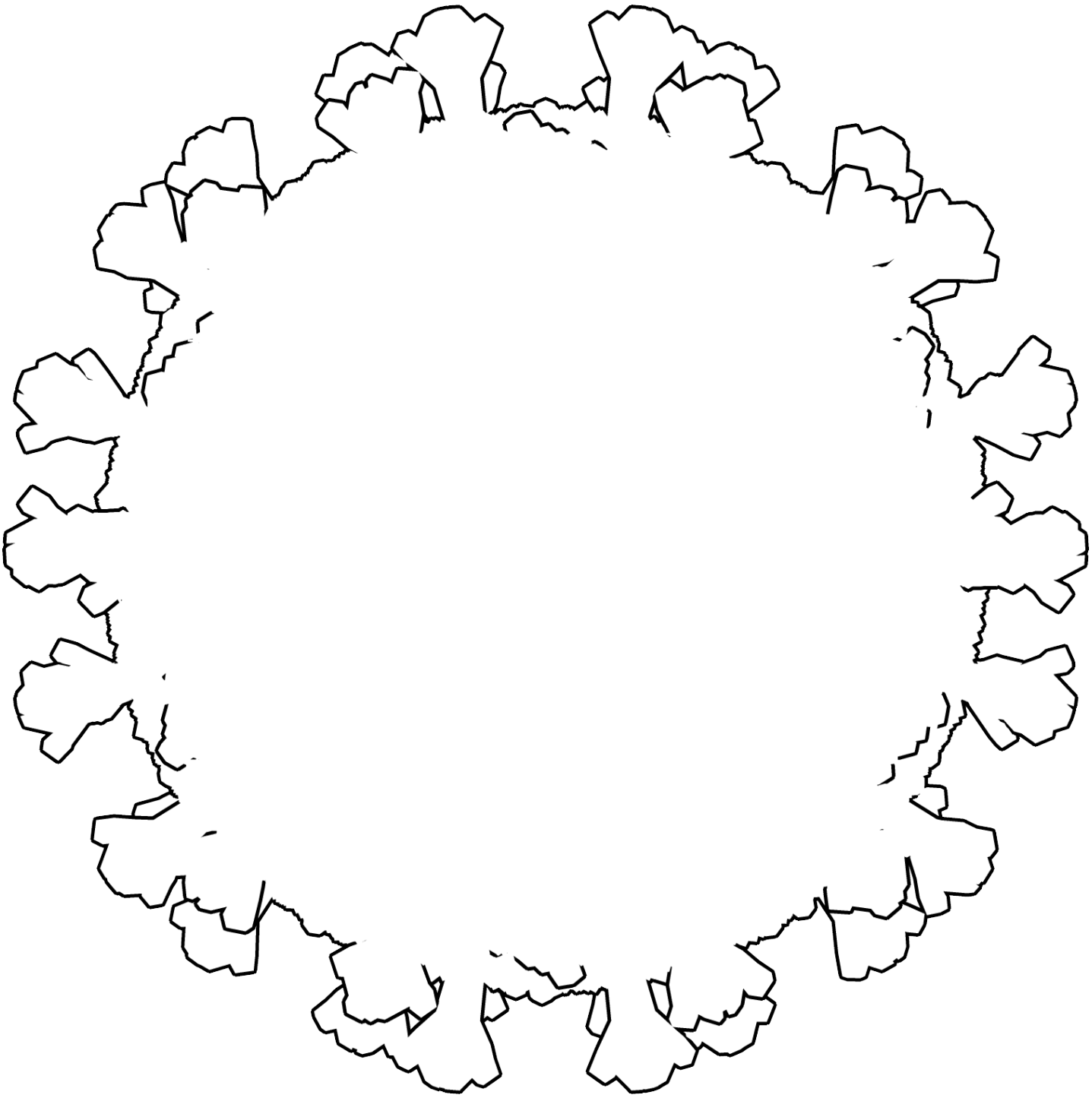
3x – Meshlab

Figure 9: View down 3x axis. From outside. Meshlab

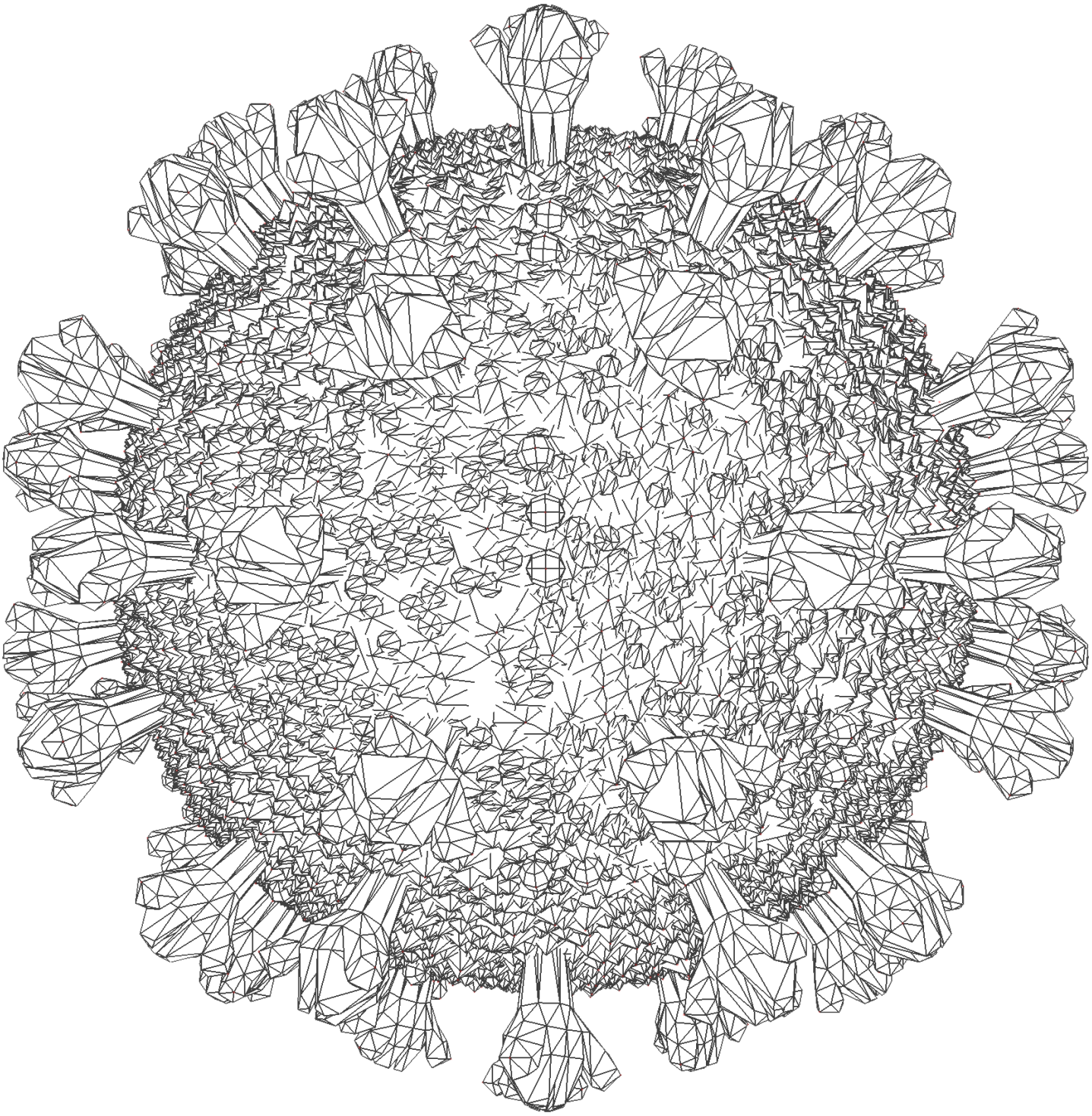




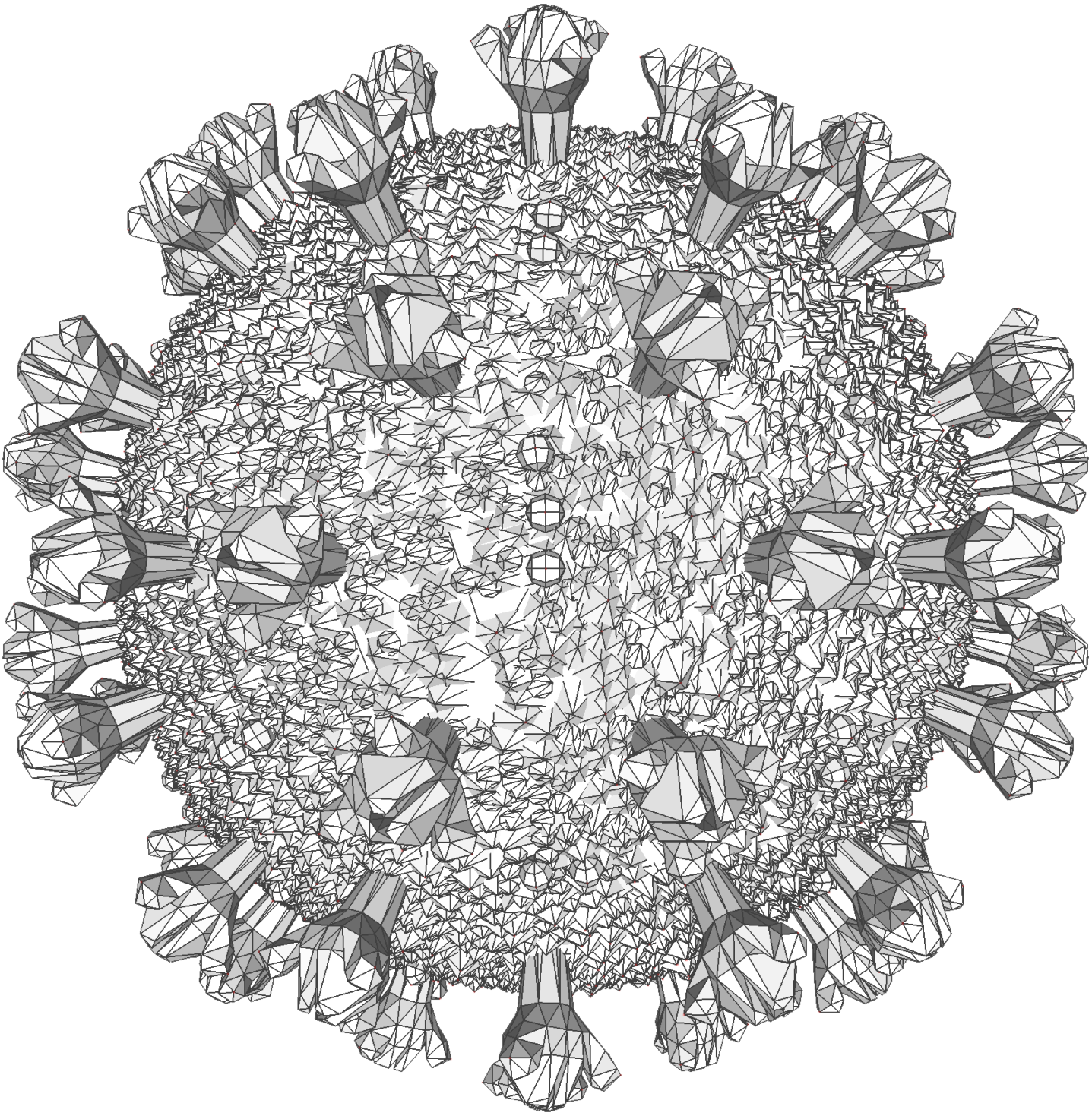


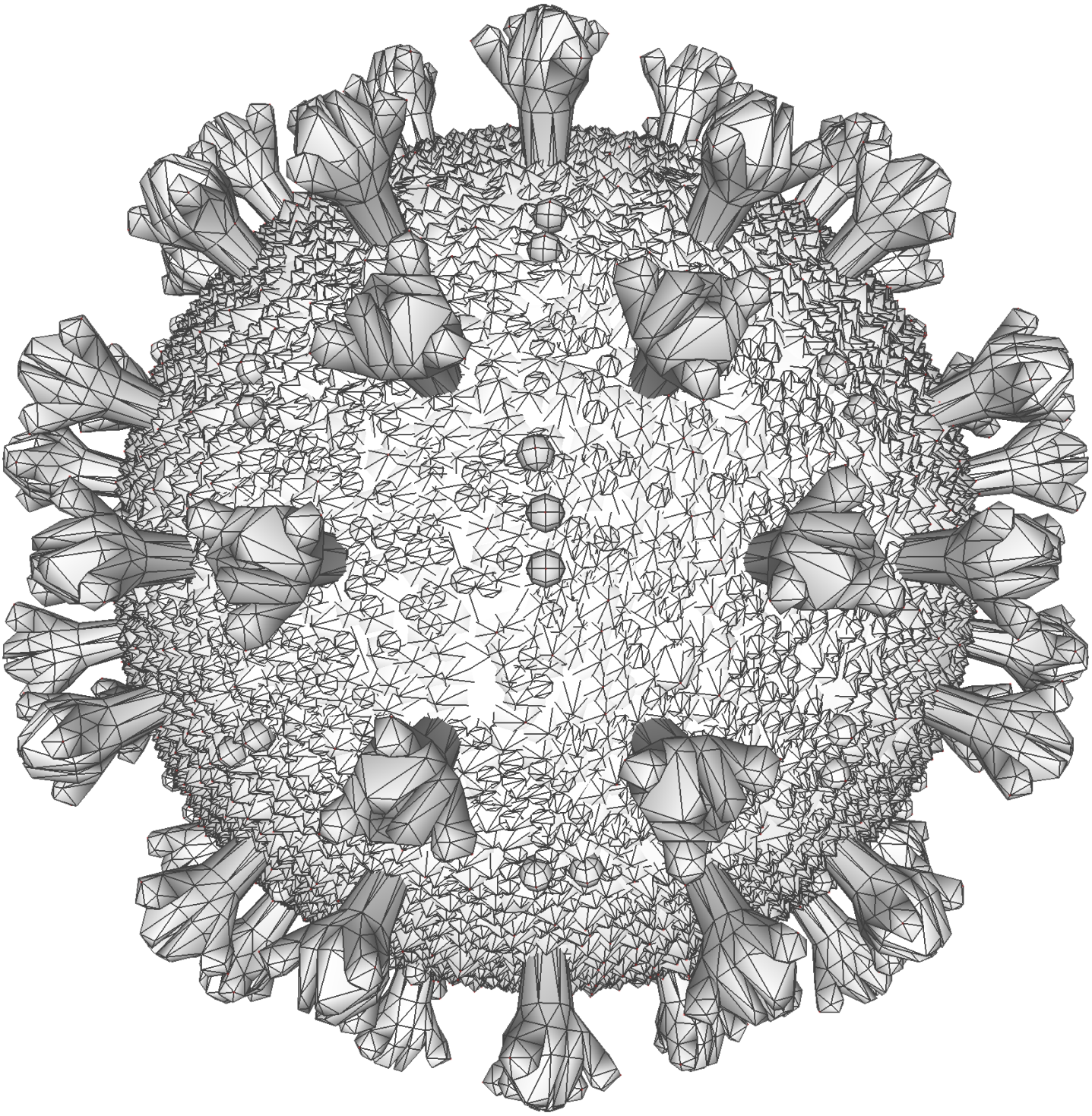


SARS-COV-2 MODEL - 3X



SARS-COV-2 MODEL - 3X





6

SARS-COV-2 MODEL - 2X

