SUPPLEMENTARY INFORMATION

Below we provide the supplementary information and figures detailed in our investigation, and report.

1. Temporal Evolution of SARS-CoV-2 Spike Across Different Experimental Conditions

1.1 Apo pH 5

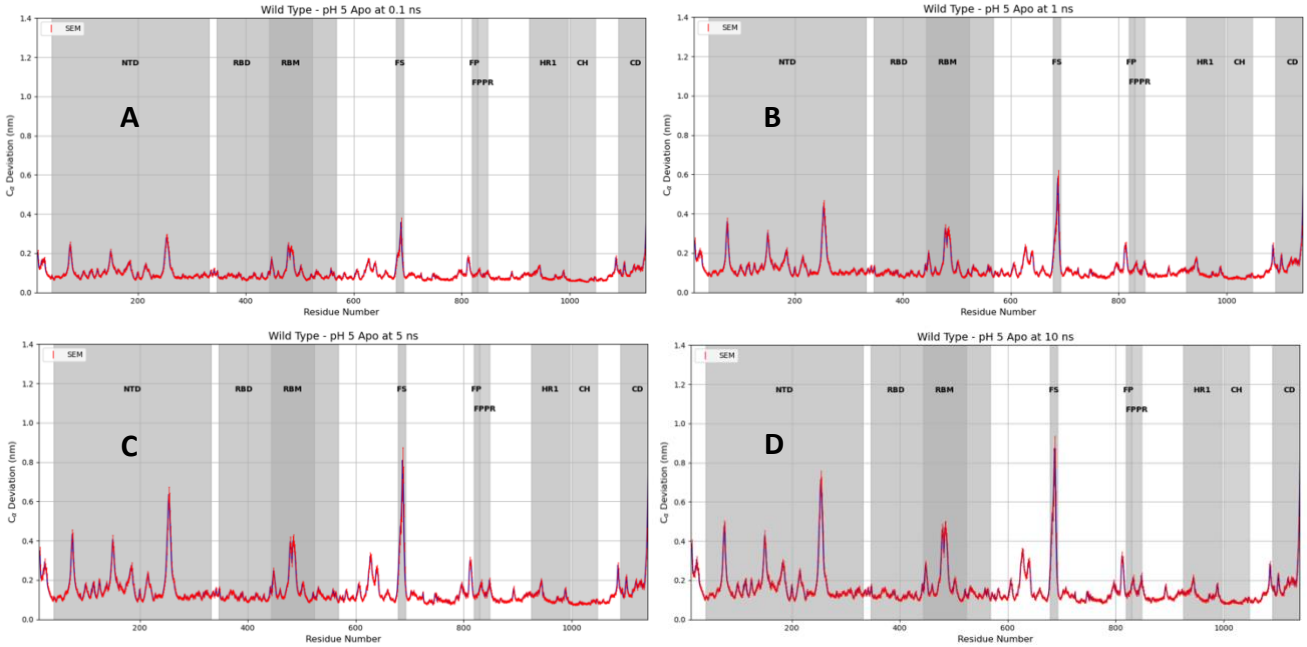

Figure 1 – Comparison of the Average Deviation (RMSD) for Carbon Alpha (Cα) atoms in nanometres (nm) along the sequence of the spike protein's residues, averaged across the spike monomers for different simulation time points at pH 5 without the presence of Linoleic Acid (LA), apo condition.

Dynamic Non-Molecular Equilibrium Molecular Dynamic Simulations (D-NEMD) were conducted using pH 7 as the equilibrium reference Molecular Dynamics (MD) simulation at pH 7. Short 105 NEMD simulations were introduced with a perturbation of pH 5. The average RMSD between the extracted equilibrium MD frames at pH 7 and NEMD frames were determined at 0.1 ns (A), 1 ns (B), 5 ns (C), and 10 ns (D). The y-axis represents the mean Cα deviation (RMSD), and the x-axis represents the residue number within the spike protein. Key domains are highlighted with shaded areas, indicating the N-terminal domain (NTD), receptor binding domain (RBD), receptor binding motif (RBM), furin site (FS), fusion peptide (FP), fusion peptide proximal region (FPPR), heptad repeat 1 (HR1), central helix (CH), and connector domain (CD). Standard error bars are illustrated in red representing the standard error of the mean (SEM) for each deviation. Please zoom in for greater detail.

1.2 Apo pH 10

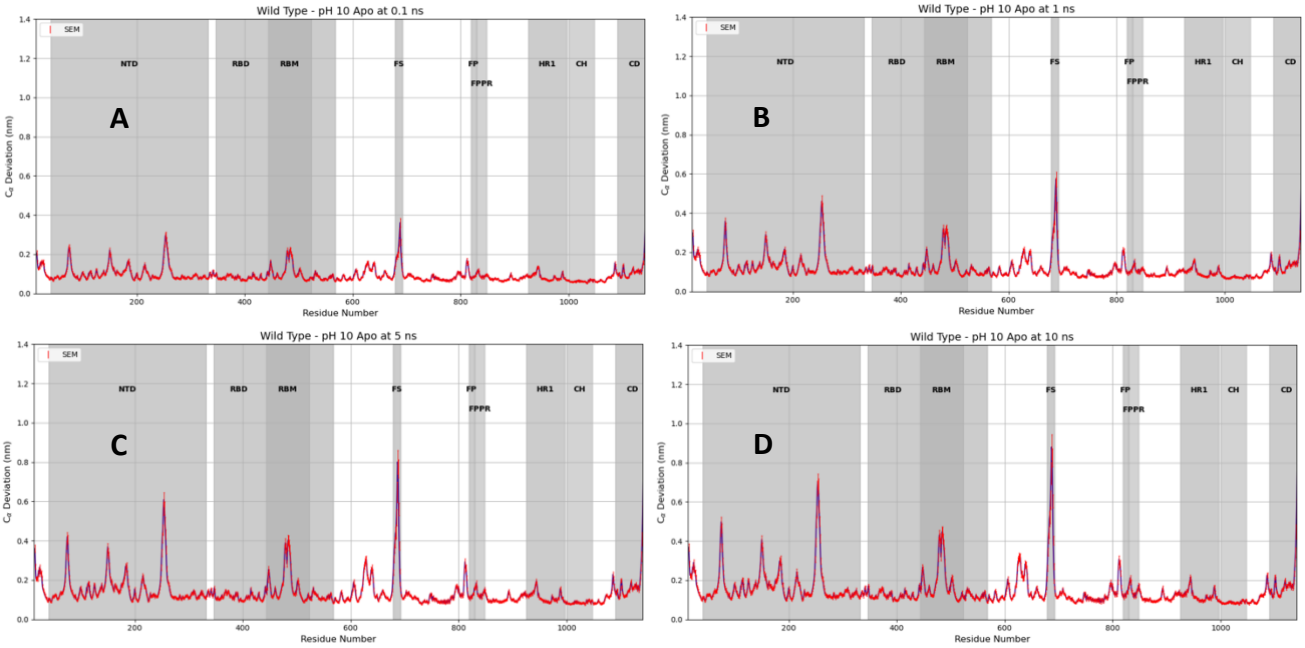

Figure 2 – Comparison of the Average Deviation (RMSD) for Carbon Alpha (Cα) atoms in nanometres (nm) along the sequence of the spike protein's residues, averaged across the spike monomers for different simulation time points at pH 5 with Linoleic Acid (LA) bound to the fatty acid (FA) site.

D-NEMD simulations were conducted using pH 7 as the reference Molecular Dynamics (MD) simulation at pH 7. 105 NEMD simulations were introduced with a perturbation of pH 10. The average RMSD between equilibrium MD frames at pH 7 and NEMD frames were determined at 0.1 ns (A), 1 ns (B), 5 ns (C), and 10 ns (D). The y-axis represents the mean Cα deviation (RMSD), and the x-axis represents the residue number within the spike protein. Key domains are highlighted with shaded areas, indicating the N-terminal domain (NTD), receptor binding domain (RBD), receptor binding motif (RBM), furin site (FS), fusion peptide (FP), fusion peptide proximal region (FPPR), heptad repeat 1 (HR1), central helix (CH), and connector domain (CD). Standard error bars are illustrated in red representing the standard error of the mean (SEM) for each deviation. Please zoom in for greater detail.

1.3 LA-Bound pH 5

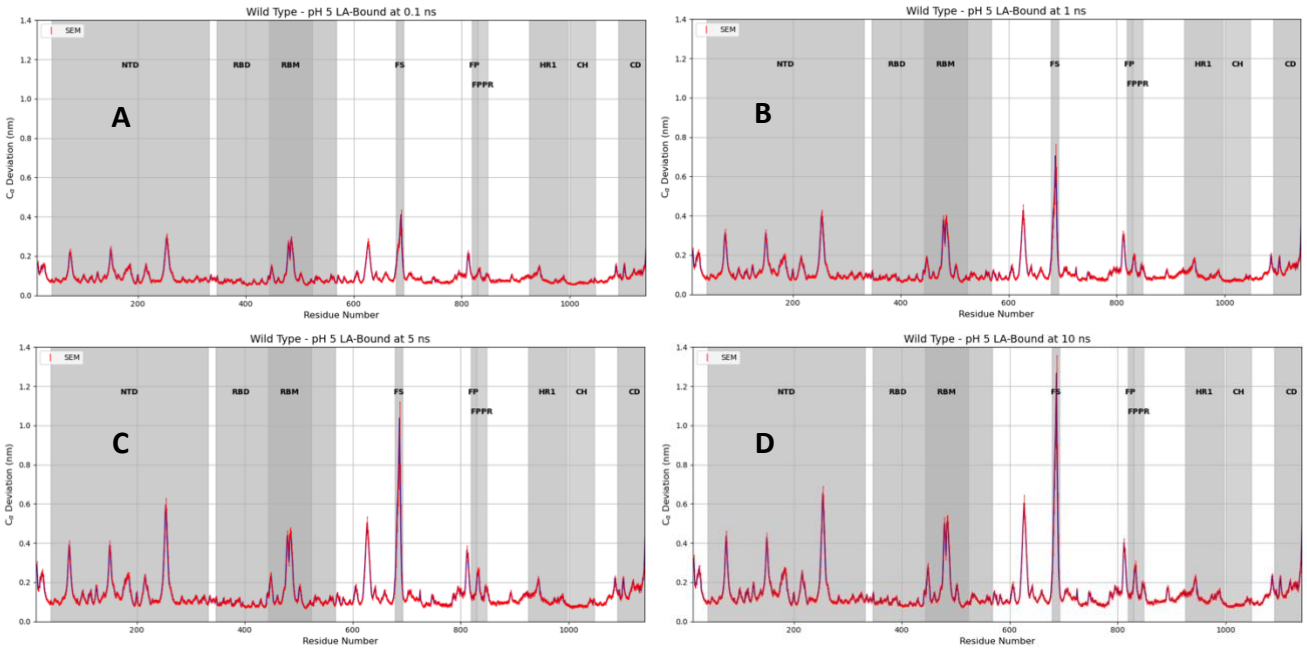

Figure 3 – Comparison of the Average Deviation (RMSD) for Carbon Alpha (Cα) atoms in nanometres (nm) along the sequence of the spike protein's residues, averaged across the spike monomers for different simulation time points at pH 5 with Linoleic Acid (LA) bound to the fatty acid (FA) site.

