

# Department of Energy Response to COVID-19 Pandemic

J.P. Hill, Director, NSLS-II

National Bureau of Economics, Panel Discussion: July 16<sup>th</sup> 2020

# Department of Energy

- Traces its history back to the Manhattan project in WWII
- Mission: to ensure America's security and prosperity by addressing its energy, environmental and nuclear challenges through transformative science and technology solutions
- Network of 17 National labs tackle critical scientific challenges from climate change to origin of the universe
- It is in its DNA to address large-scale complex challenges with large teams and large facilities

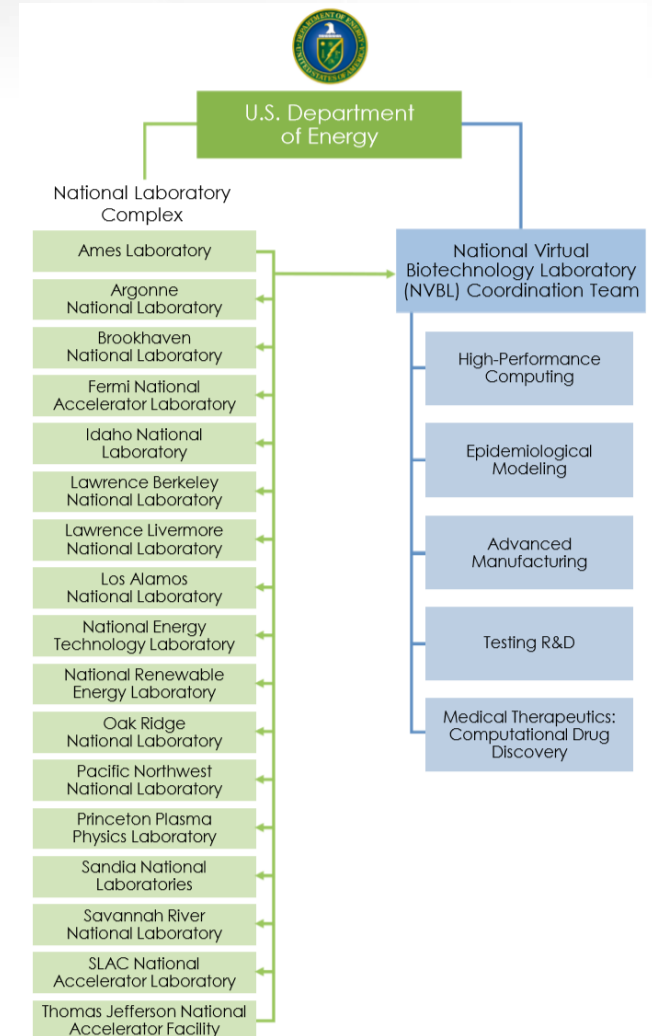
# DoE and National Emergencies

- DOE has a history of responding to urgent National need:
  - Fukushima
  - Hurricane Sandy
  - Deep Water Horizon
- In response to COVID-19 Pandemic and the range of challenges it presents, DOE stood up the *National Virtual Biotechnology Laboratory (NVBL)*

# National Virtual Biotechnology laboratory

- Consortium of DOE National laboratories
- “Front Door” for DOE’s COVID response
- Takes advantage of DOE user facilities
- Initial activities include:
  - Epidemiological and logistical support
  - Addressing supply chain bottlenecks by harnessing advanced manufacturing
  - Medical therapeutics: computational drug discovery and structural biology
  - Innovations in testing capabilities
  - Viral fate and transport

<https://science.osti.gov/nvbl>



# CARES act funding for DOE Office of Science

\$99.5 M

**User facilities:** \$19.6 M

Light sources

Neutron sources

CryoEM facilities

**Leadership Computing:** \$36.2 M

ALCF

OLCF

NERSC

**Multi-lab research sprints:** \$43.7 M

Epidemiology

Advanced manufacturing

Viral fate and transport

Molecular drug design

Testing R&D



*National Synchrotron Light Source II  
Brookhaven National Laboratory*



*National Energy Research Scientific  
Computing Center  
Lawrence Berkeley National Laboratory*



Tubes and  
swabs

# Light Source Operations

93% of all drugs approved by FDA in last 15 years had structures solved at a synchrotron

Imperative to keep the light sources running. CARES act funding helped this happen.