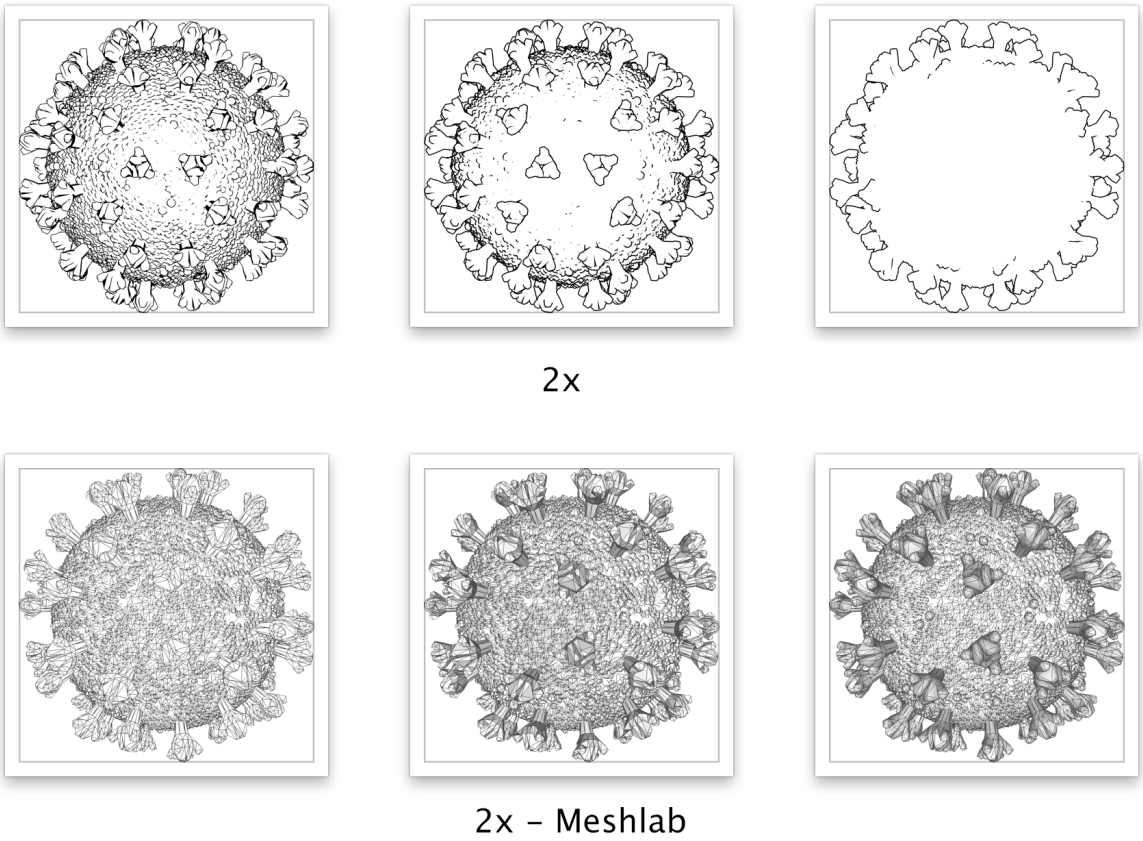
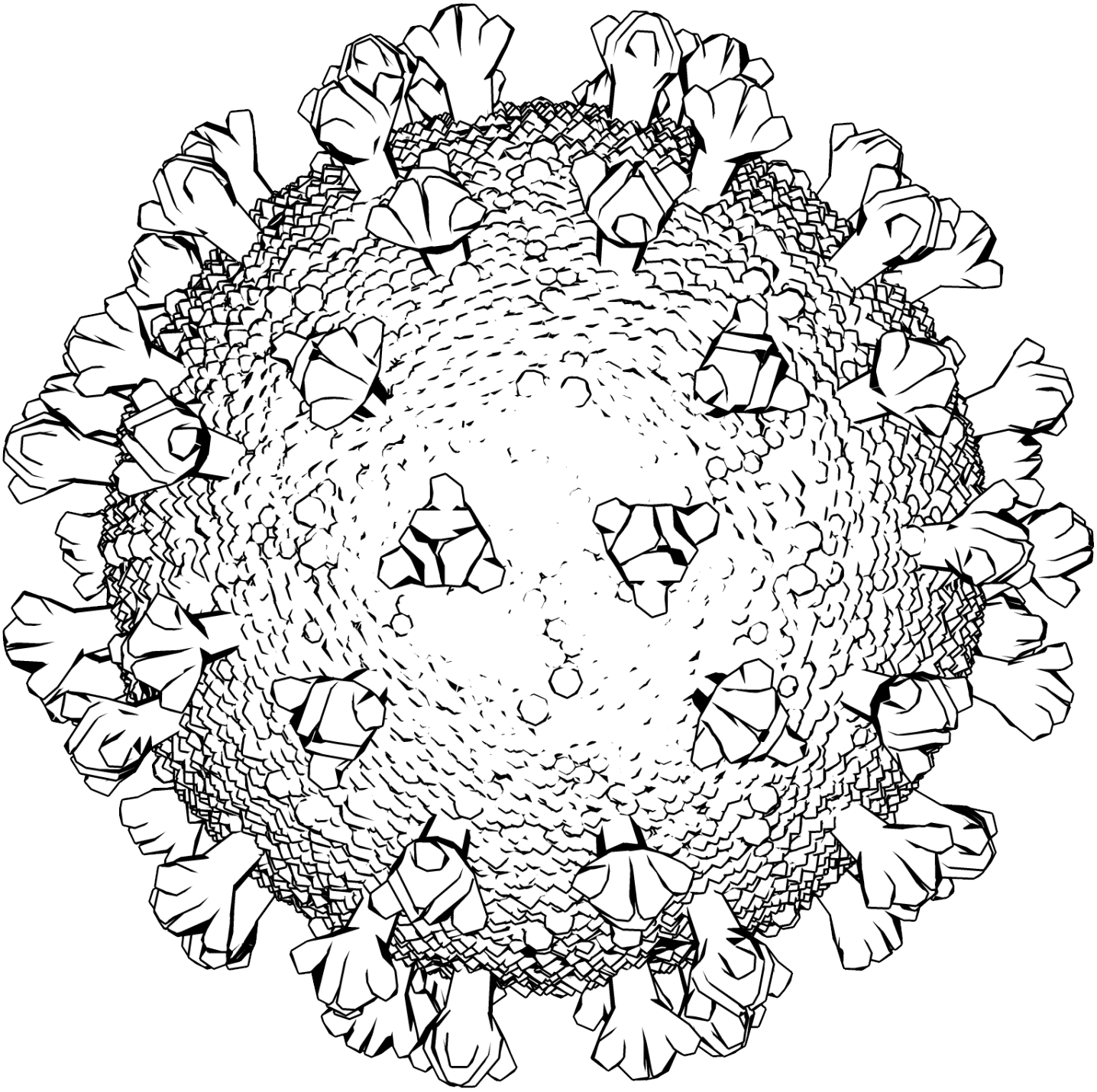
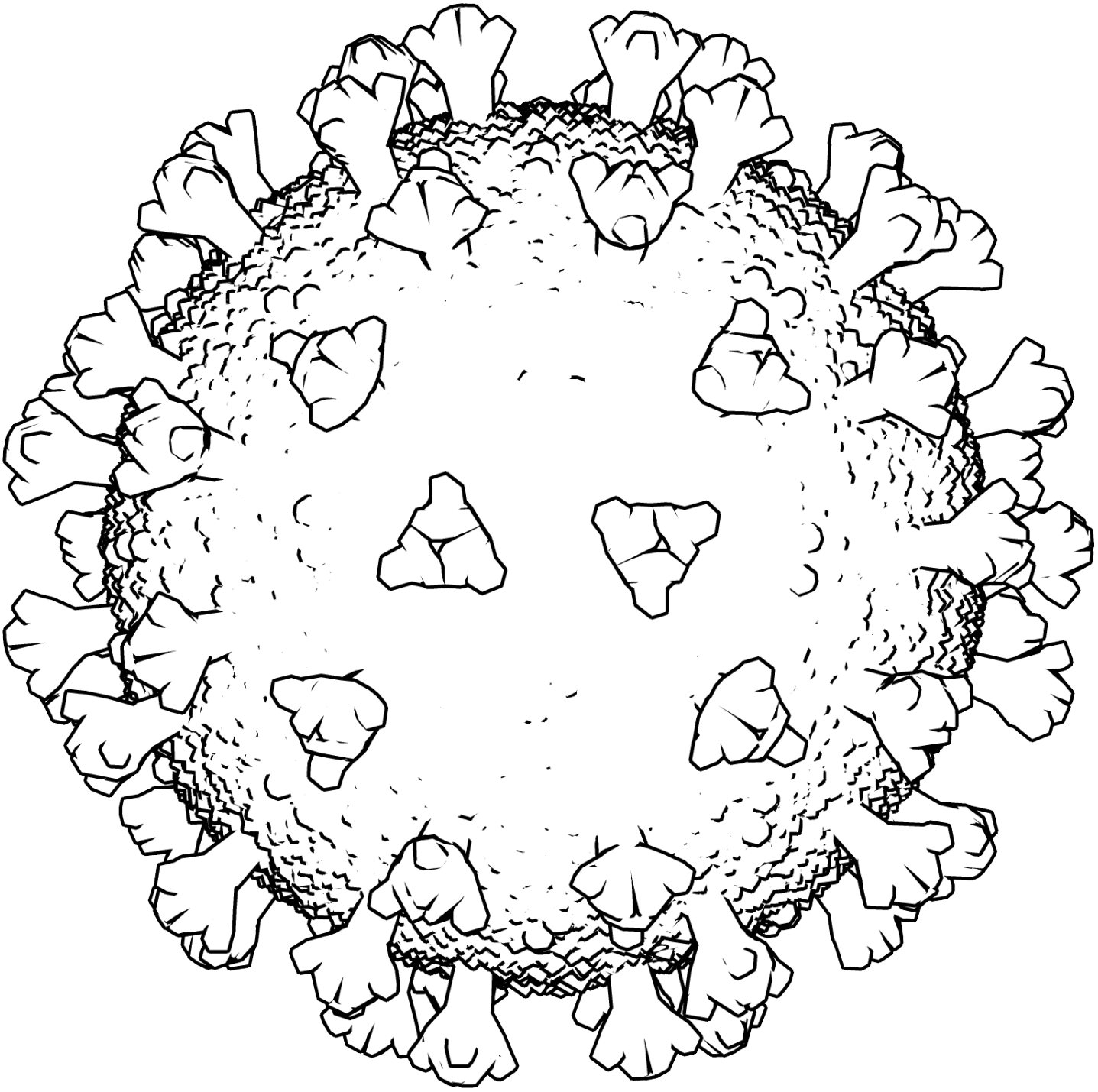
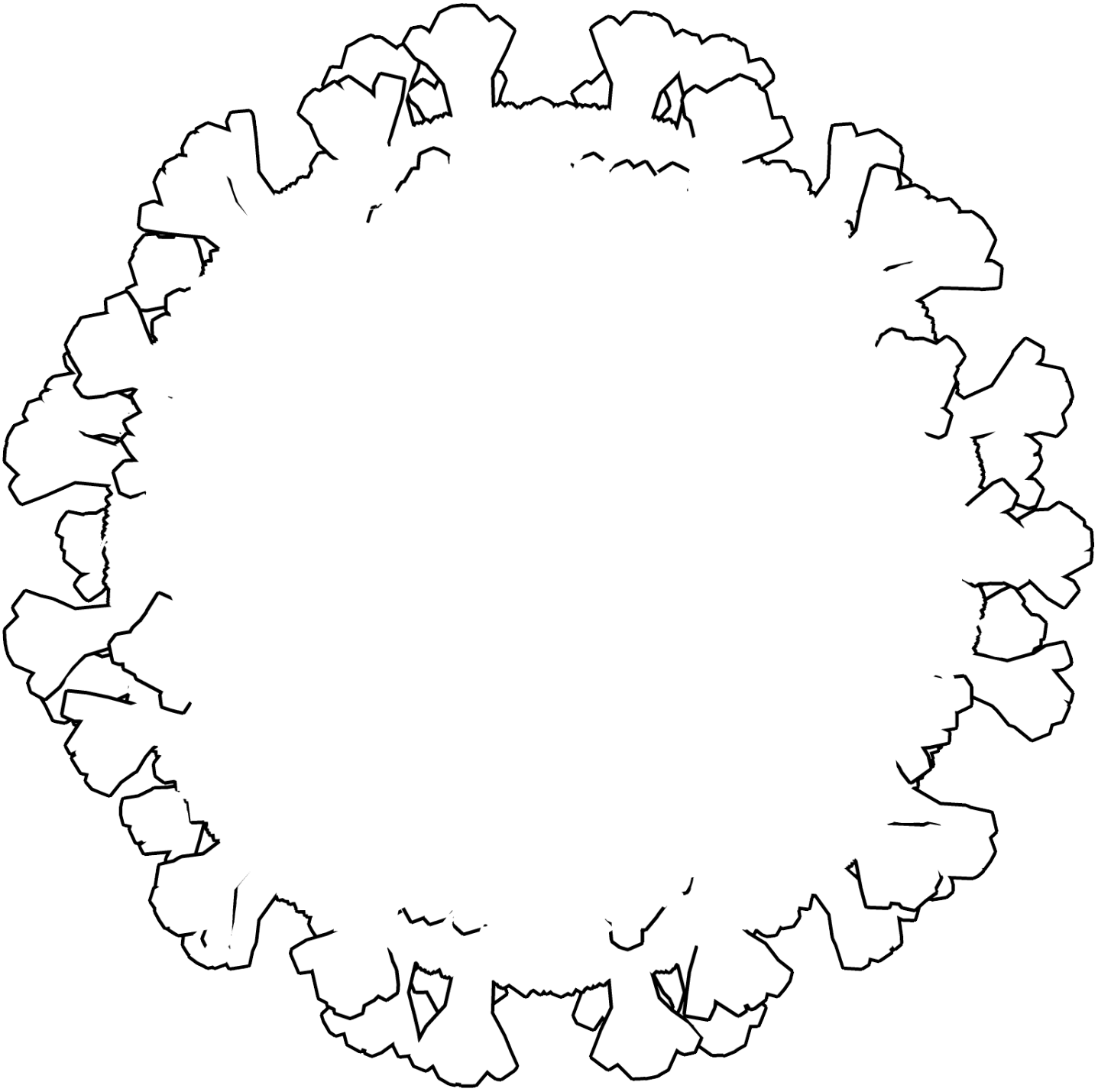


Figure 10: View down 2x axis. From outside. Meshlab

SARS-COV-2 MODEL - 2X







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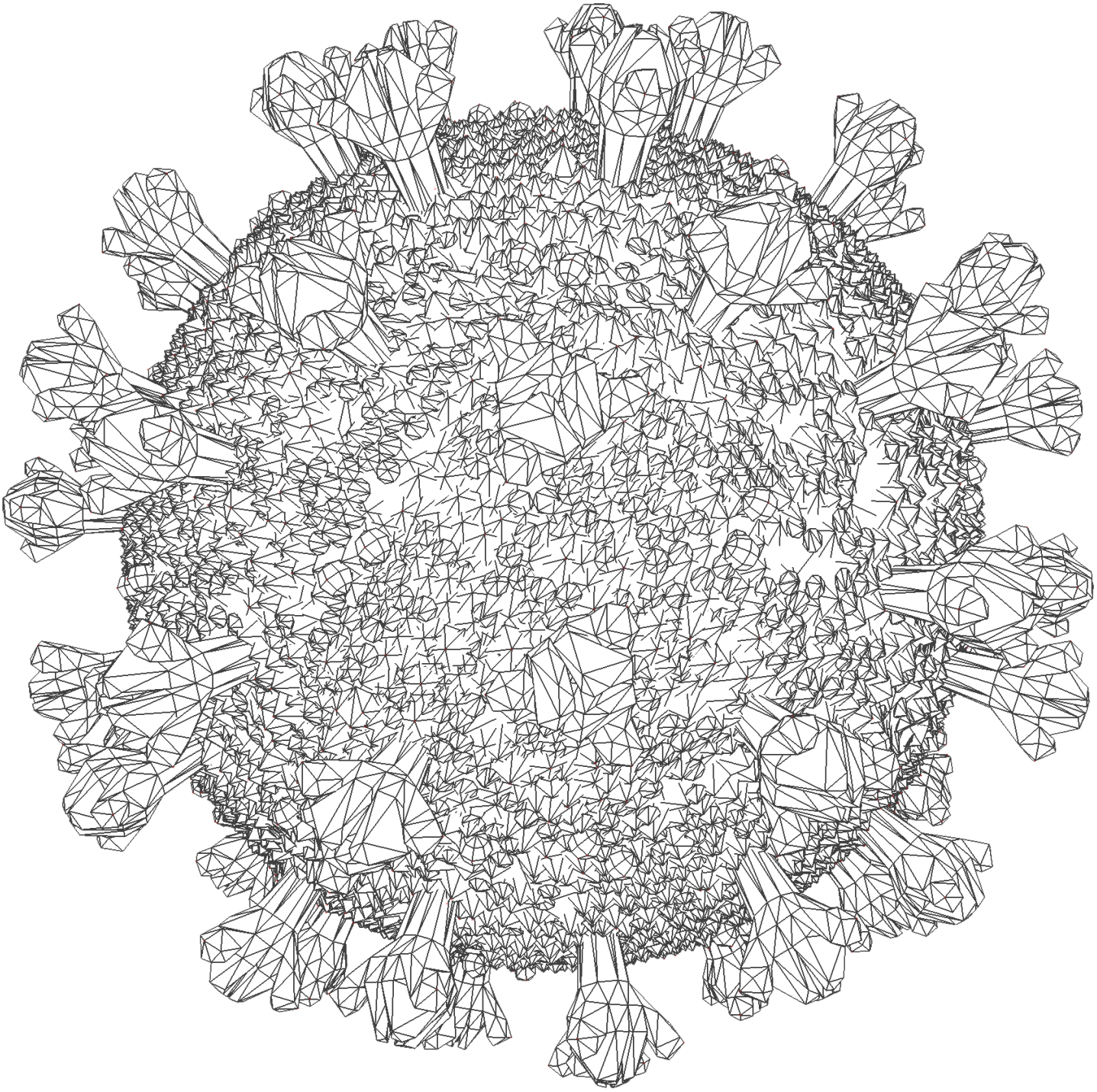