D-NEMD simulations were conducted using pH 7 as the reference Molecular Dynamics (MD) simulation at pH 7. 105 NEMD simulations were introduced with a perturbation of pH 5. The average RMSD between equilibrium MD frames at pH 7 and NEMD frames were determined at 0.1 ns (A), 1 ns (B), 5 ns (C), and 10 ns (D). The y-axis represents the mean Cα deviation (RMSD), and the x-axis represents the residue number within the spike protein. Key domains are highlighted with shaded areas, indicating the N-terminal domain (NTD), receptor binding domain (RBD), receptor binding motif (RBM), furin site (FS), fusion peptide (FP), fusion peptide proximal region (FPPR), heptad repeat 1 (HR1), central helix (CH), and connector domain (CD). Standard error bars are illustrated in red representing the standard error of the mean (SEM) for each deviation. Please zoom in for greater detail.

1.4 LA-Bound pH 10

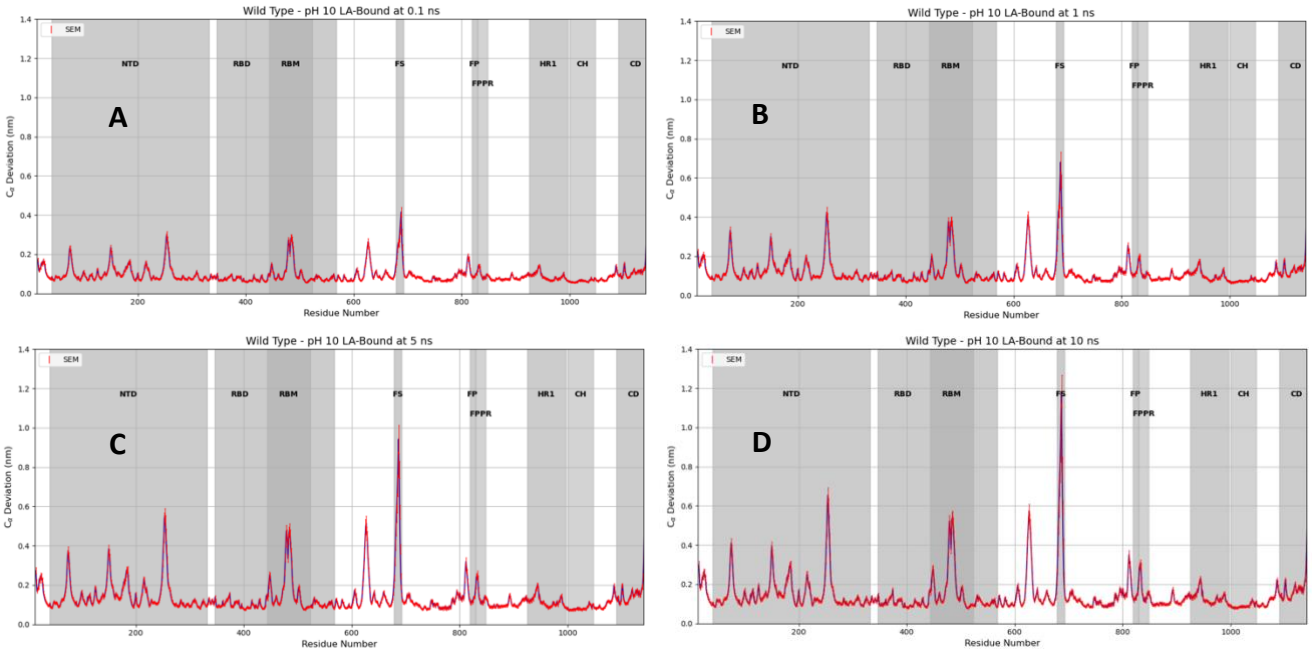

Figure 4 – Comparison of the Average Deviation (RMSD) for Carbon Alpha (Cα) atoms in nanometres (nm) along the sequence of the spike protein's residues, averaged across the spike monomers for different simulation time points at pH 10 with Linoleic Acid (LA) bound to the fatty acid (FA) site.

D-NEMD simulations were conducted using pH 7 as the reference Molecular Dynamics (MD) simulation at pH 7. 105 NEMD simulations were introduced with a perturbation of pH 10. The average RMSD between equilibrium MD frames at pH 7 and NEMD frames were determined at 0.1 ns (A), 1 ns (B), 5 ns (C), and 10 ns (D). The y-axis represents the mean Cα deviation (RMSD), and the x-axis represents the residue number within the spike protein. Key domains are highlighted with shaded areas, indicating the N-terminal domain (NTD), receptor binding domain (RBD), receptor binding motif (RBM), furin site (FS), fusion peptide (FP), fusion peptide proximal region (FPPR), heptad repeat 1 (HR1), central helix (CH), and connector domain (CD). Standard error bars are illustrated in red representing the standard error of the mean (SEM) for each deviation. Please zoom in for greater detail.

1.5 Comparison of Temporal Evolutions for Different Experimental Conditions

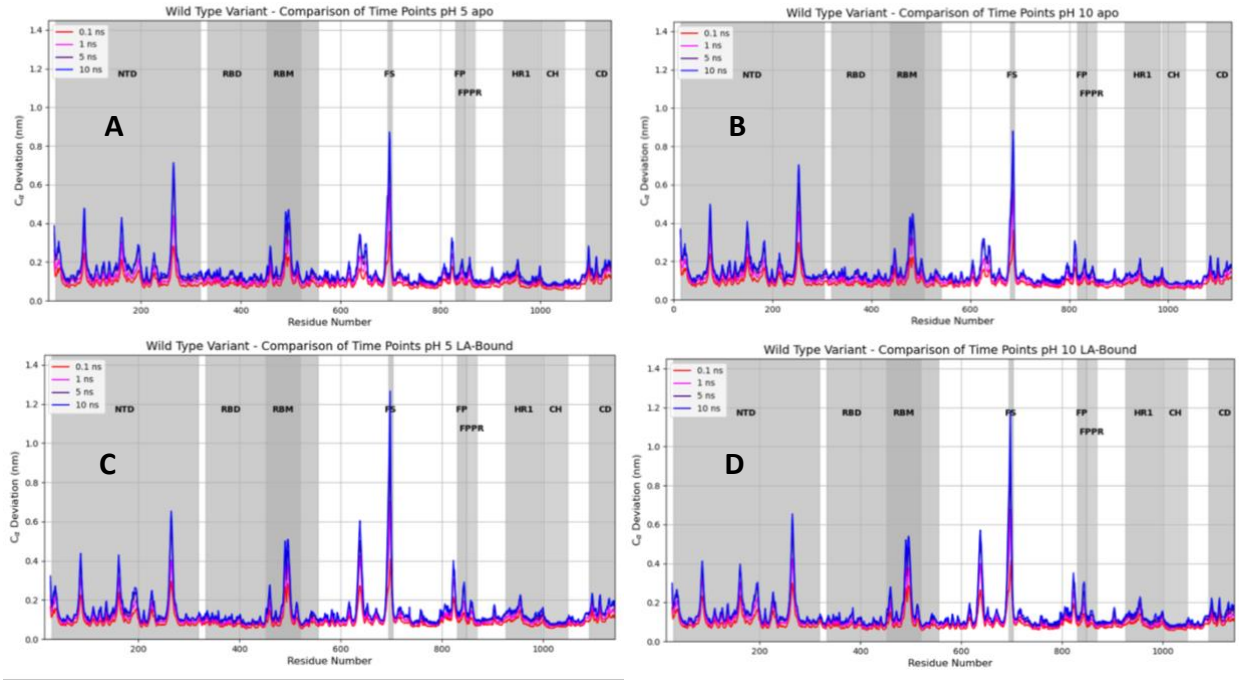

Figure 5 – Comparison of the Average Deviation (RMSD) for Carbon Alpha (Cα) atoms in nanometres (nm) along the sequence of the spike protein's residues, averaged across the spike monomers for different simulation time points at pH 5 and 10 without the presence of Linoleic Acid (LA), apo condition (A and B), and in the presence of LA at pH 5 and 10 (C and D).

Exhibits the allosteric response of the spike protein and it's key functional domains across time when not bound to linoleic acid (Apo) at pH 5 (A) and pH 10 (B), and when also bound to linoleic acid (LA-Bound) at pH 5 (C) and pH 10 (D). Dynamic Non-Molecular Equilibrium Molecular Dynamic Simulations (D-NEMD) were conducted using pH 7 as the equilibrium reference Molecular Dynamics (MD) simulation at pH 7. Short 105 NEMD simulations were introduced with a perturbation of pH 5 and 10. The average RMSD between the extracted equilibrium MD frames at pH 7 and NEMD frames were determined at 0.1 ns (red), 1 ns (magenta), 5 ns (black), and 10 ns (blue). The y-axis represents the mean Cα deviation (RMSD), and the x-axis represents the residue number within the spike protein. Key domains are highlighted with shaded areas, indicating the N-terminal domain (NTD), receptor binding domain (RBD), receptor binding motif (RBM), furin site (FS), fusion peptide (FP), fusion peptide proximal region (FPPR), heptad repeat 1 (HR1), central helix (CH), and connector domain (CD). Please zoom in for greater detail.