From March to mid-June the 5 DOE light sources collectively:

- Ran over 4000 hours of operations dedicated to COVID-19 research

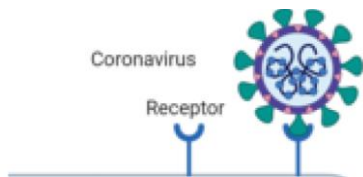
- Ran over 7000 samples

- Solved over 50 new structures

- Supported 24 proprietary groups from pharmaceutical companies

- Supported 66 Academic groups

Anti-viral drugs aim to break the infection cycle:



First step in infection is virus “spike” protein binds with receptor in human cell



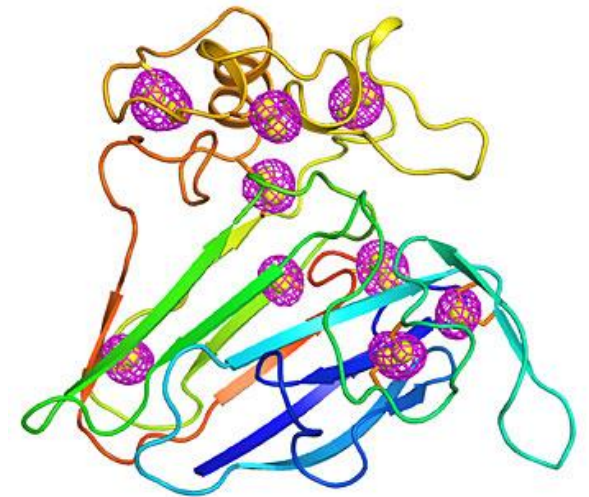
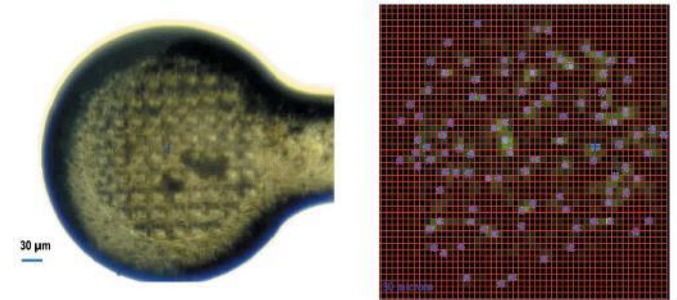
Spike protein Receptor Binding Domain complexed with human ACE2

Structure solved at the Advanced Photon Source, April 2020

# NSLS-II Strength: Microbeams

- Growing large enough single crystals is the bottleneck in determining structure
- Automation and intense x-ray beams at NSLS-II allow the study of crystals 200 x smaller in volume than anywhere else in the world.
- Down to  $\sim 2$  micron. This greatly speeds up solving the structure and searching for new drugs

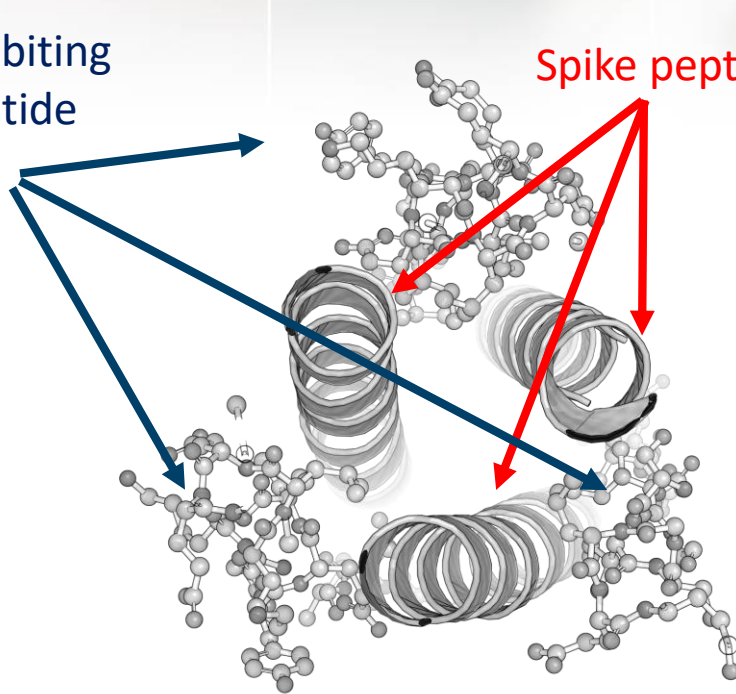
Guo et al. *IUCr J.* 6, Part 4, July 2019.