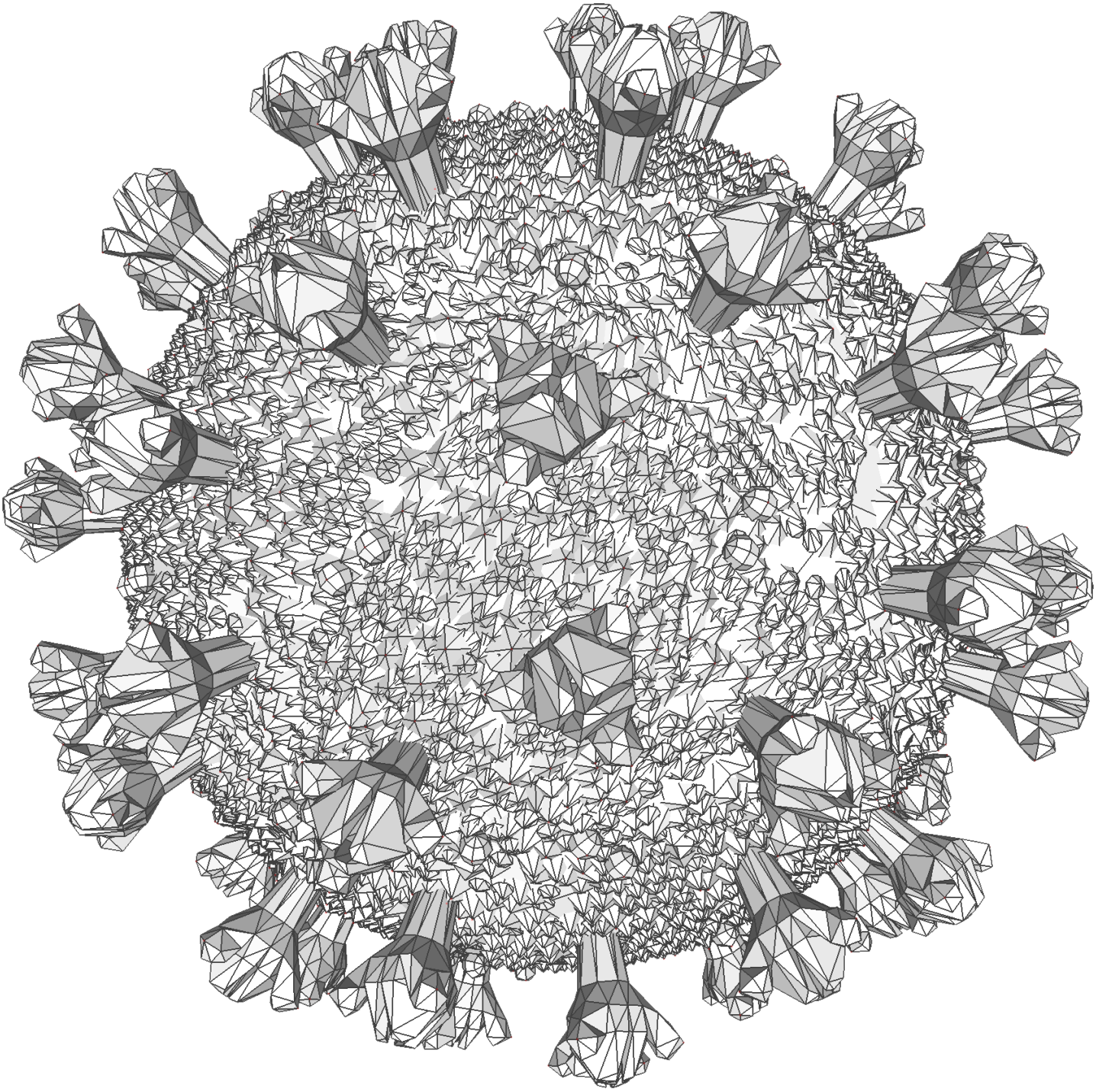

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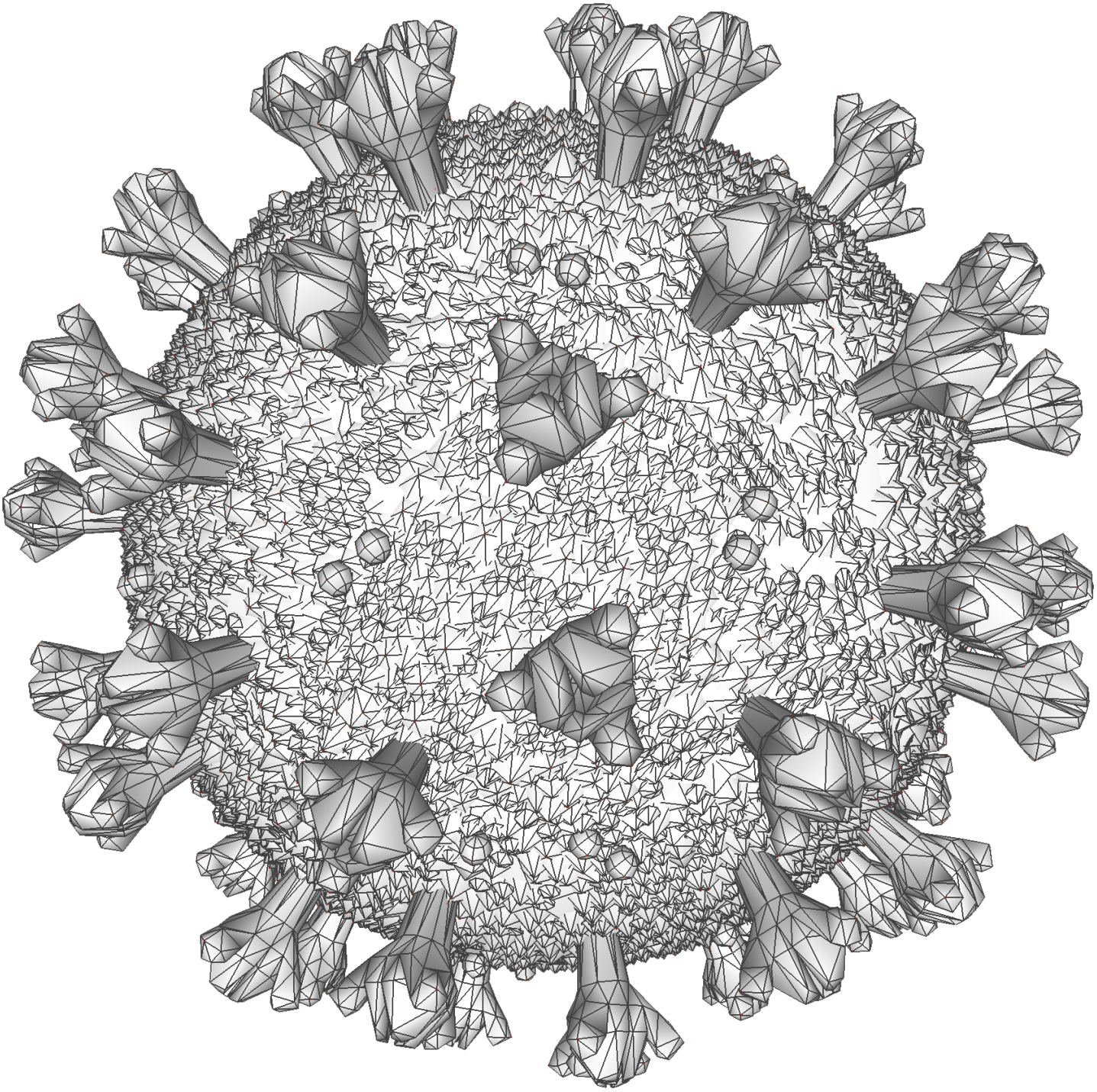


7

SARS-COV-2 SPIKE MOLECULE AND RECEPTOR

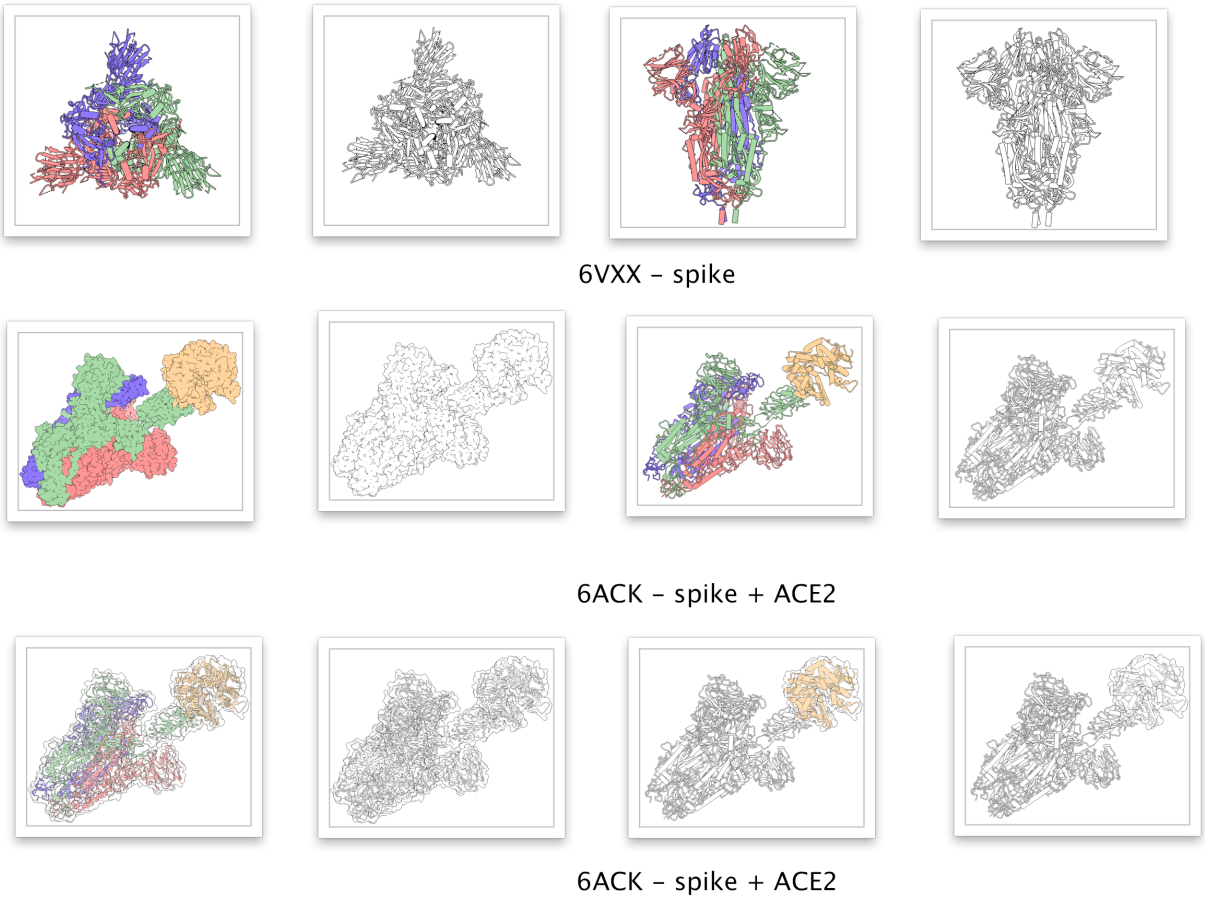
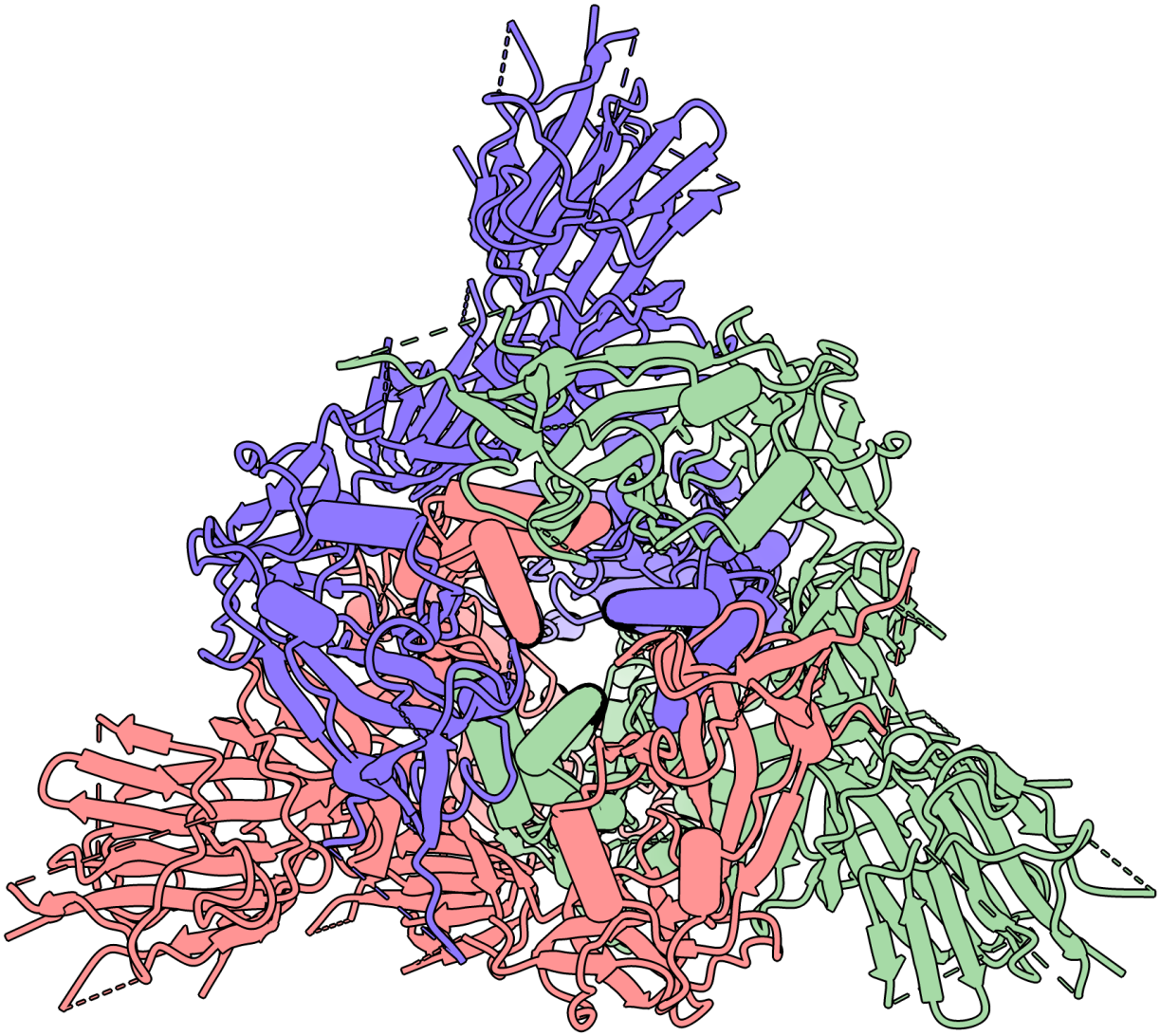
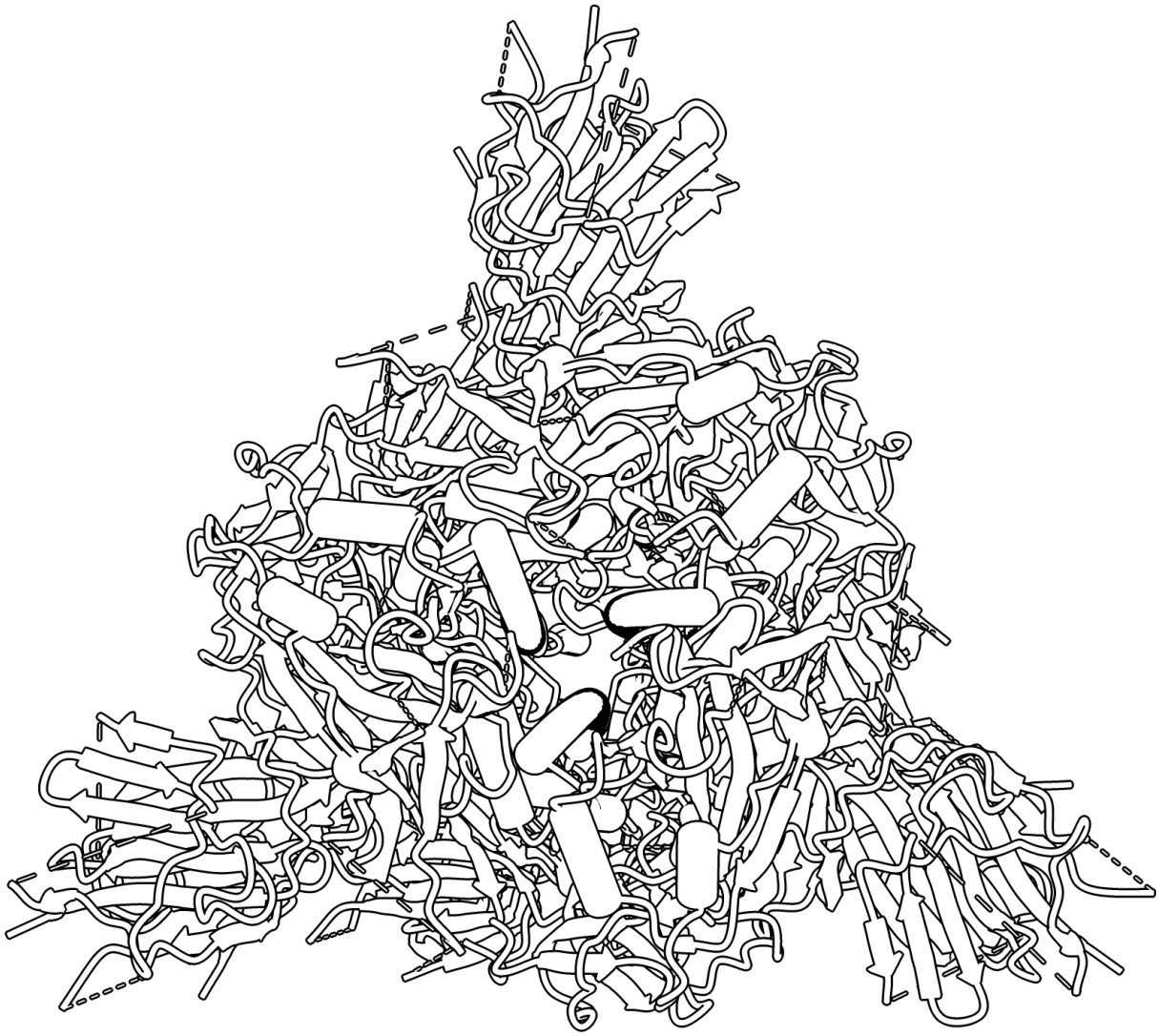
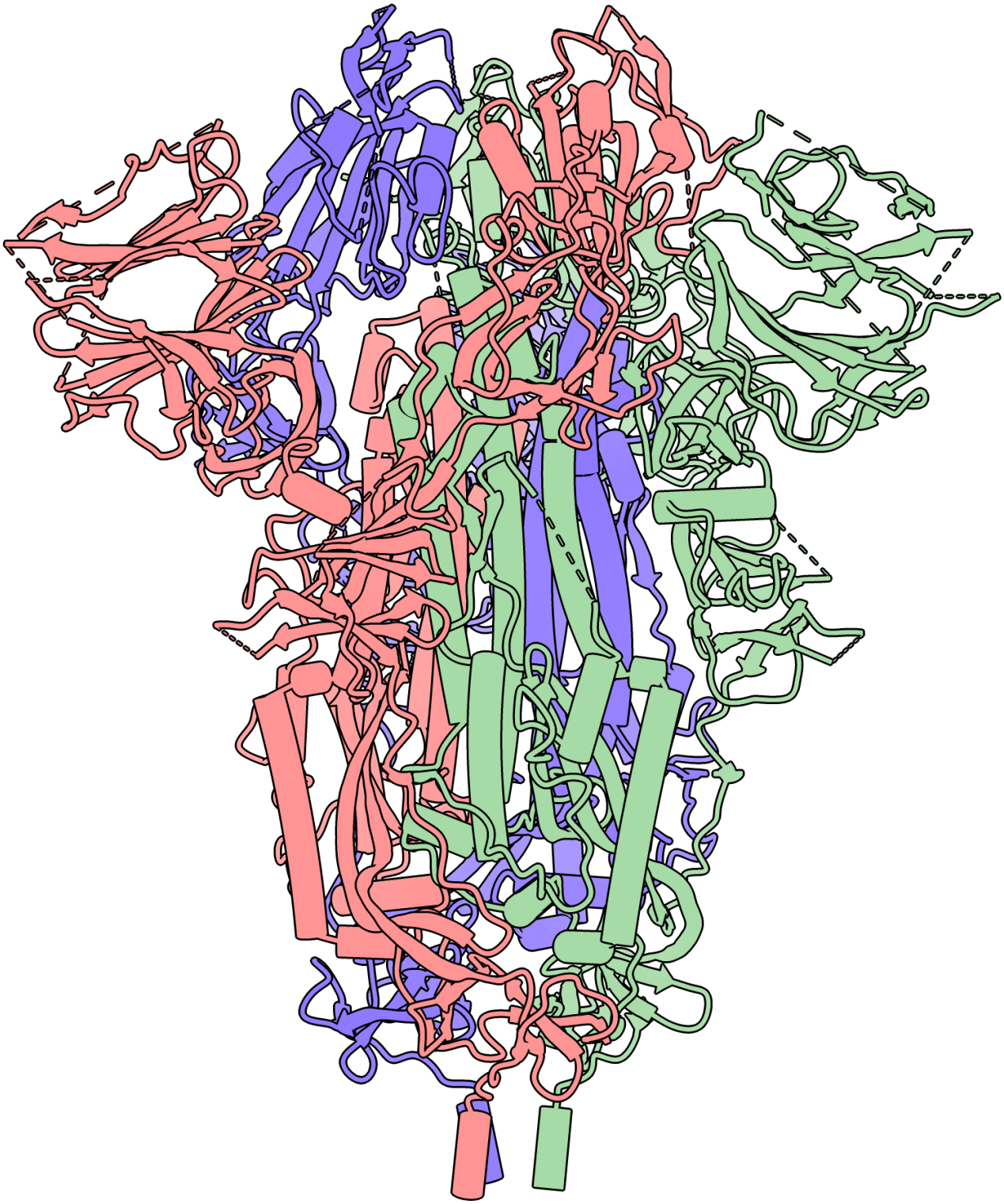