1.6 Pymol Visualisation

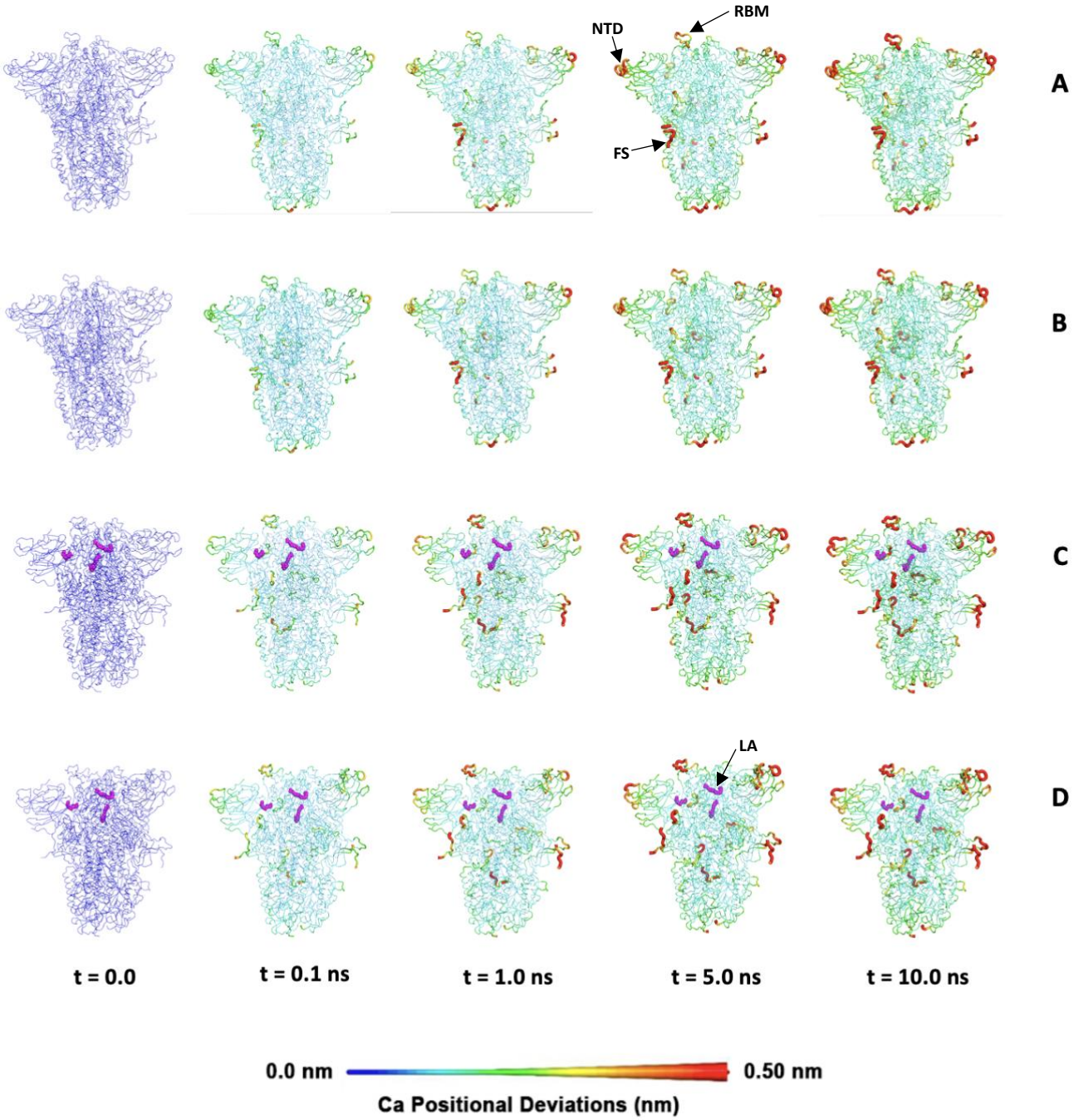

Figure 6 – Visual Illustration of the temporal deviation evolution of the SARS-CoV-2 Spike in varying conditions of pH whilst bound to LA. (A): Apo pH 5 (B): Apo pH 10 (C): LA-Bound pH 5 (D) LA-Bound pH 10. The illustration exhibits the deviations at time points of 0.0 ns, 0.1 ns, 1.0 ns, 5.0 ns, and 10.0 ns from left to right. The colour scale provides a scale for deviation up to 0.50 nm to facilitate visualisation, with regions of increasing deviations being illustrated with increasing thickness. Regions of deviations which are > 0.500 nm will be the same colour and thickness. Functional domains: NTD, RBM, FS, FPPR are labelled. LA is illustrated and labelled in C and D witnessed through magenta spheres respectively. Note: Glycan chains are not included within these visualisations to enhance the visualisation of deviations for the SARS-CoV-2 spike. Please zoom in for greater detail. This illustration was created using Pymol.

2. Effects of pH Whilst Bound to Linoleic Acid (LA)

2.1 The N-Terminal Domain (NTD)

2.1.1 S71-R78 Segment

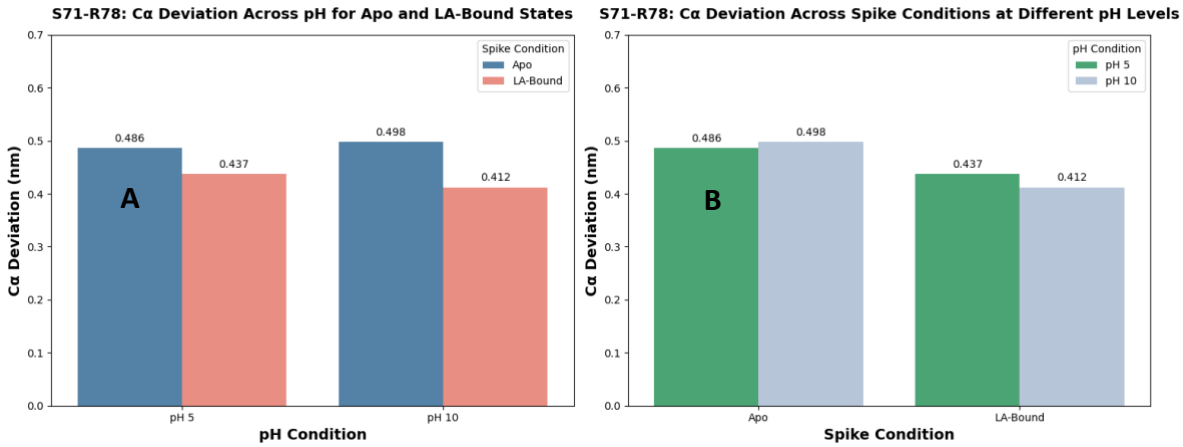

Figure 7 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the S71-R78 segment of the NTD: At pH 5 and pH 10 for Apo spikes, the S71-R78 exhibited greater deviation responses of 0.486 nm and 0.498 nm relative to the LA-Bound spikes. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the S71-R78 segment of the NTD:** For the LA-Bound spikes, the greatest deviation response of 0.437 nm was observed at pH 5, whilst at pH 10 the deviation response was 0.412 nm. The green bars represent pH 5, the light blue bars represent pH 10.

2.1.2 H146-E156 Segment

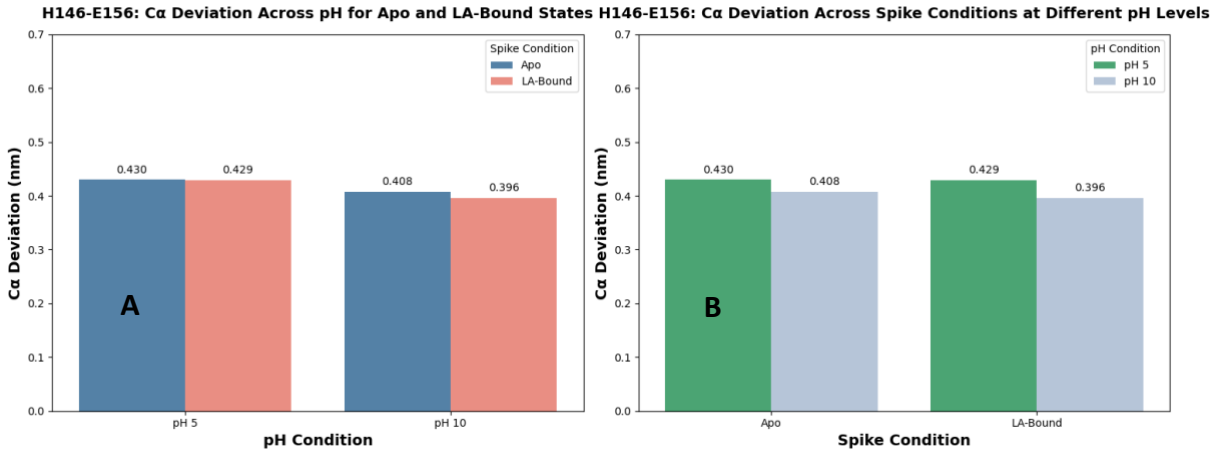

Figure 8 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the H146-E156 segment of the NTD: At both pH 5 and 10, the Apo spikes exhibited greater deviation responses of 0.430 nm and 0.408 nm for the H146-E156 segment, relative to the LA-bound spikes. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the H146-E156 segment of the NTD:** Across both pH 5 and 10, LA-bound spikes exhibited reduced deviation responses of 0.429 nm and 0.396 nm relative to the Apo spikes. The green bars represent pH 5, the light blue bars represent pH 10.