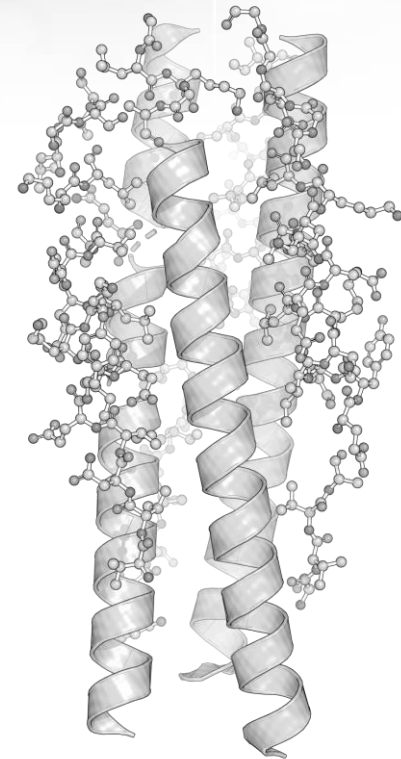
# Spike protein receptor binding domain

Inhibiting peptide

Spike peptide



Top view



Side view

Kreitler, McSweeney et al, unpublished

100's of microcrystals studied

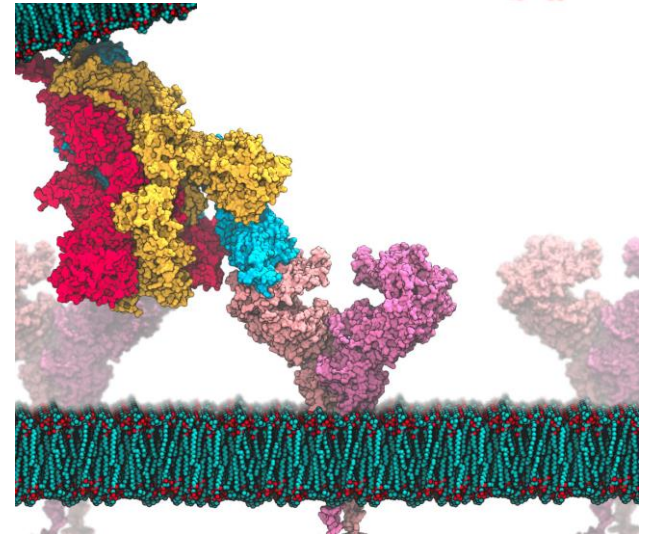
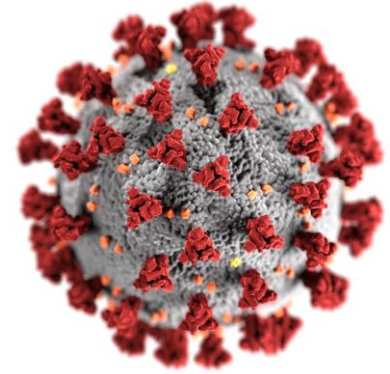
Peptide = piece of a protein

Goal is to find something that binds with the spike protein and prevents it fusing with our cell membrane



# Computer-based Drug Discovery

- There are 68 'Pockets' on the spikes where a potential vaccine/drug could 'bind' to stop the virus from connecting
- 4 billion drug compounds that could potentially 'bind' to those pockets
- Gives **68 x 4 billion** possibilities!
- 200 million tested to date. 40 targets identified
- Next steps are to test the binding experimentally and solve the structures before moving to drug trials



Work funded by DOE's National Virtual Biotechnology Laboratory

# Challenges of operating a user facility in a post-COVID world

- Risks associated with COVID-19 can be managed with hygiene plans, social distancing and new habits. These will be distractions at first, but should “bed in” over a few months.
- User travel likely to be highly restricted in the future. Increased emphasis on remote user operations. Need to find ways to make this as rich an experience as possible for the users.
- Scientific interactions between staff and users and users and users, particularly the impromptu informal ones that can be so creative, much less likely
- User experience risks becoming very transactional “measure this for me” which would be a great loss, reducing the opportunity for facility staff to engage scientifically and thereby reducing the impact of the work
- Potential long term consequences for workforce development

# Summary

- DOE has significant R&D expertise and capabilities that can be brought to bear on scientific and technical challenges at a time of national emergency
- In the case of COVID-19, these efforts have been coordinated through the newly-created National Virtual Biotechnology Laboratory
- CARES act funding of \$99 M was instrumental in the short term response
- Long term consequences on the way research is performed, traditionally biased on extended person-to-person interactions likely to be profound.