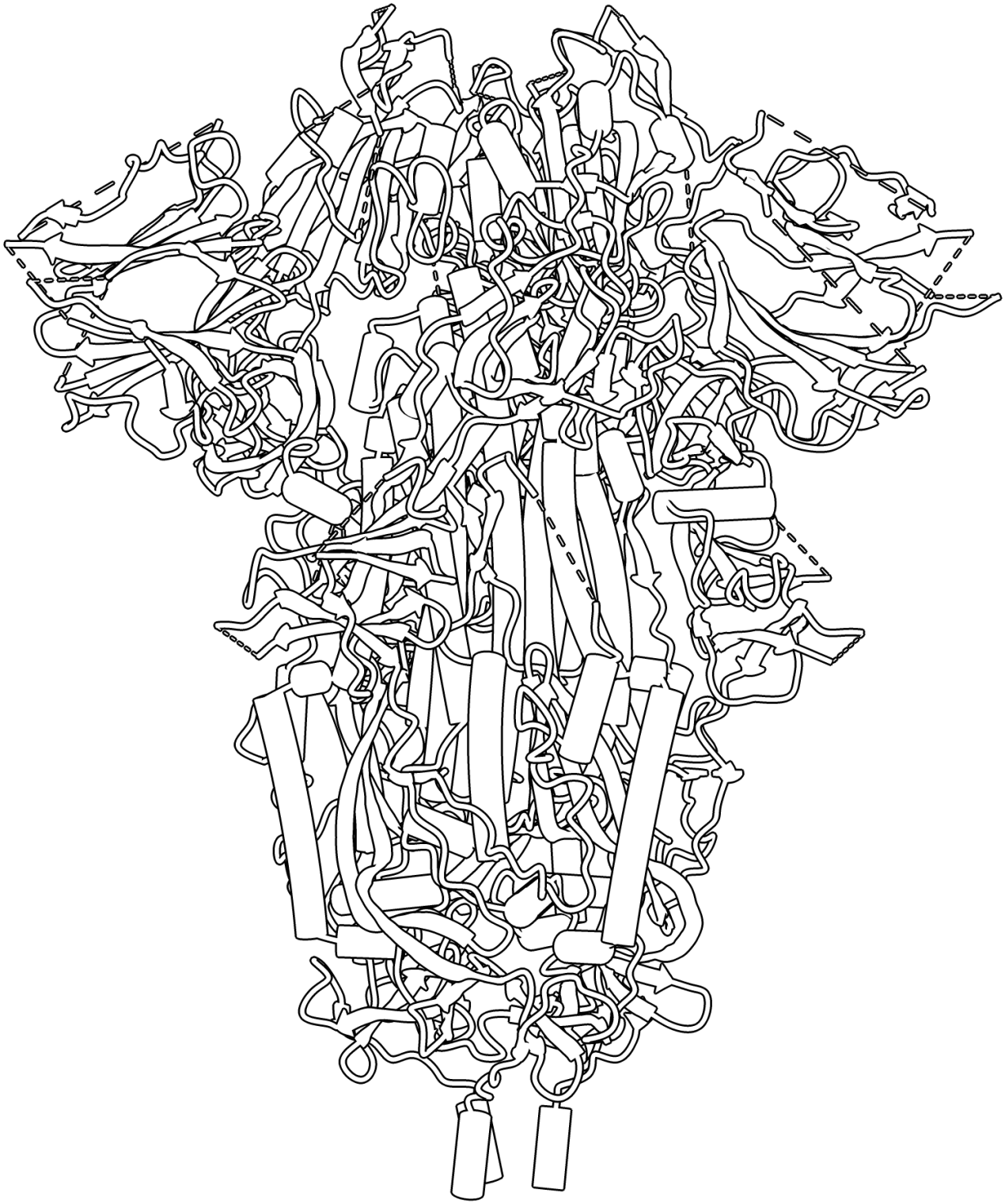
Figure 11: Trimeric spike glycoprotein with and without ACE2 receptor (yellow.)



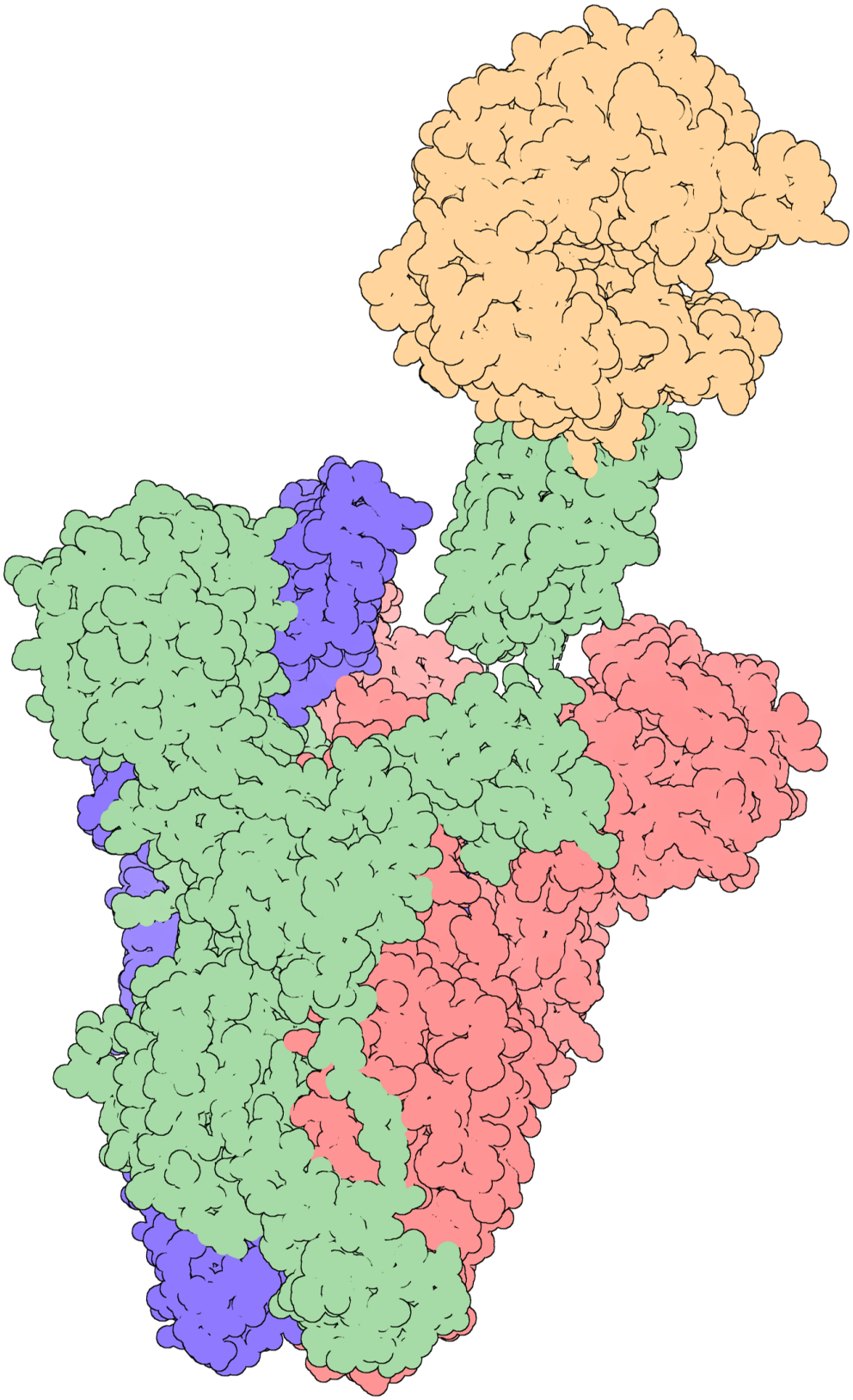


SARS-COV-2 SPIKE MOLECULE AND RECEPTOR





SARS-COV-2 SPIKE MOLECULE AND RECEPTOR



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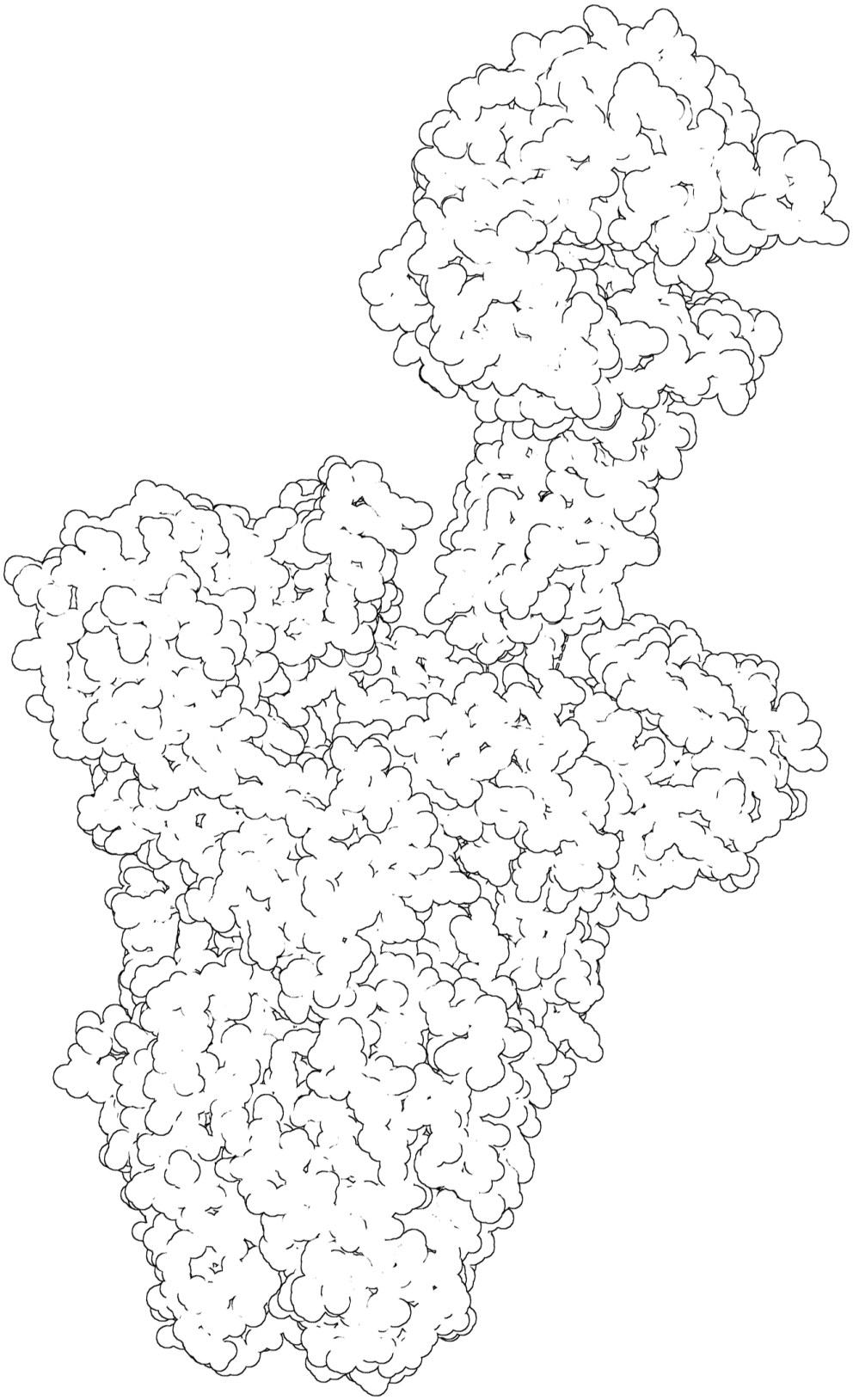