2.1.3 L249-G257 Segment

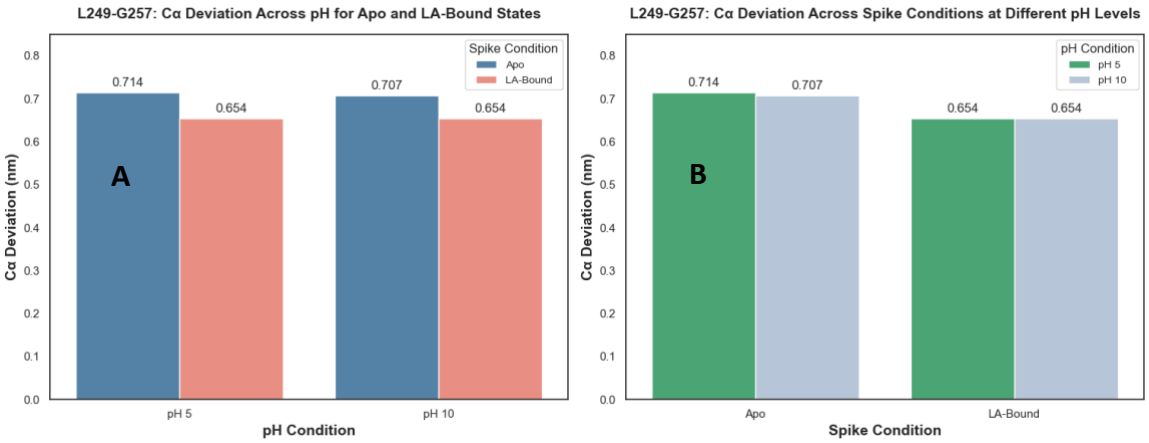

Figure 9 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the L249-G257 segment of the NTD: At both pH 5 and 10, LA-bound spikes witnessed reduced deviations for the L249-G257 segment relative to the Apo spikes. The deviations of the LA-bound spikes at pH 5 and pH 10 witnessed a notably lower deviation relative to the Apo condition, being 0.654 nm; a significantly reduced deviation compared to 0.714 nm and 0.704 nm witnessed at pH 5 and 10, respectively. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the L249-G257 segment of the NTD:** For the Apo the L249-G257 segment appears to be more responsive to pH, witnessed through greater deviation responses of 0.714 nm and 0.707 nm at pH 5 and 10 respectively compared to the Apo spikes. The green bars represent pH 5, the light blue bars represent pH 10.

2.2 Receptor Binding Motif (RBM)

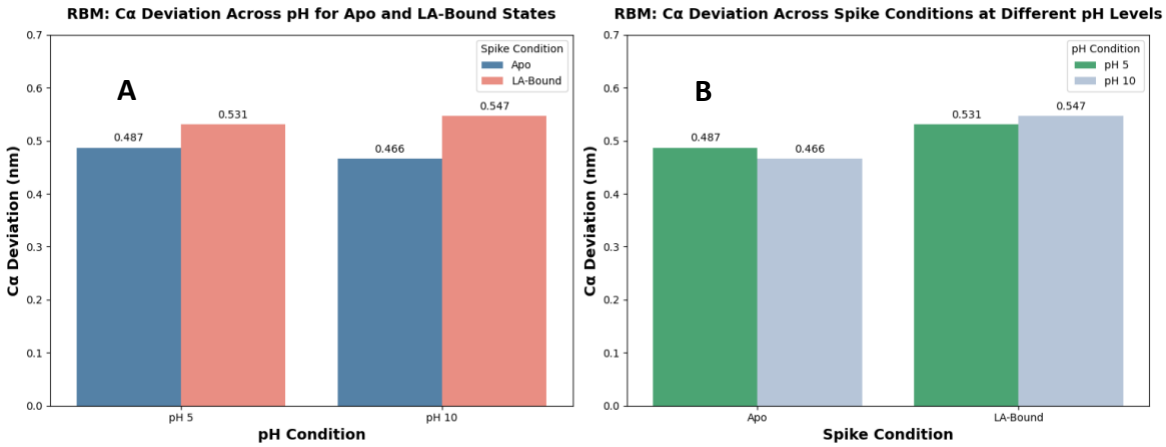

Figure 10 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the RBM: At pH 5 and pH 10 for the LA-Bound state, the RBM exhibited a greater response witnessed through greater deviations of 0.531 nm and 0.547 nm, respectively relative to the Apo condition. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the RBM:** In Apo conditions, at pH 5 the RBM exhibited a greater deviation of 0.487 nm compared to pH 5 where a deviation response of 0.466 nm was observed. The greatest deviation of 0.547 nm was witnessed at pH 10 for the RBM whilst bound to LA, which was greater than the deviation response of 0.531 nm reported at pH 5 whilst bound to LA. The green bars represent pH 5, the light blue bars represent pH 10.

2.3 Furin Cleavage Site (FS)

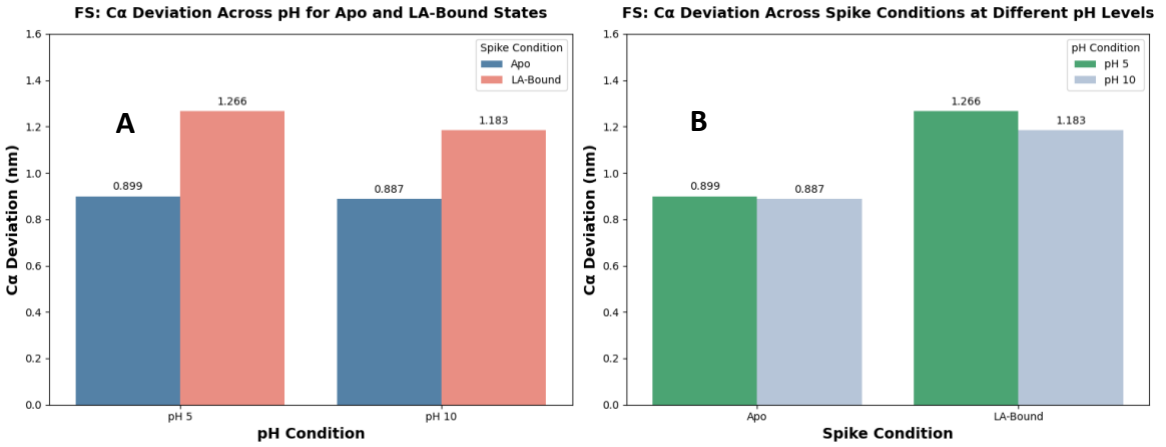

Figure 11 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the FS: At pH 5 and pH 10 for the LA-Bound state, the FS exhibited greater deviation response compared to the Apo conditions witnessed through deviations of 1.266 nm and 1.183 nm, respectively. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the FS:** In Apo conditions, at pH 5 the FS exhibited a greater deviation of 0.899 nm compared to pH 10 where a deviation of 0.887 nm was reported. In LA-bound conditions, the greatest deviation was observed at 1.266 nm at pH 10, whilst pH 5 reported a deviation response of 1.183 nm. The green bars represent pH 5, the light blue bars represent pH 10.

2.4 V622-L629 Segment

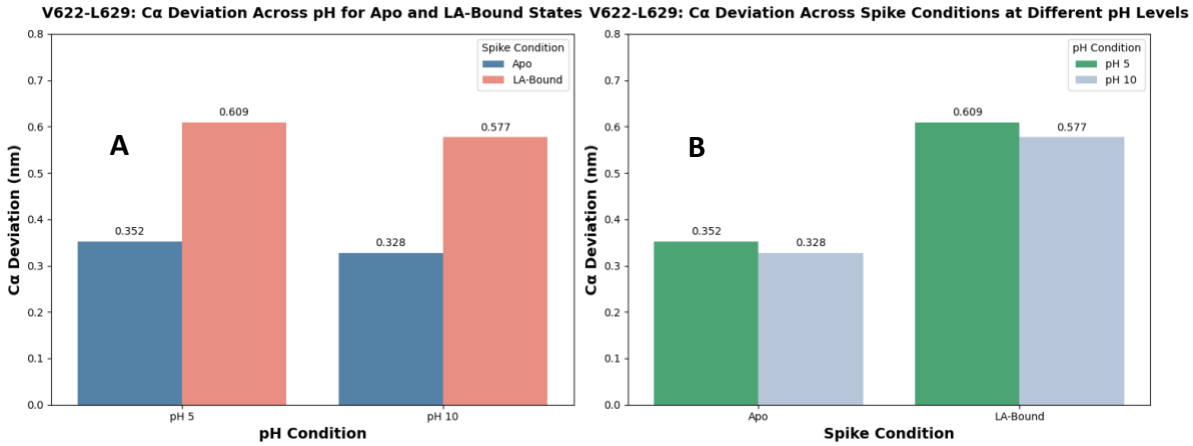

Figure 12 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the V622-L629: At pH 5 and pH 10 for the LA-Bound state, the V622-L629 exhibited a greater response compared to the Apo condition, witnessed through greater deviations of 0.609 nm and 0.577 nm, respectively. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the V622-L629:** In Apo conditions, at pH 5 the V622-L629 segment exhibited a greater deviation of 0.352 nm compared to the deviation of 0.328 nm witnessed at pH 10. The green bars represent pH 5, the light blue bars represent pH 10.