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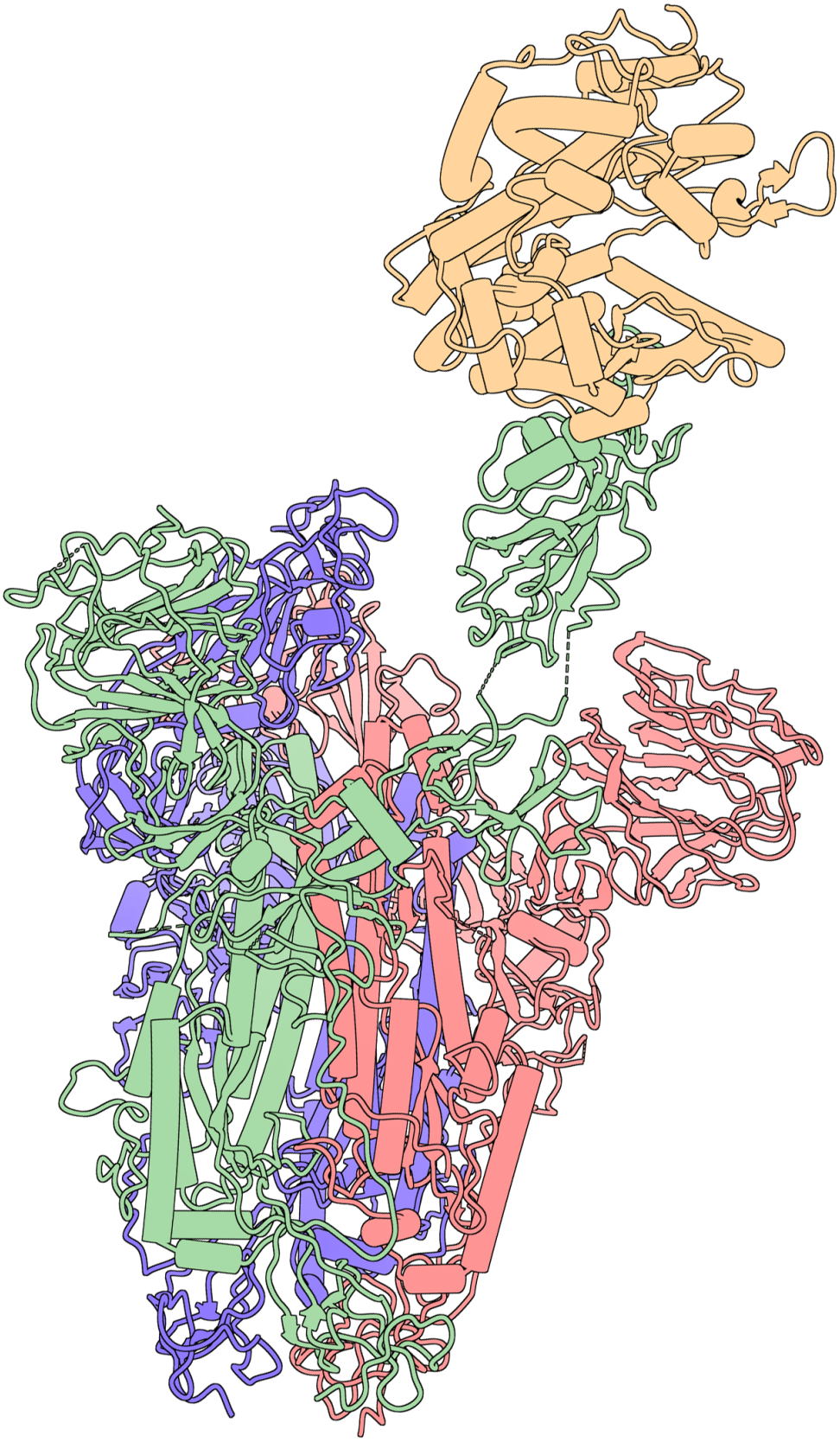
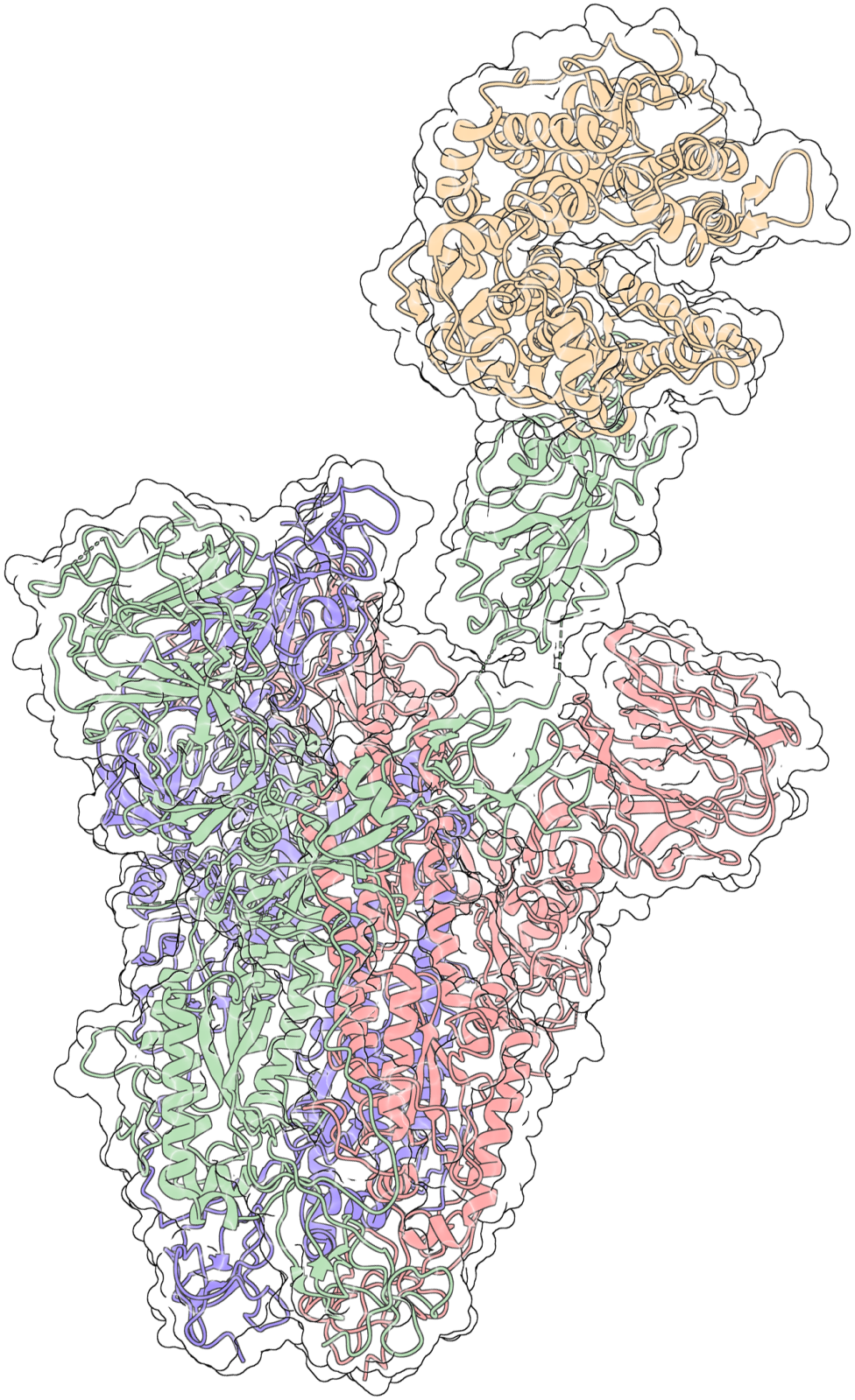


SARS-COV-2 SPIKE MOLECULE AND RECEPTOR

SARS-COV-2 SPIKE MOLECULE AND RECEPTOR



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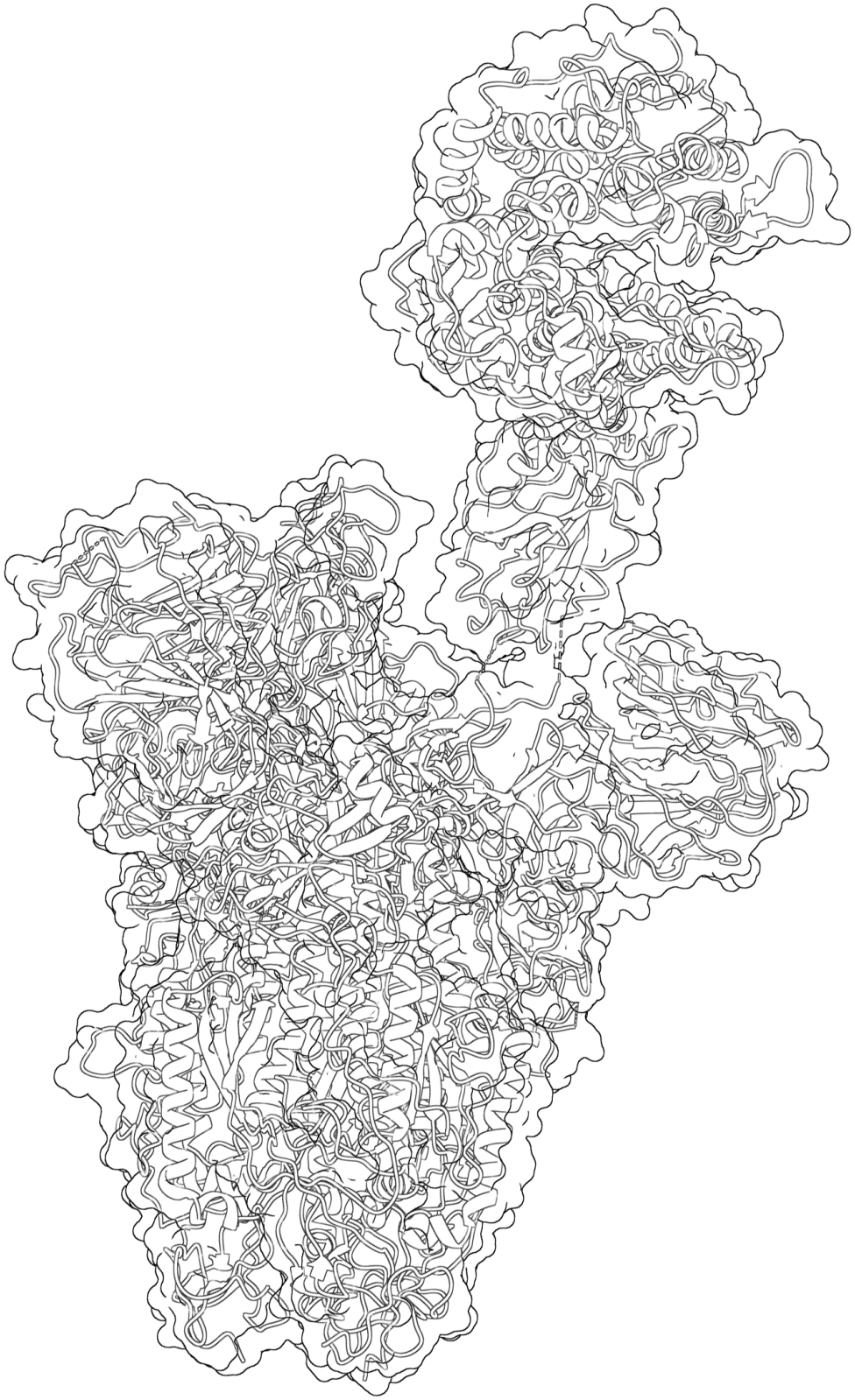

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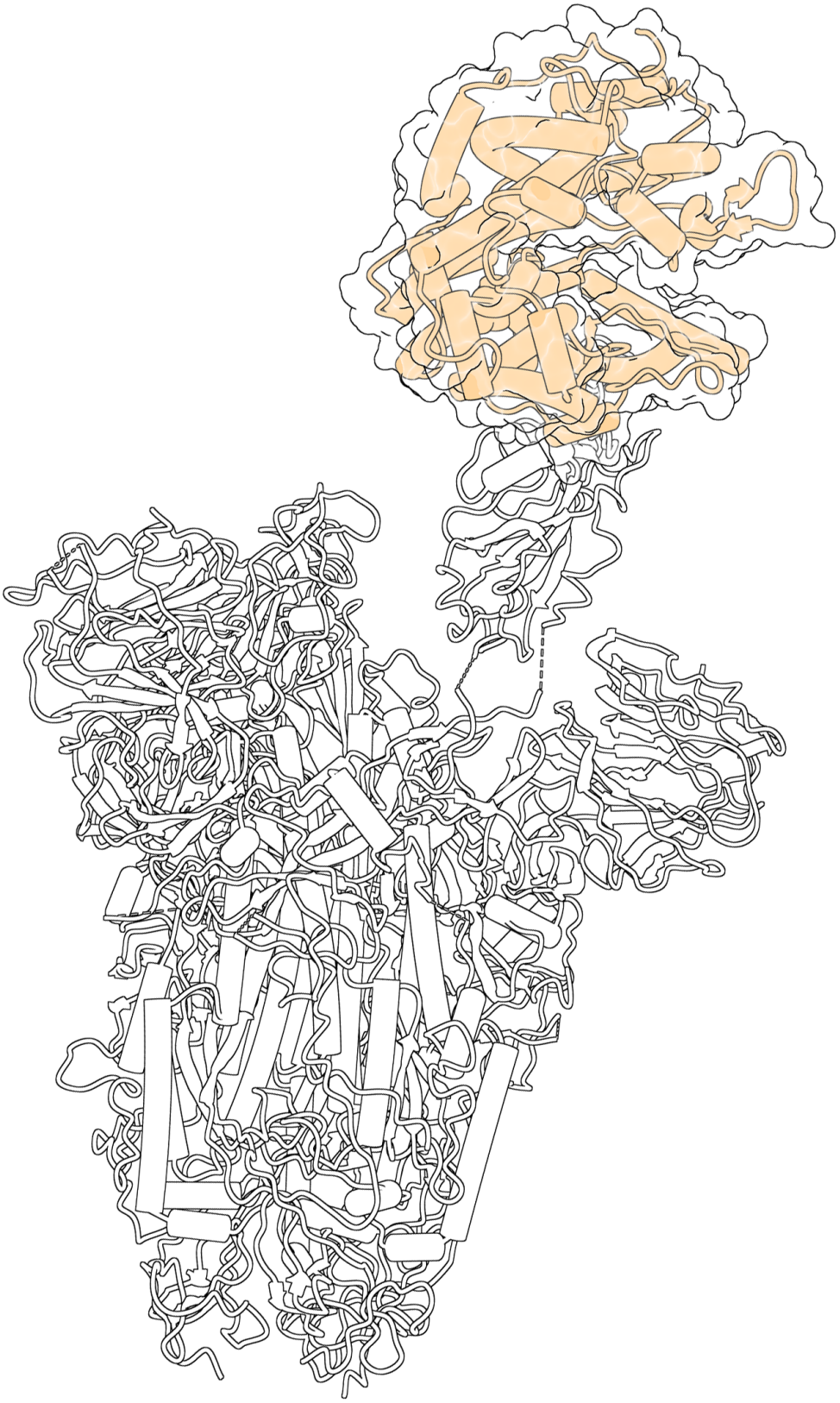