2.5 D803-S813 Segment

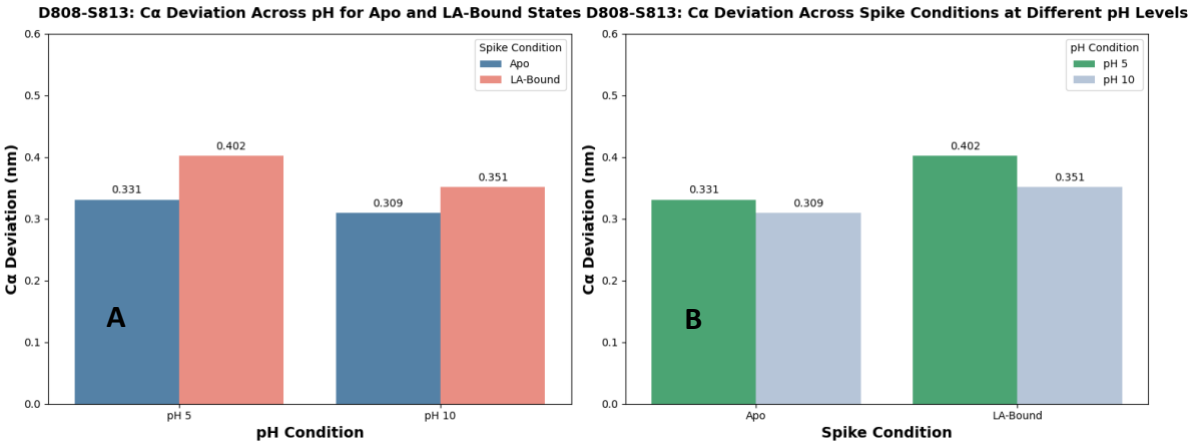

Figure 13 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the D808-S813: At pH 5 and pH 10 for the LA-Bound state, the D808-S813 exhibited greater flexibility witnessed through greater deviations than the Apo state of 0.402 nm and 0.351 nm, respectively with the latter being observed at pH 10. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the D818-S813:** In Apo conditions, at pH 5 the D808-S813 segment exhibited a greater deviation of 0.331 nm relative to pH 10 where the deviation response was 0.309 nm. The green bars represent pH 5, the light blue bars represent pH 10.

2.6 Fusion-Peptide Proximal Region (FPPR)

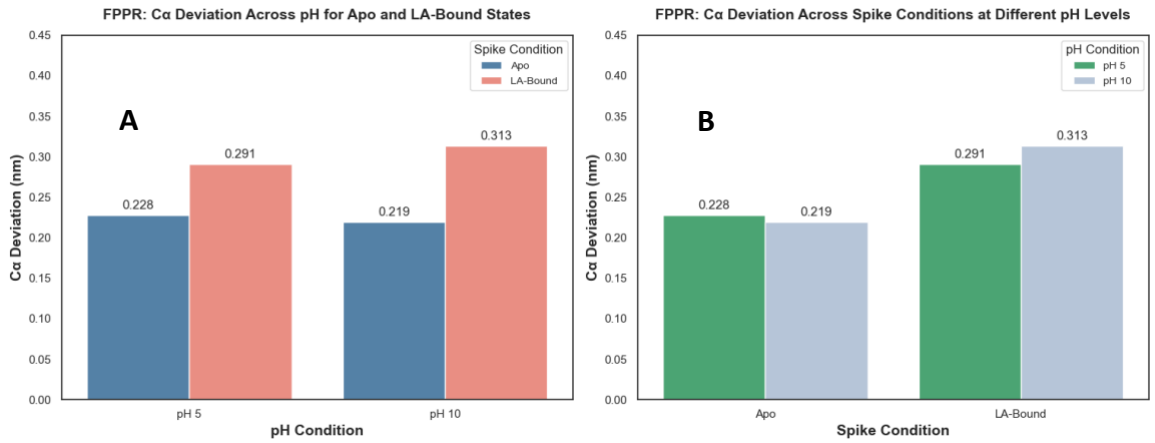

Figure 14 – (A) Illustration of the CA deviation across pH for Apo and LA-Bound spike states for the FPPR: At pH 5 and pH 10 for the LA-Bound state, the FPPR exhibited greater flexibility witnessed through greater deviations than the Apo state of 0.291 nm and 0.313 nm, respectively. The dark blue bars represent Apo conditions, the orange bars represent LA-Bound conditions. **(B) Illustration of the CA deviation across spike conditions of Apo and LA-Bound across pH 5 and pH 10 conditions for the FPPR:** In Apo conditions, at pH 5 the FPPR segment exhibited a greater deviation of 0.228 nm relative to pH 10 where the deviation response was 0.219 nm. Whilst bound to LA, the greatest deviation of 0.313 nm was witnessed at pH 10 for the FPPR segment, whereas at pH 5 the deviation response was 0.291 nm. The green bars represent pH 5, the light blue bars represent pH 10.

3. The Variation in Response Between Monomers

3.1 Apo pH 5

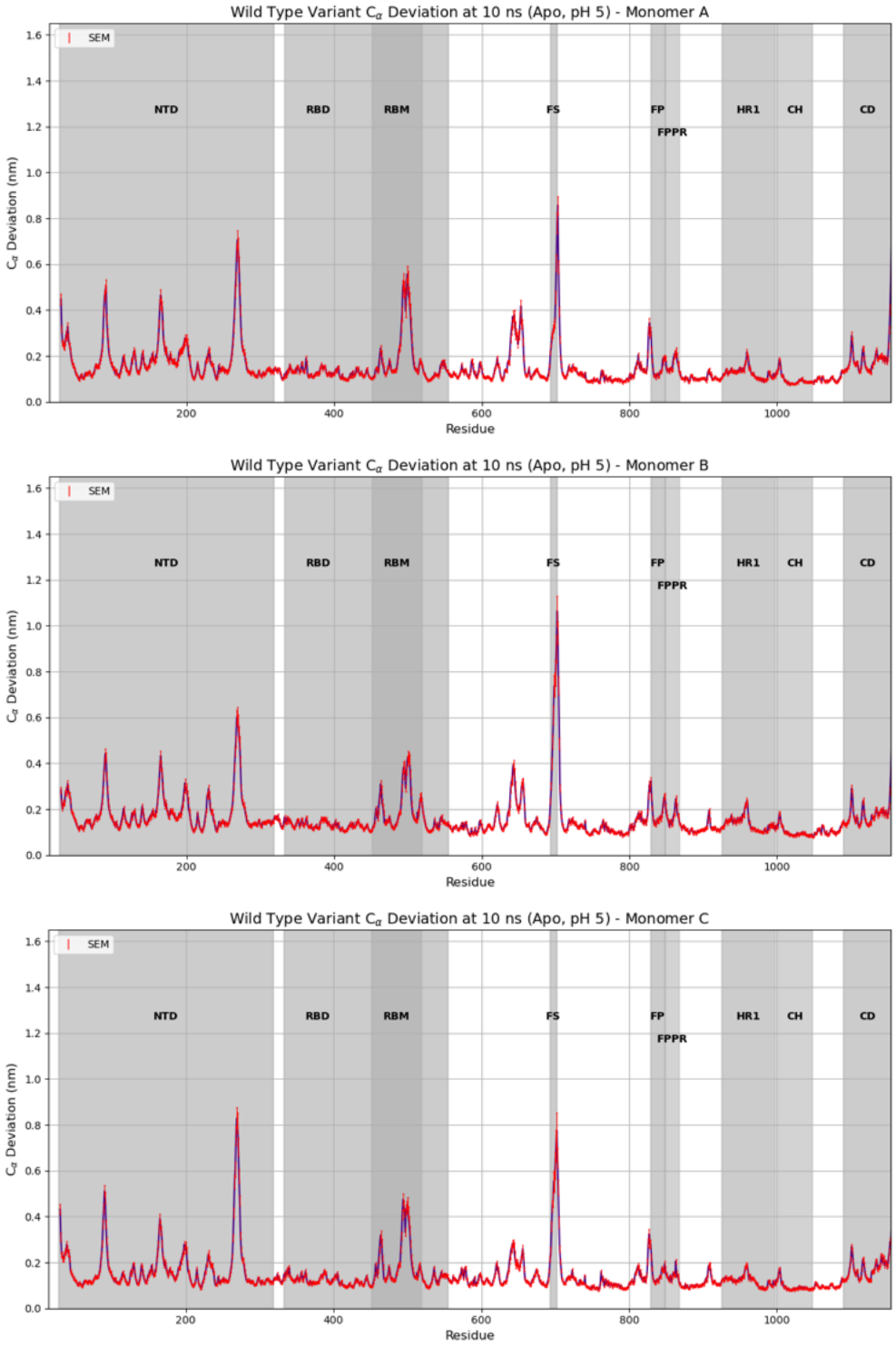

Figure 15 – (A) Illustration of the CA deviation across at 10 ns for Apo condition at pH 5 for each monomer of the spike. (A): Monomer A. (B): Monomer B. (C) Monomer C. The y-axis represents the CA deviation in nanometres, nm and the x-axis represents the residue number along the SARS-CoV-2 spike. The standard error of the mean (SEM) bar for each residue is highlighted in red.

3.2 Apo pH 10

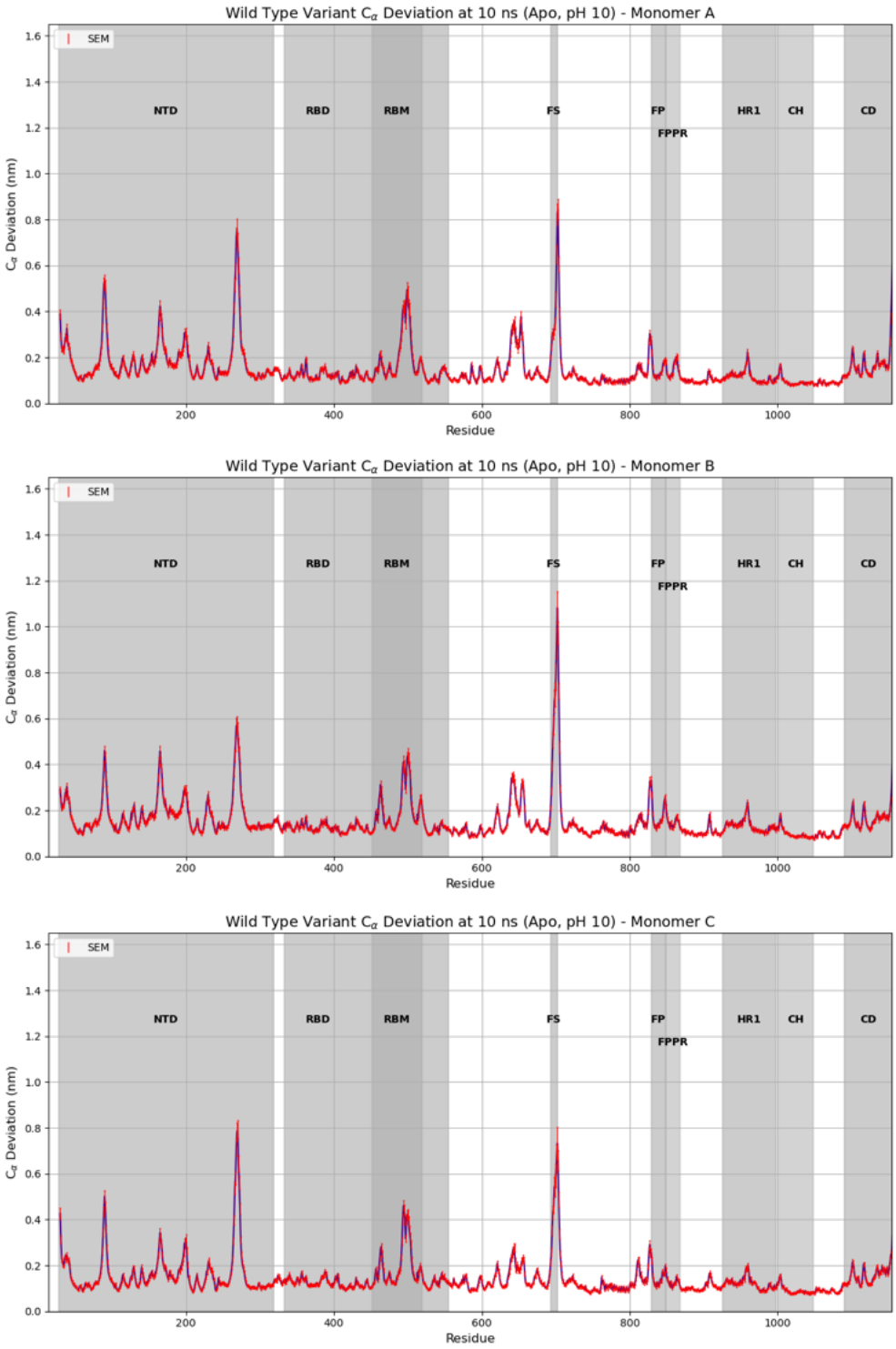

Figure 16 – (A) Illustration of the CA deviation across at 10 ns for Apo condition at pH 10 for each monomer of the spike. (A): Monomer A. (B): Monomer B. (C) Monomer C. The y-axis represents the CA deviation in nanometres, nm and the x-axis represents the residue number along the SARS-CoV-2 spike. The standard error of the mean (SEM) bar for each residue is highlighted in red.

3.3 LA-Bound pH 5

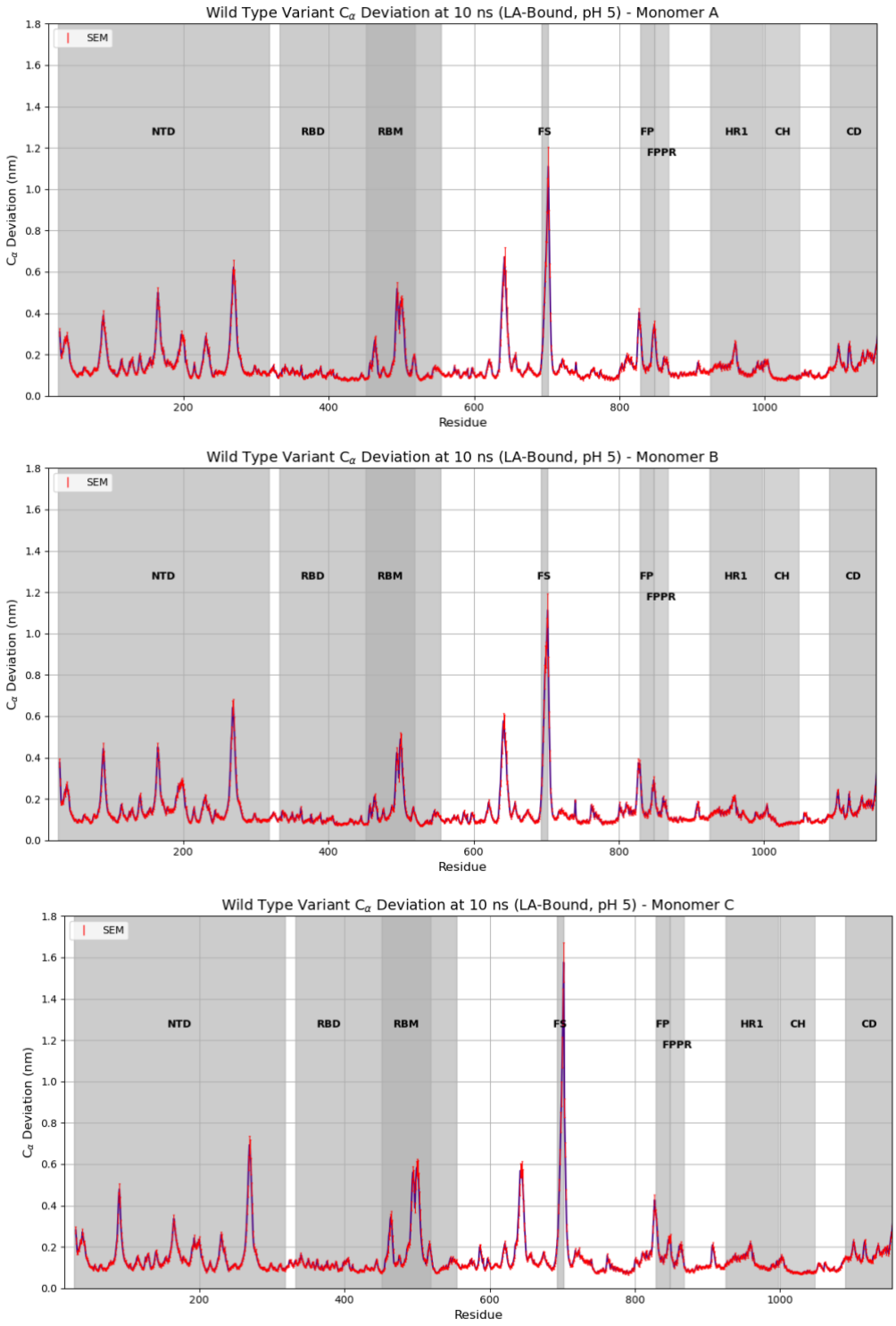

Figure 17 – (A) Illustration of the CA deviation across at 10 ns for LA-Bound condition at pH 5 for each monomer of the spike. (A): Monomer A. (B): Monomer B. (C) Monomer C. The y-axis represents the CA deviation in nanometres, nm and the x-axis represents the residue number along the SARS-CoV-2 spike. The standard error of the mean (SEM) bar for each residue is highlighted in red.

3.4 LA-Bound pH 10

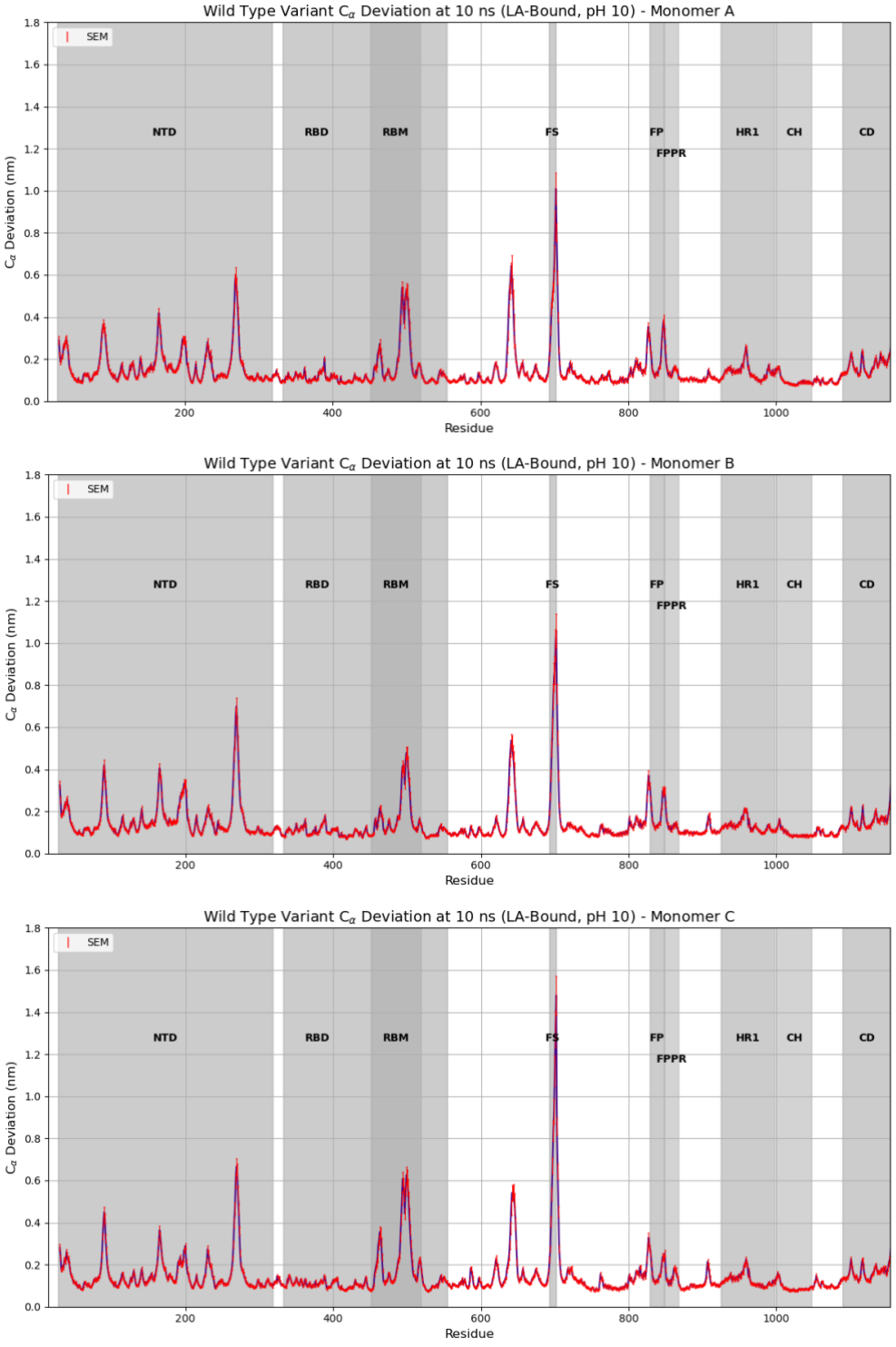

Figure 18 – (A) Illustration of the CA deviation across at 10 ns for LA-Bound condition at pH 10 for each monomer of the spike. (A): Monomer A. (B): Monomer B. (C) Monomer C. The y-axis represents the CA deviation in nanometres, nm and the x-axis represents the residue number along the SARS-CoV-2 spike. The standard error of the mean (SEM) bar for each residue is highlighted in red.