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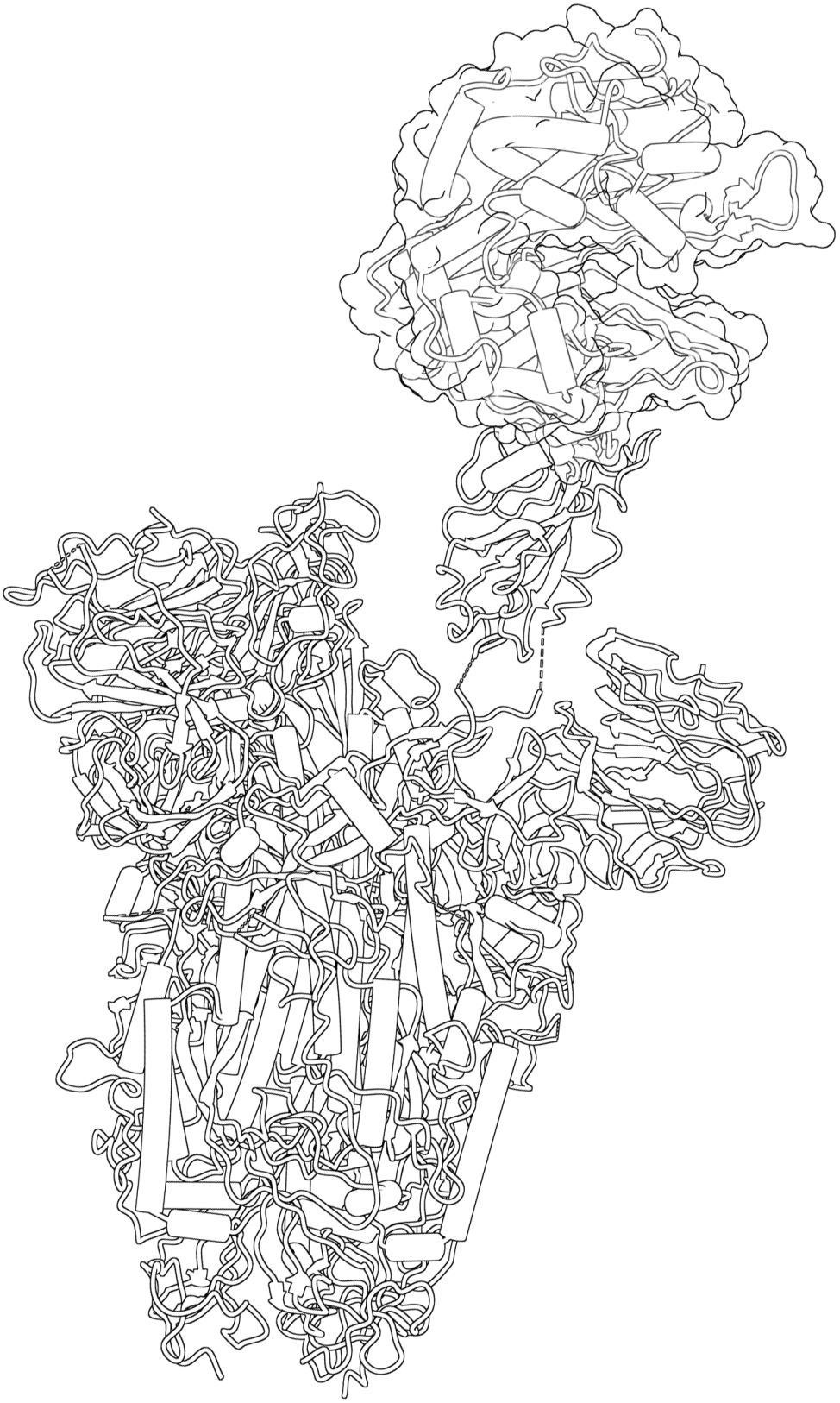

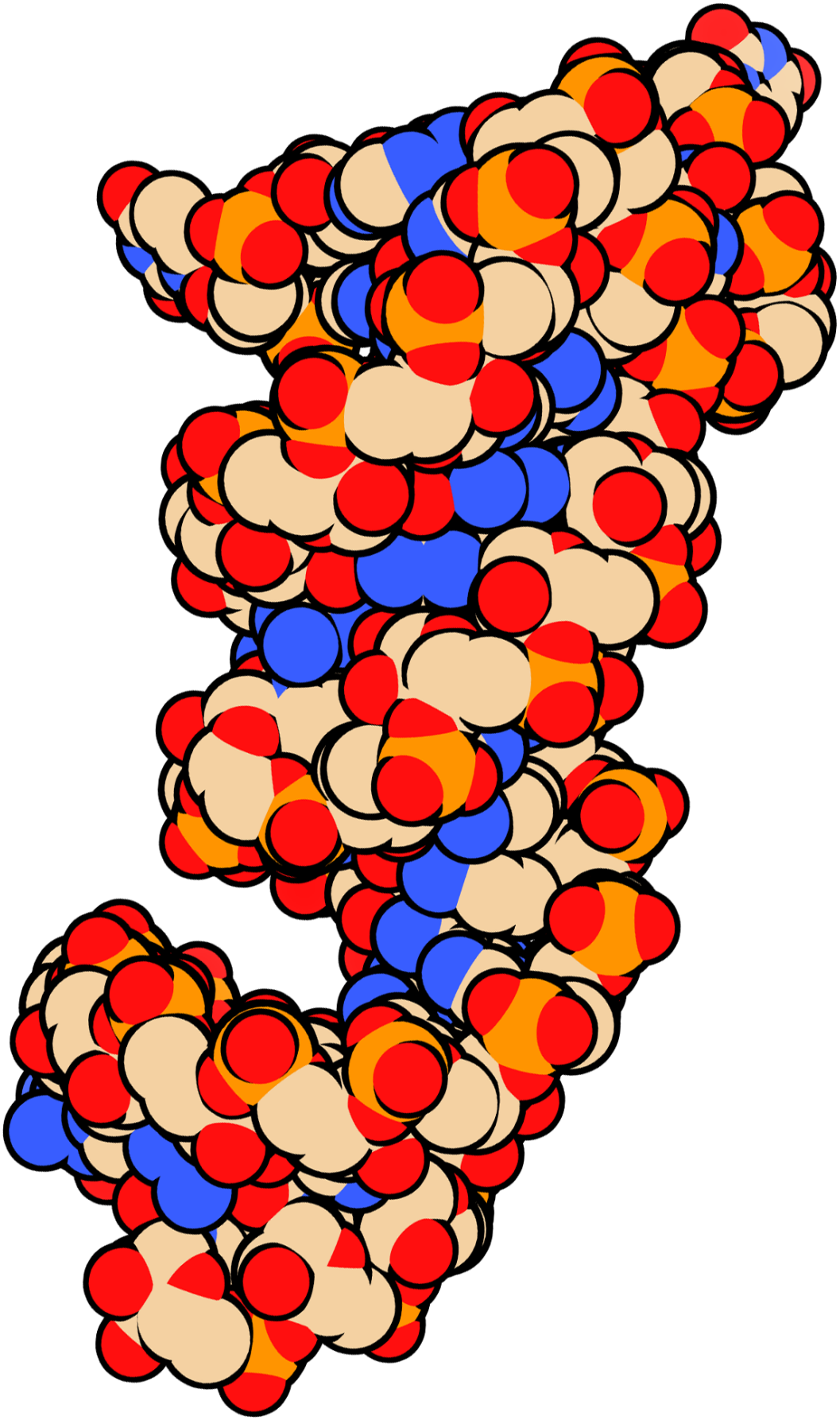

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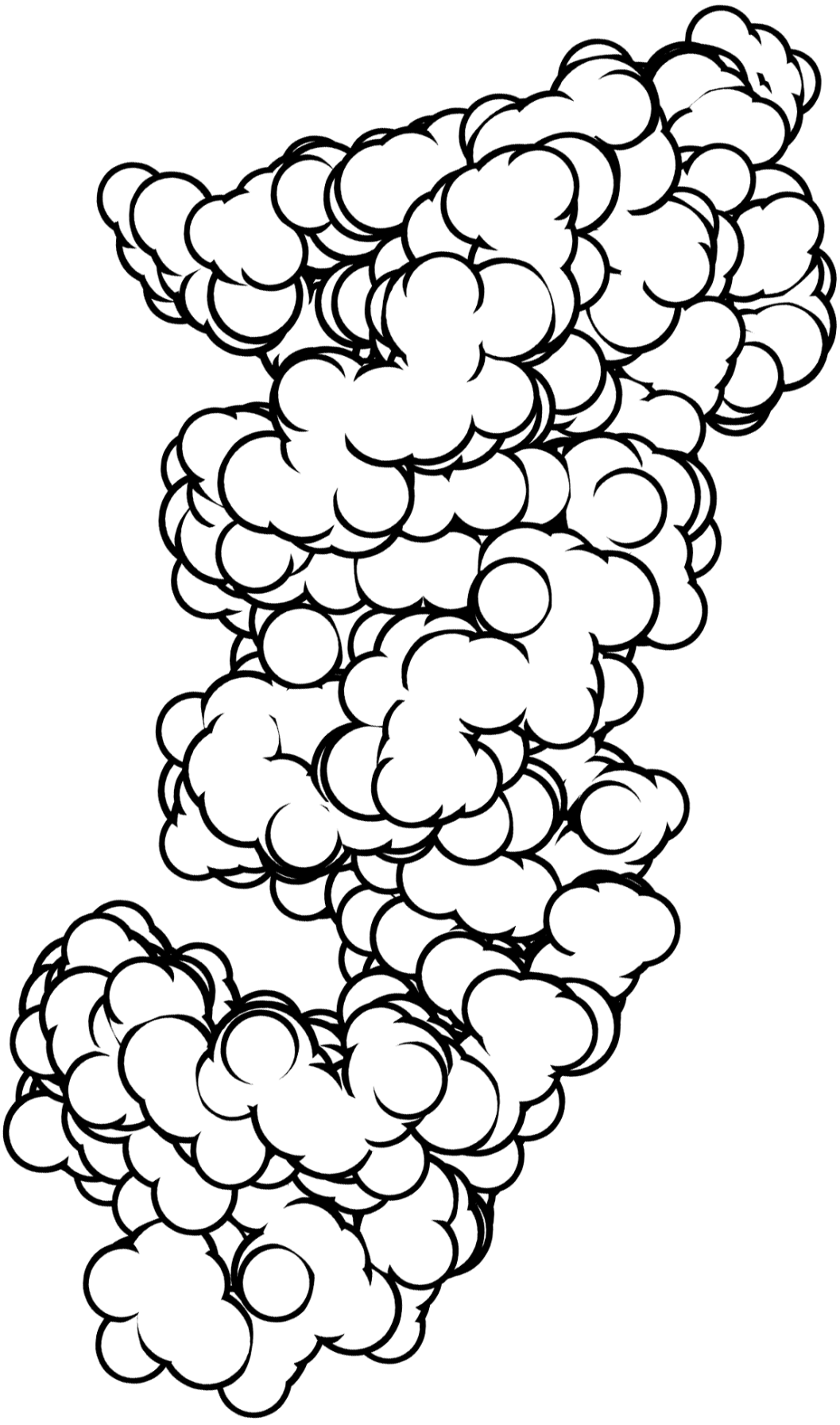