4. Apo Monomer Analysis

4.1 The NTD

4.1.1 S71-R78 Segment

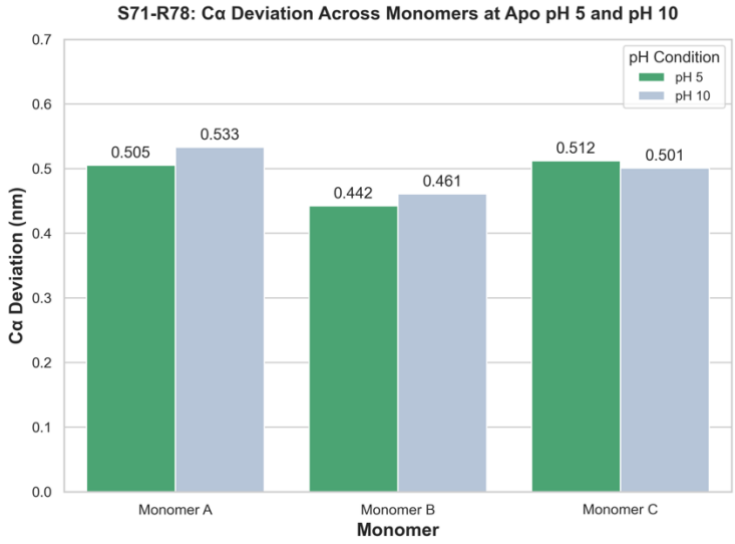

Figure 19 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's S71-R78 Segment of the NTD for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

4.1.2 H146-E156

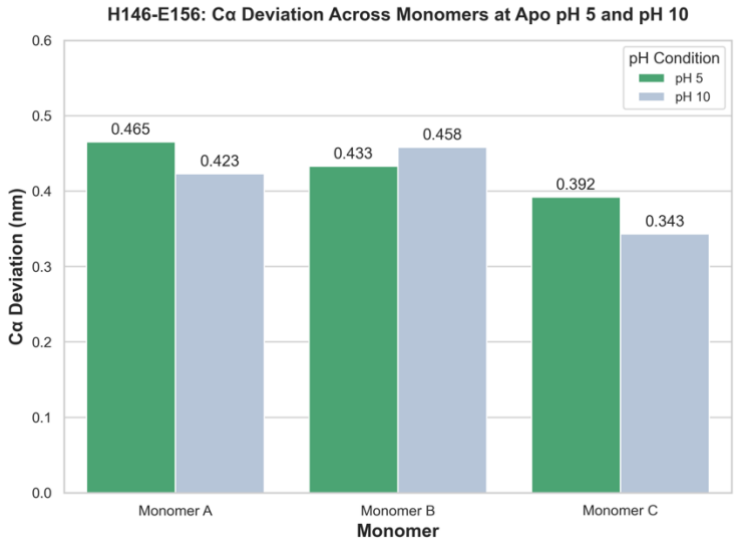

Figure 20 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's H146-E156 Segment of the NTD for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

4.1.3 L249-G257

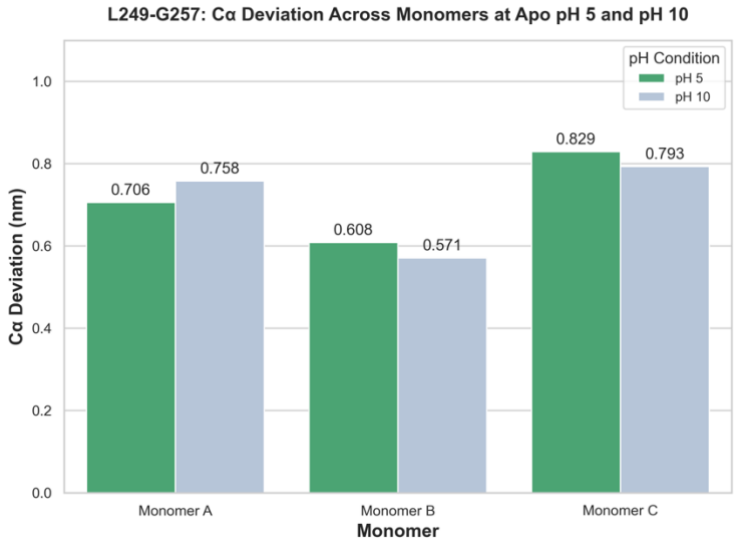

Figure 21 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's L249-G257 Segment of the NTD for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

4.2 Receptor Binding Motif (RBM)

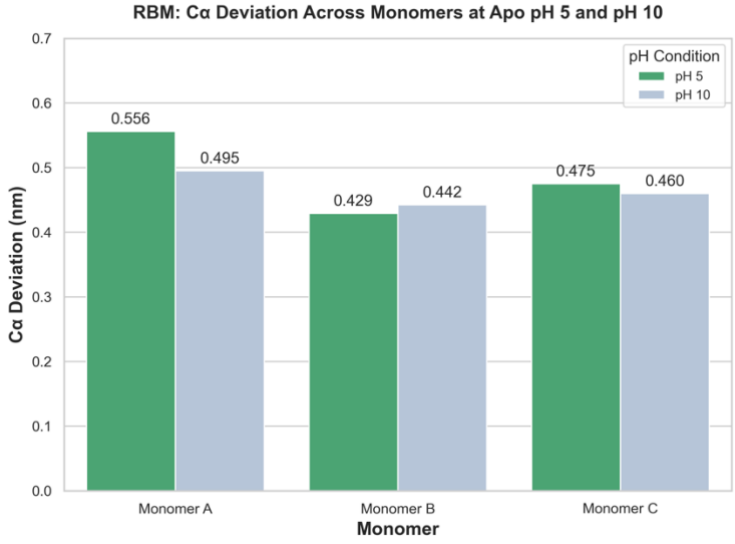

Figure 22 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's RBM for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

4.3 Furin Cleavage Site (FS)

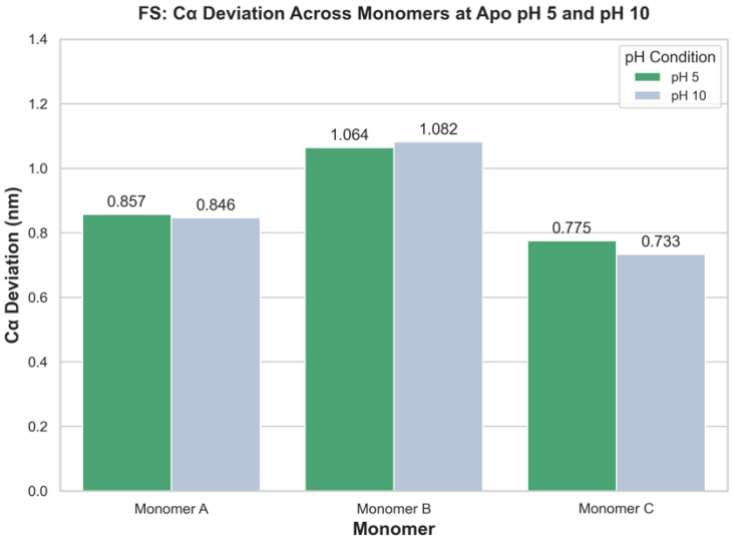

Figure 23 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's FS for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

4.4 V622-L629

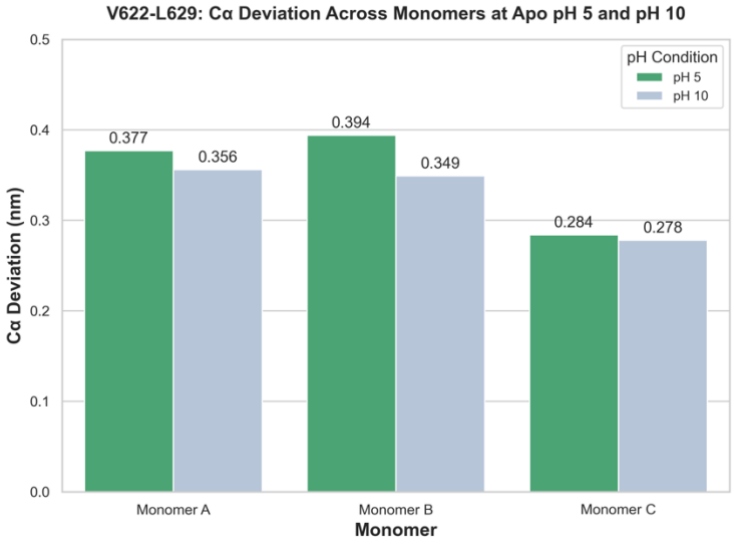

Figure 24 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's V622-L629 for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