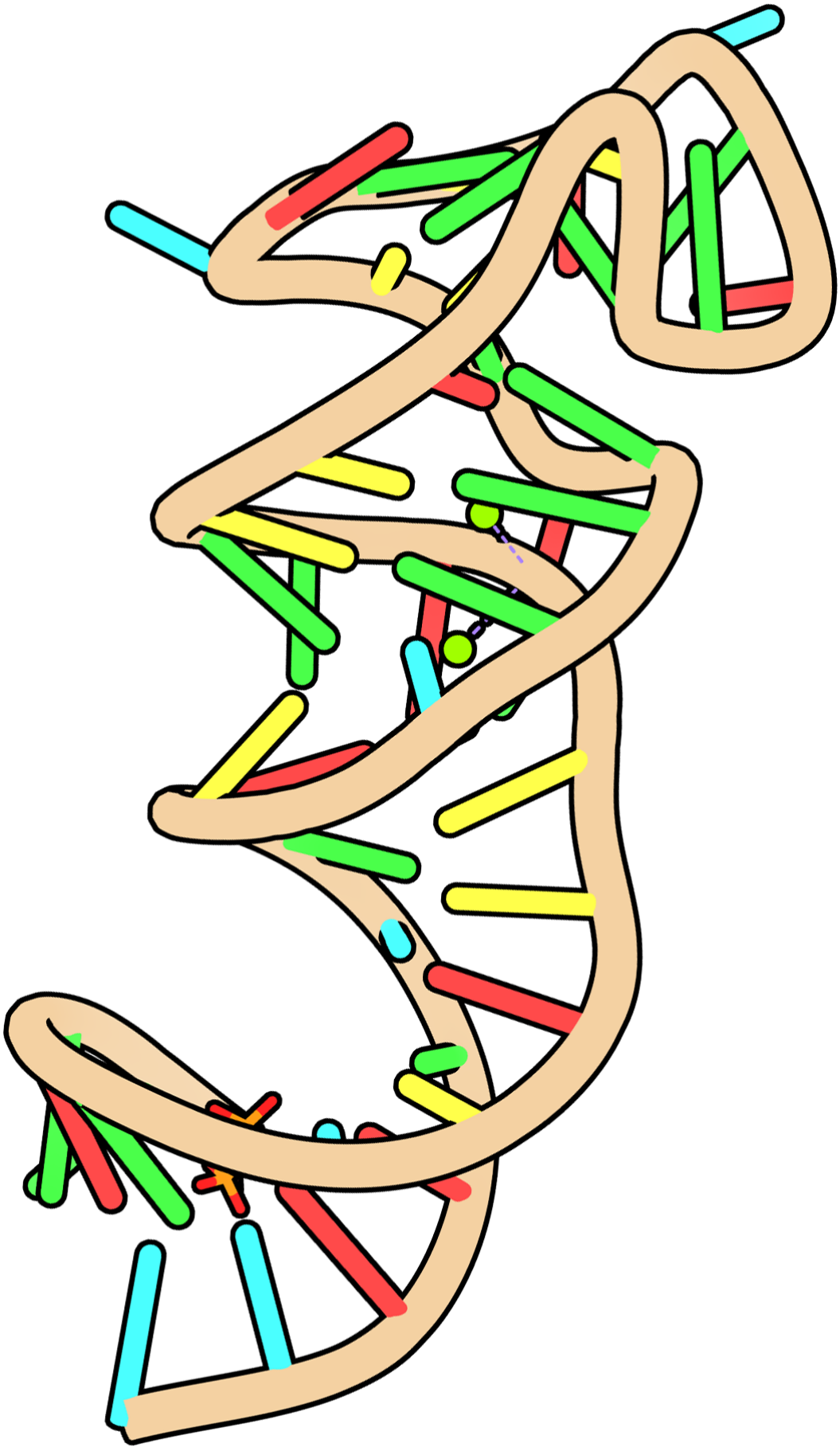

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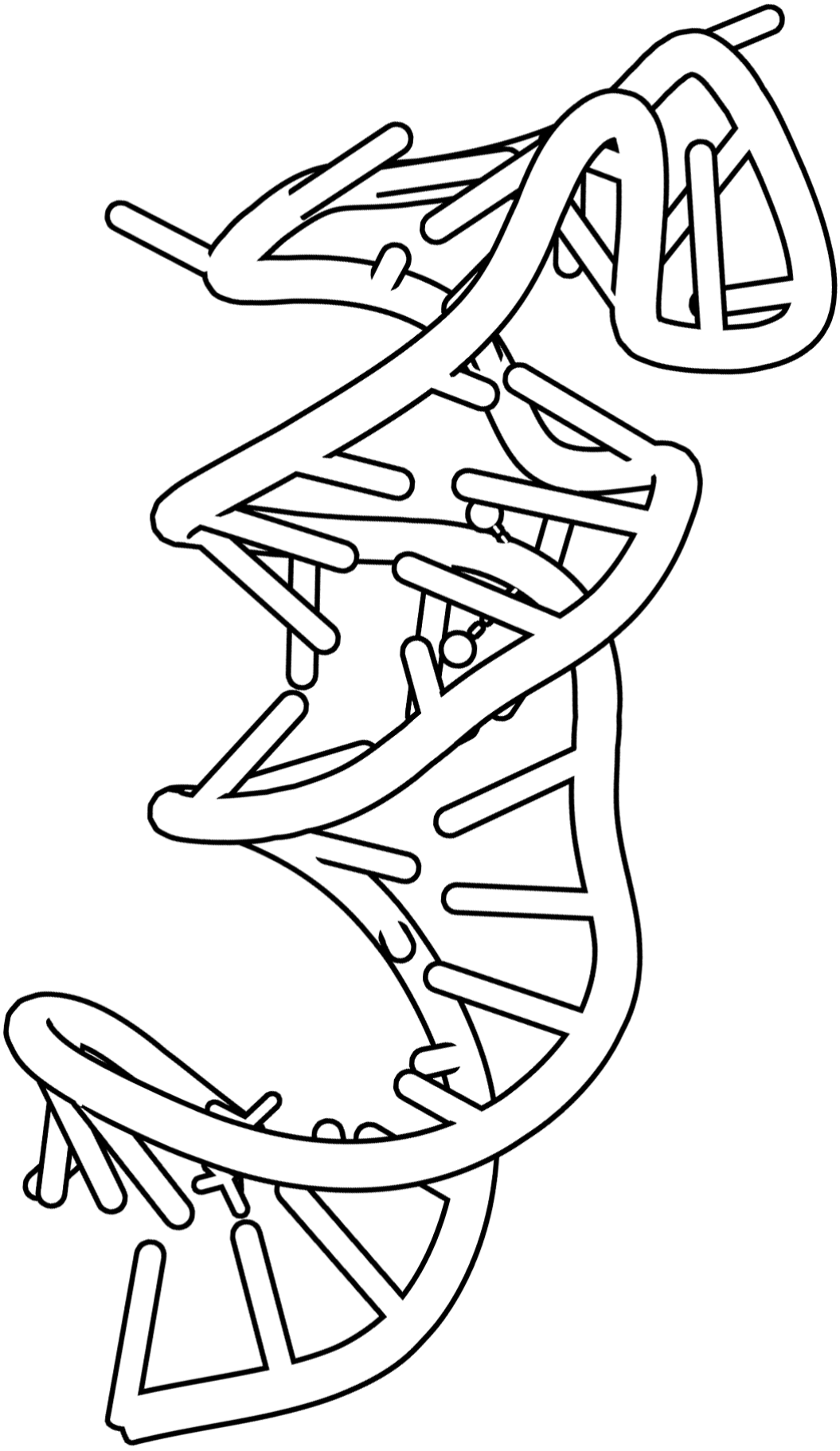

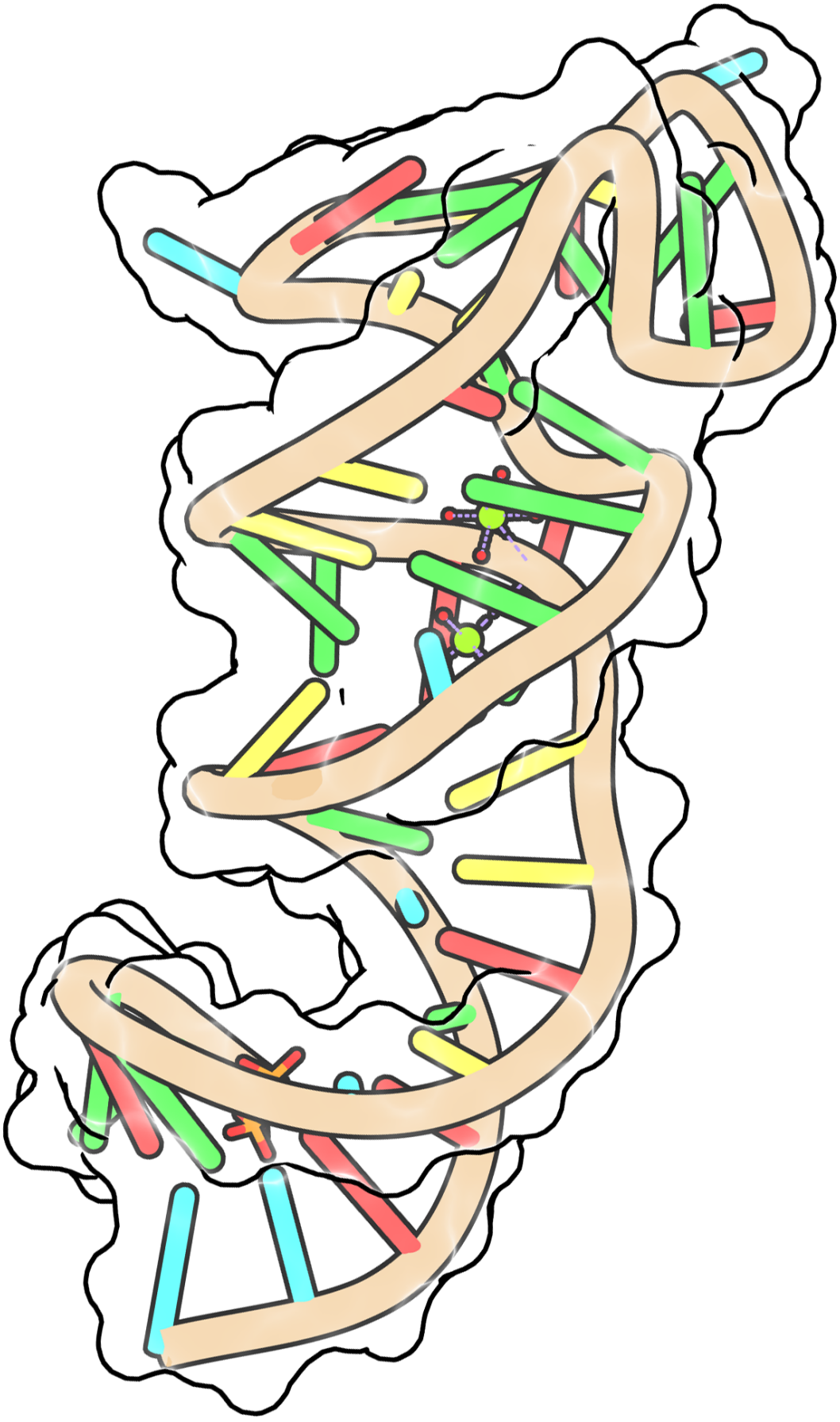

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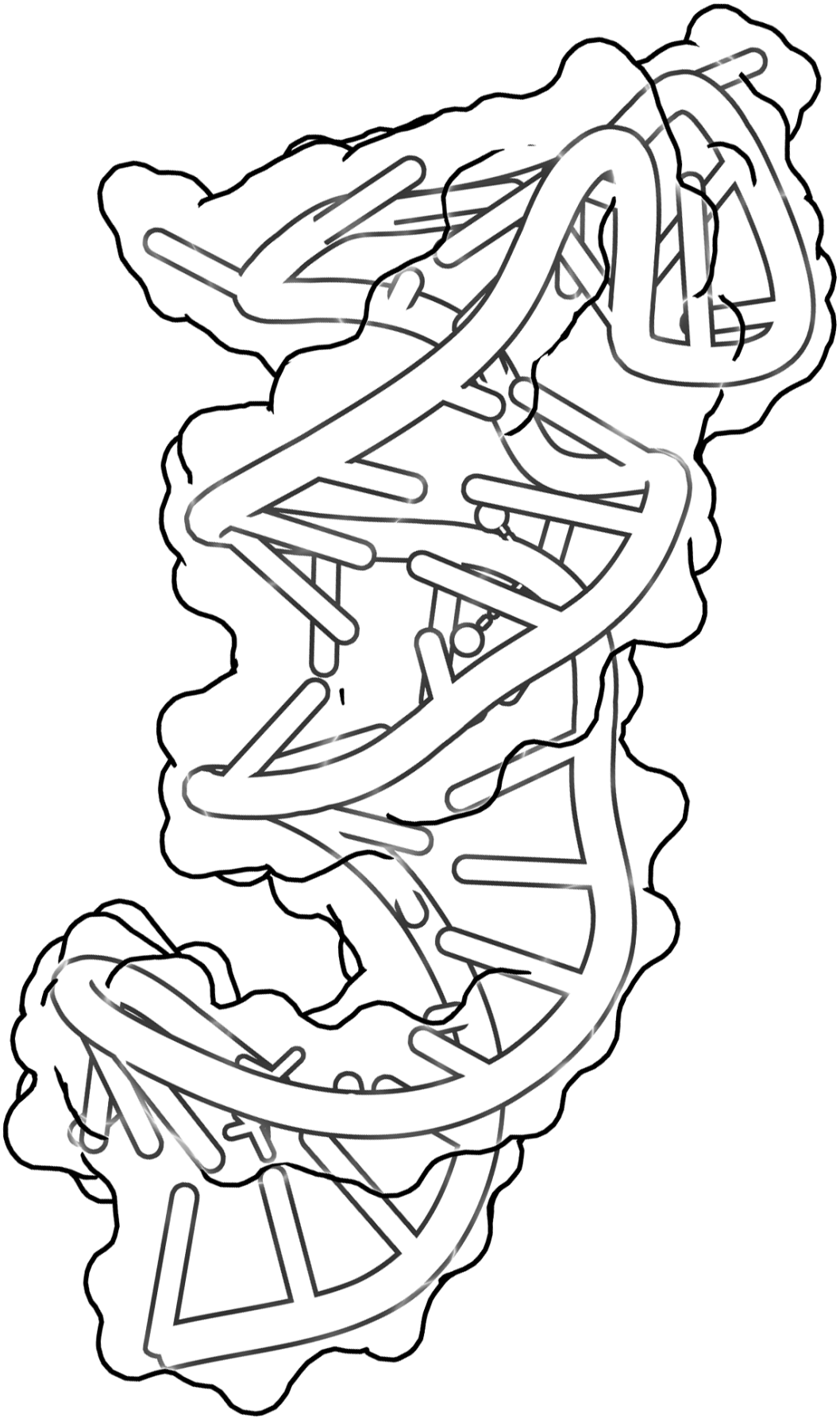
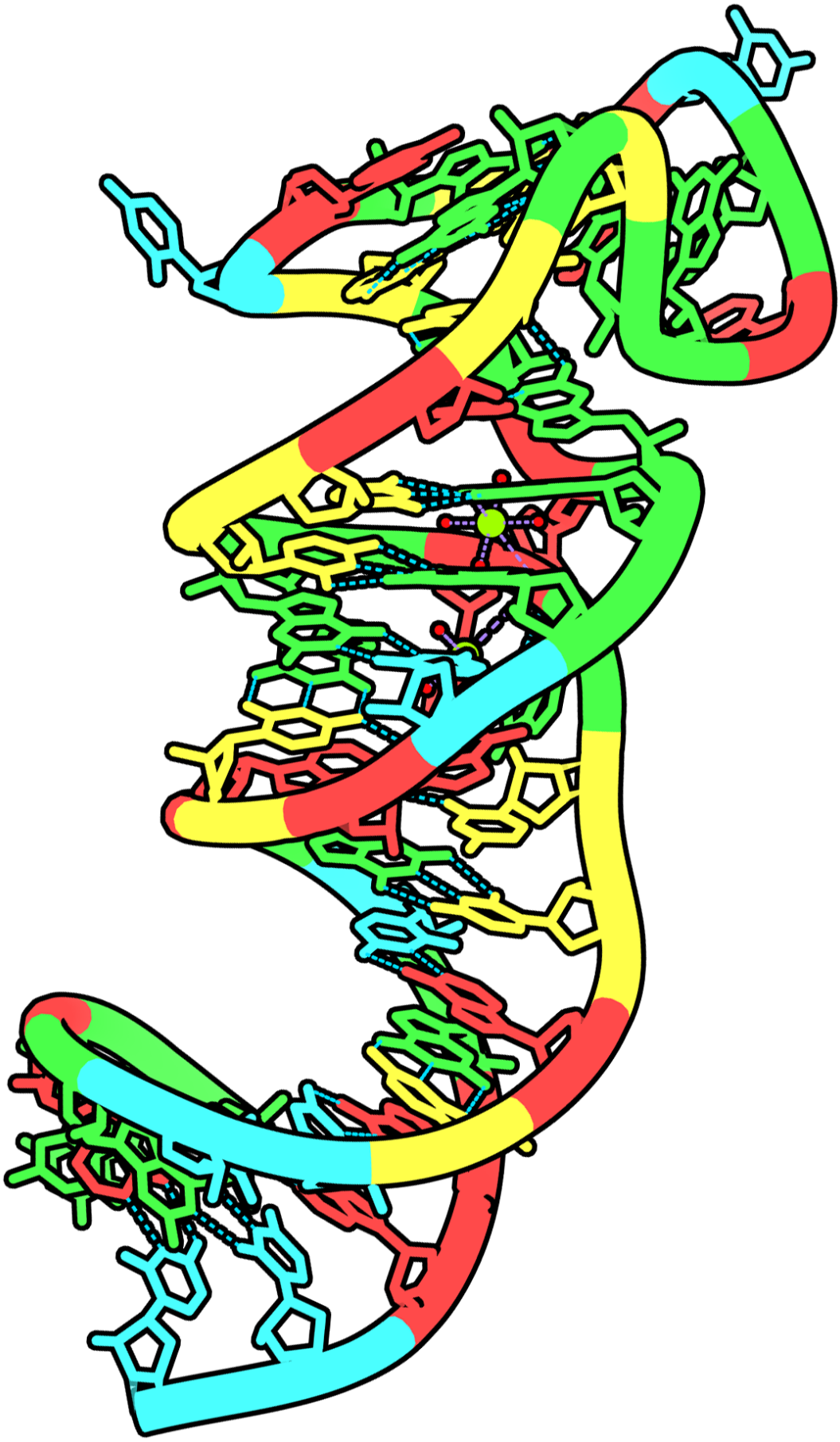
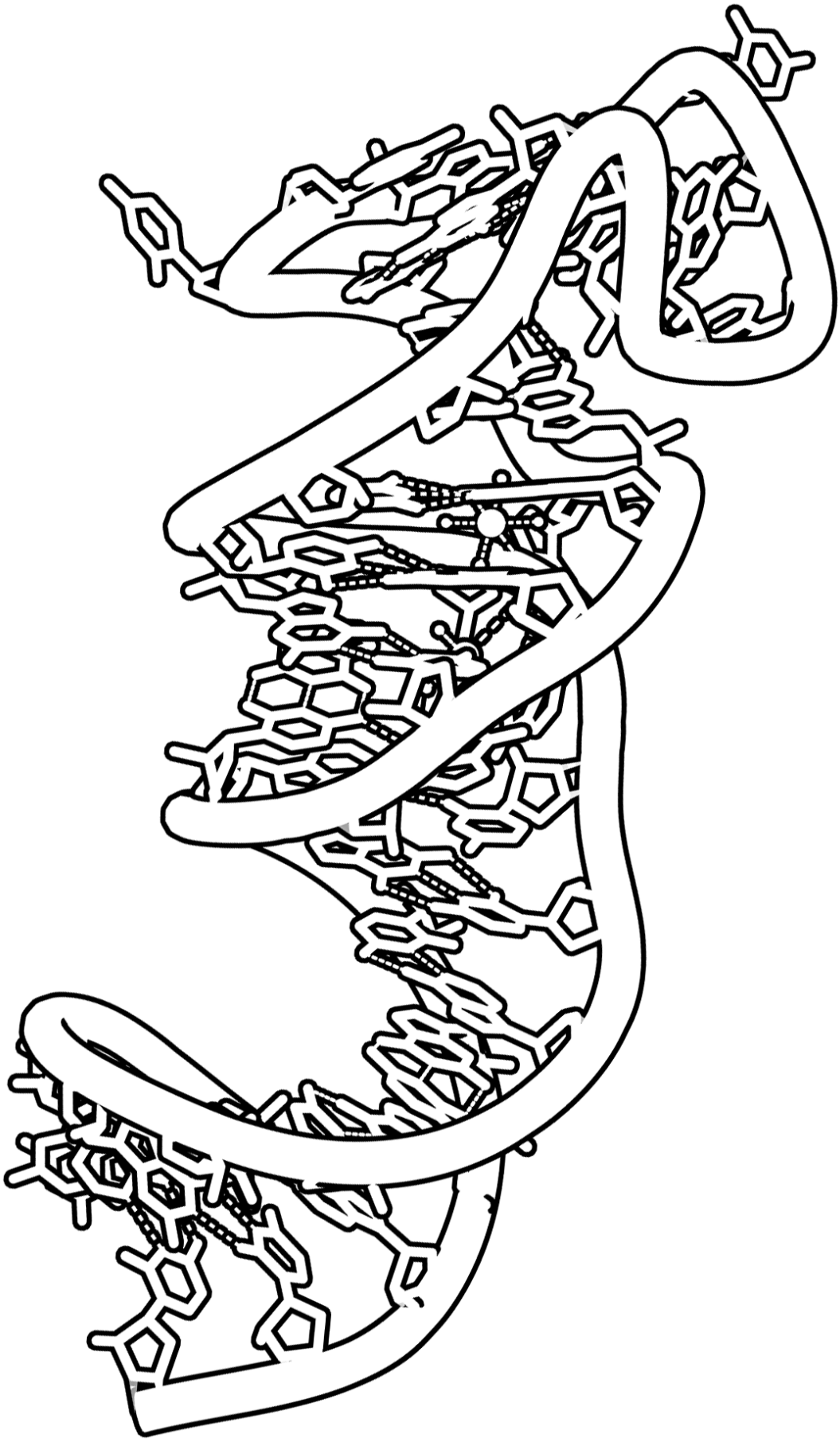
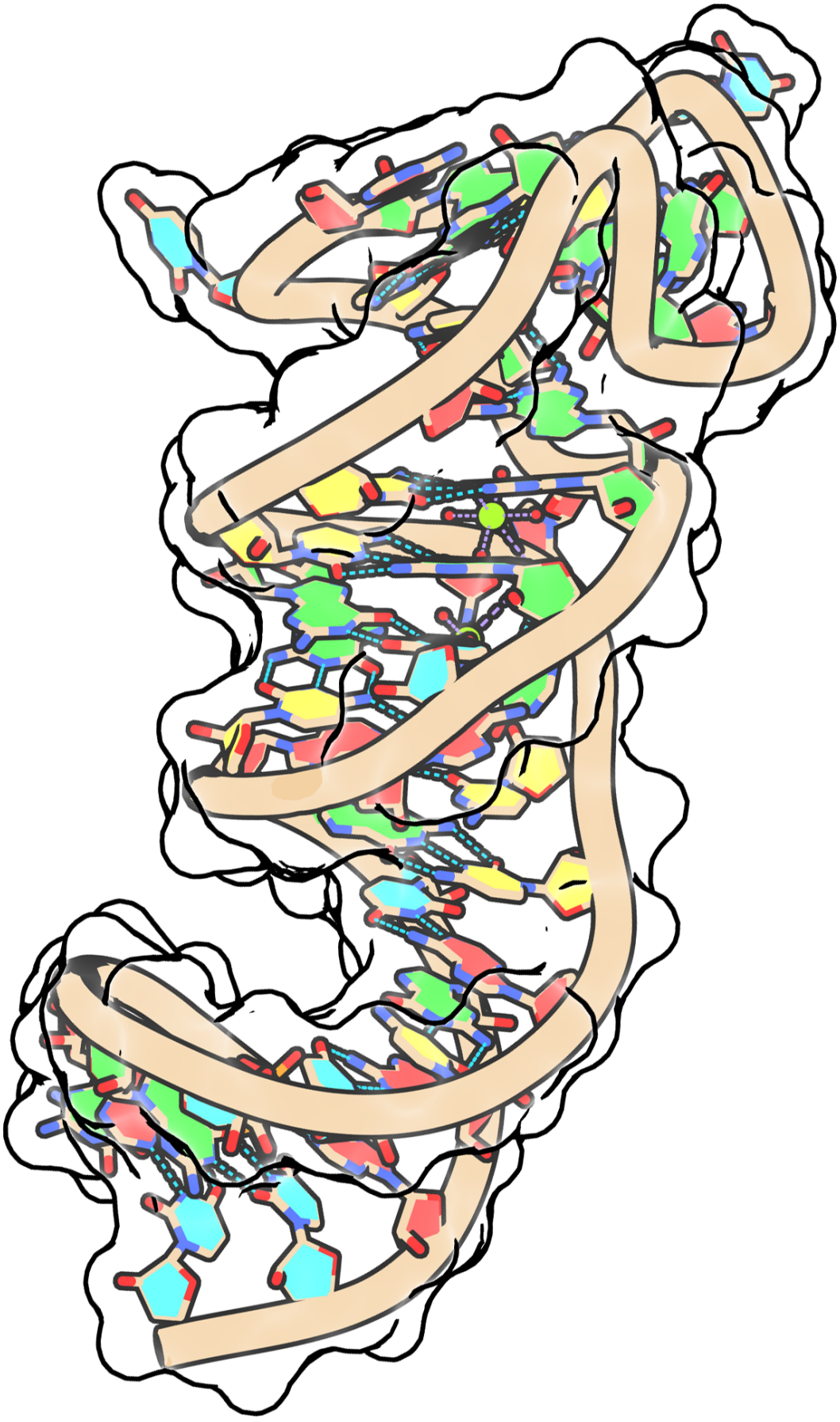
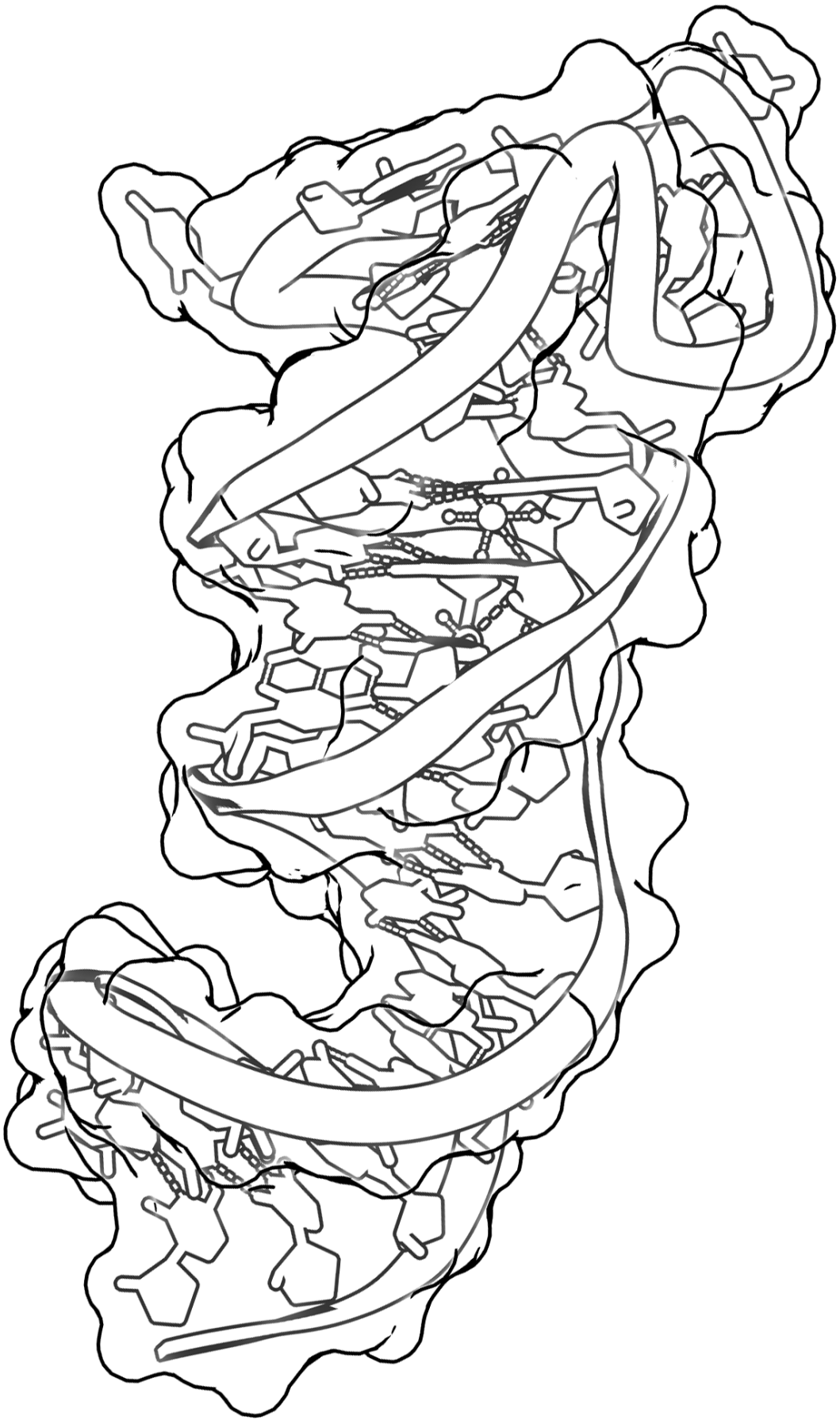


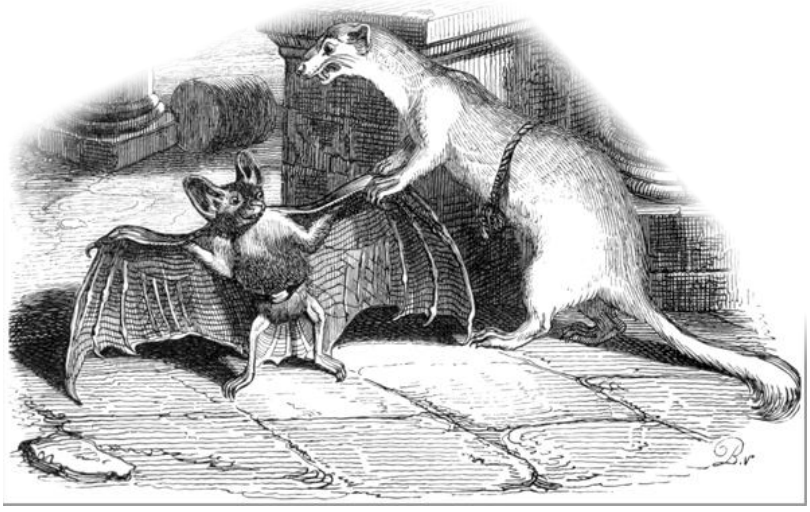






SARS-COV-2 SPIKE MOLECULE AND RECEPTOR





ACKNOWLEDGEMENTS

PHOTOS CREDITS

Figure 2: Illustration by David S. Goodsell, RCSB Protein Data Bank; doi: 10.2210/rcsb_pdb/goodsell-gallery-019

Figure 6: By Photo Credit: Content Providers(s): CDC/Dr. Fred Murphy - This media comes from the Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #4814. Note: Not all PHIL images are public domain; be sure to check copyright status and credit authors and content providers., Public Domain, https://commons.wikimedia.org/w/index.php?curid=822112

Figure 7 based on: 3D medical animation still shot showing 2019 novel Coronavirus Structure. Created: 30 January 2020. Image in article: https://en.wikipedia.org/wiki/Coronavirus Image: https://upload.wikimedia.org/wikipedia/commons/9/96/3D_medical_animation_coronavirus_structure.jpg ORIGIN: "https://www.scientificanimations.com/ coronavirus-symptoms-and-prevention-explained-through-medical-animation/"

Bat and weasel cartoon: portion of illustration of fable "*la chauve-souris et les deux belettes.*" (the bat and the two weasels) within 1868 edition of "Fables de la Fontaine, illustrations par Grandville" [1] (de La Fontaine and Grandville [2] .)

1 http://www.gutenberg.org/files/56327/56327-h/56327-h.htm

SOFTWARE

Coronavirus model and molecules from the Protein Data Bank were rendered as black outlines with software **UCSF ChimeraX**[2] (Goddard et al. [3],) developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco, with support from National Institutes of Health R01-GM129325 and the Office of Cyber Infrastructure and Computational Biology, National Institute of Allergy and Infectious Diseases.

Some renderings were also done with **MeshLab** (Cignoni et al. [1])

The booklet was assembled within **RStudio** (RStudio Team [6]) with the *classic* template of R package `bookdownplus` [10] which is an extension of package `bookdown` [9] .

This also required Latex

3D MODEL AND 3D MOLECULES

3D model by Alejandro Le'on. See detail section 2.

3D coordinates of molecules are from the Protein Data Bank.

www.rcsb.org

- `6ACK`: Cryo-EM structure of the SARS coronavirus spike glycoprotein in complex with its host cell receptor ACE2: Song et al. [7] .
- `6VXX`: Structure of the SARS-CoV-2 spike glycoprotein (closed state): Walls et al. [8] .
- `1XJR`: The Structure of a Rigorously Conserved RNA Element Within the SARS Virus Genome: Robertson et al. [5] .

2 https://www.cgl.ucsf.edu/chimerax/

BIBLIOGRAPHY

[1] Paolo Cignoni, Marco Callieri, Massimiliano Corsini, Matteo Dellepiane, Fabio Ganovelli, and Guido Ranzuglia. MeshLab: an Open-Source Mesh Processing Tool. In Vittorio Scarano, Rosario De Chiara, and Ugo Erra, editors, *Eurographics Italian Chapter Conference*, pages 129–136. The Eurographics Association, 2008. ISBN 978-3-905673-68-5. doi: 10.2312/LocalChapterEvents/ItalChap/ItalianChapConf2008/129-136.

[2] Jean de La Fontaine and J. J. Grandville. *Fables: précédées de La vie d'Esope le Phrygien*. Garnier Frères, 1868. URL http://www.gutenberg.org/files/56327/56327-h/56327-h.htm.

[3] T. D. Goddard, C. C. Huang, E. C. Meng, E. F. Pettersen, G. S. Couch, J. H. Morris, and T. E. Ferrin. UCSF ChimeraX: Meeting modern challenges in visualization and analysis. *Protein Sci.*, 27(1):14–25, 01 2018. [PubMed Central:PMC5734306] [DOI:10.1002/pro.3235] [PubMed:8254673].

[4] B. W. Neuman, B. D. Adair, C. Yoshioka, J. D. Quispe, G. Orca, P. Kuhn, R. A. Milligan, M. Yeager, and M. J. Buchmeier. Supramolecular architecture of severe acute respiratory syndrome coronavirus revealed by electron cryomicroscopy. *J. Virol.*, 80(16):7918–7928, Aug 2006. [PubMed Central:PMC1563832] [DOI:10.1128/JVI.00645-06] [PubMed:10600565].

[5] M. P. Robertson, H. Igel, R. Baertsch, D. Haussler, M. Ares, and W. G. Scott. The structure of a rigorously conserved RNA element within the SARS virus genome. *PLoS Biol.*, 3(1):e5, Jan 2005. [PubMed Central:PMC539059] [DOI:10.1371/journal.pbio.0030005] [PubMed:1382577].

[6] RStudio Team. *RStudio: Integrated Development Environment for R*. RStudio, Inc., Boston, MA, 2015. URL http://www.rstudio.com/.

[7] W. Song, M. Gui, X. Wang, and Y. Xiang. Cryo-EM structure of the SARS coronavirus spike glycoprotein in complex with its host cell receptor ACE2. *PLoS Pathog.*, 14(8):e1007236, 08 2018. [PubMed Central:PMC6107290] [DOI:10.1371/journal.ppat.1007236] [PubMed:15367599].

[8] A. C. Walls, Y. J. Park, M. A. Tortorici, A. Wall, A. T. McGuire, and D. Veesler. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. *Cell*, Mar 2020. [PubMed Central:PMC7102599] [DOI:10.1016/j.cell.2020.02.058] [PubMed:16195424].

[9] Yihui Xie. *bookdown: Authoring Books and Technical Documents with R Markdown*. Chapman and Hall/CRC, Boca Raton, Florida, 2016. URL `https://github.com/rstudio/bookdown`. ISBN 978-1138700109.

[10] Peng Zhao. *bookdownplus: Generate Varied Books and Documents with R 'bookdown' Package*, 2017. URL `https://CRAN.R-project.org/package=bookdownplus`. R package version 1.0.2.