4.5 D808-S813

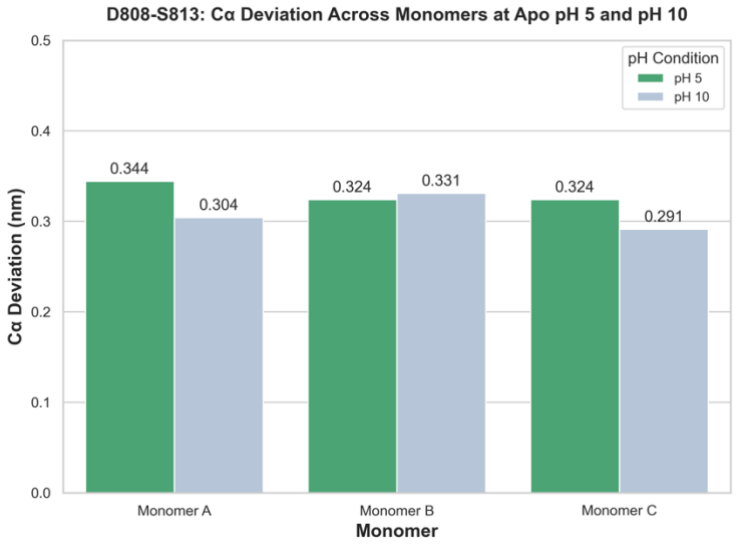

Figure 25 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's D808-S813 for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

4.6 FPPR

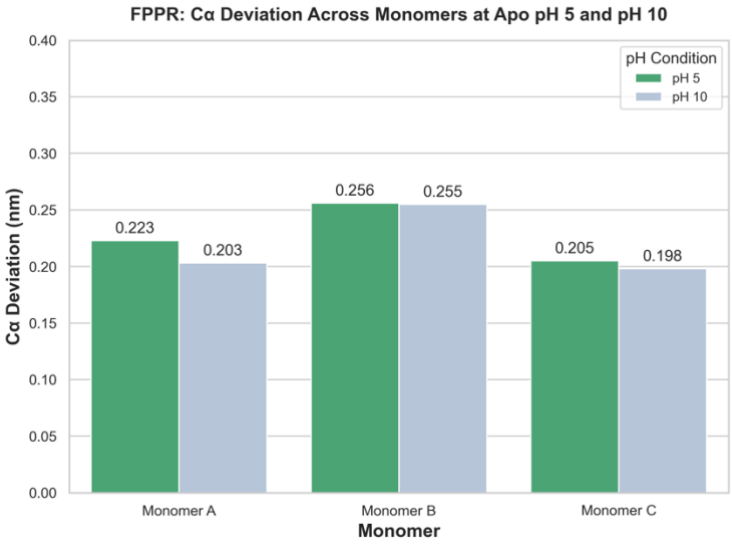

Figure 26 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's FPPR for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5. LA-Bound Monomer Analysis

5.1 The NTD

5.1.1 S71-R78 Segment

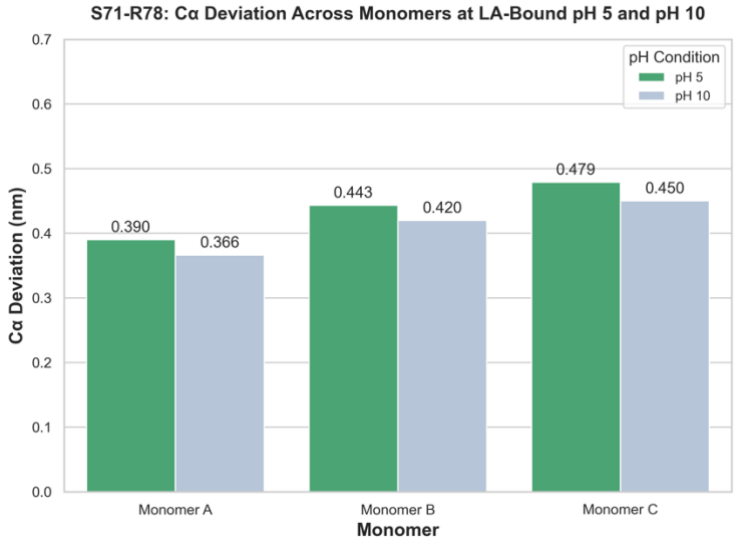

Figure 27 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's S71-R78 Segment of the NTD for LA-Bound Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5.1.2 H146-E156 Segment

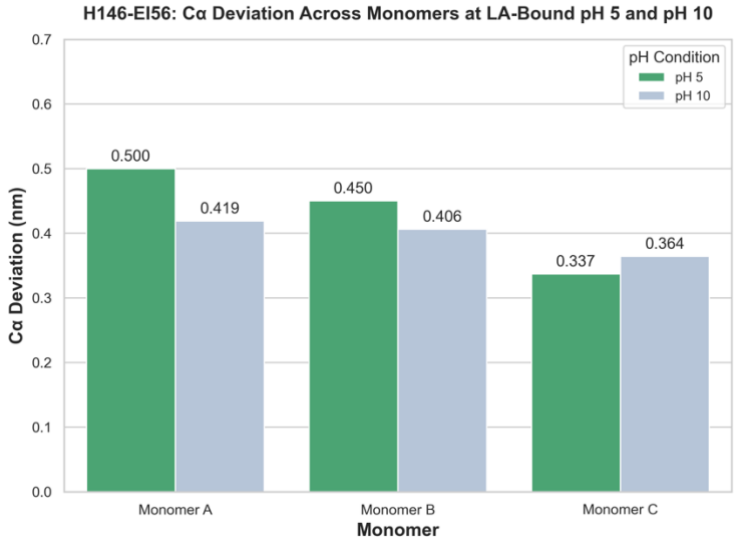

Figure 28 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's H146-E156 Segment of the NTD for LA-Bound Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5.1.3 L249-G257 Segment

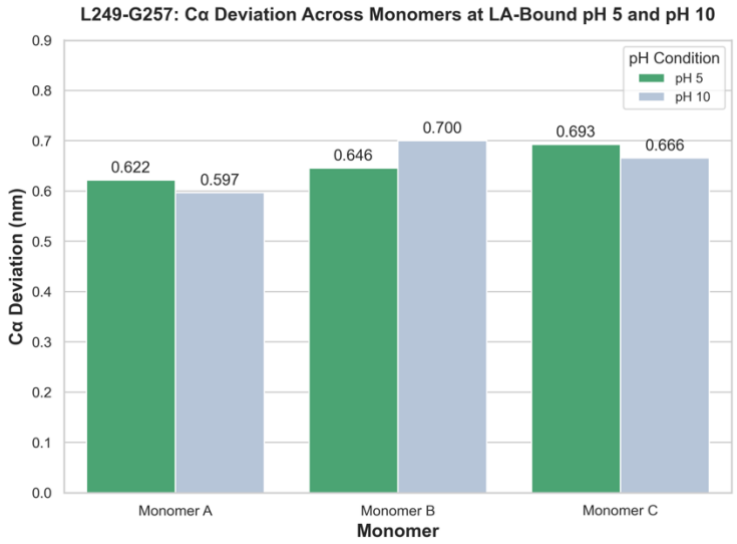

Figure 29 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's L249-G257 Segment of the NTD for Apo Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5.2 Receptor Binding Motif (RBM)

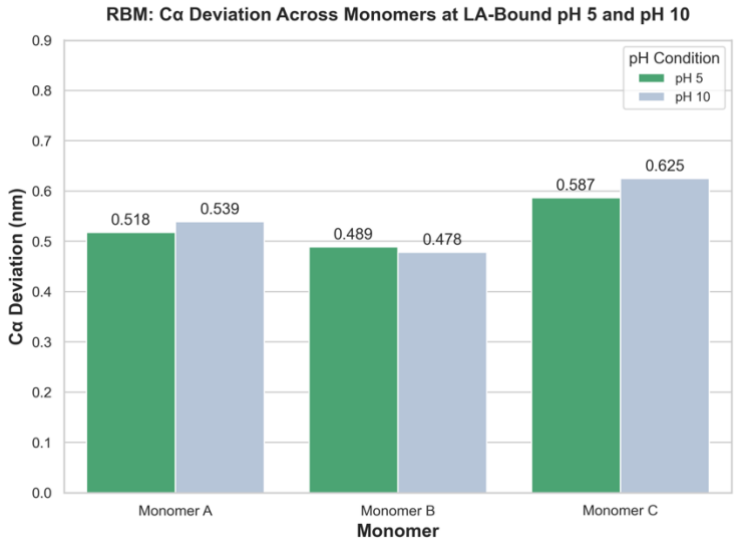

Figure 30 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's RBM for LA-Bound Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5.3 Furin Cleavage Site (FS)

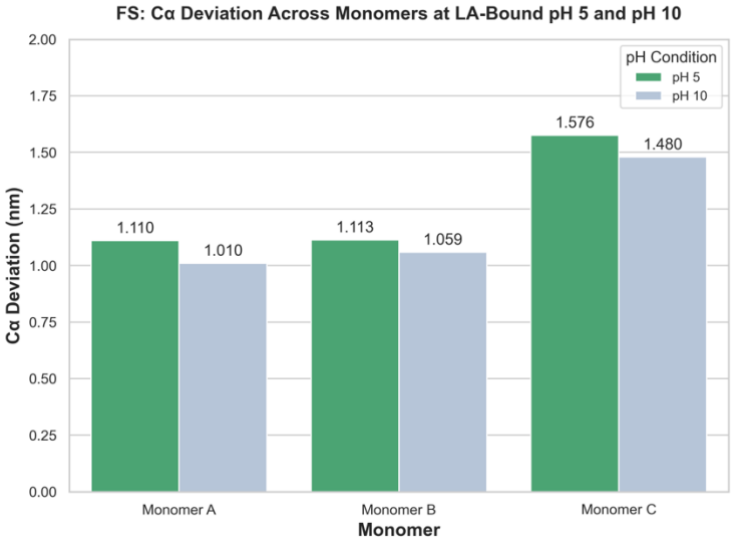

Figure 31 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's FS for LA-Bound Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5.4 V622-L629

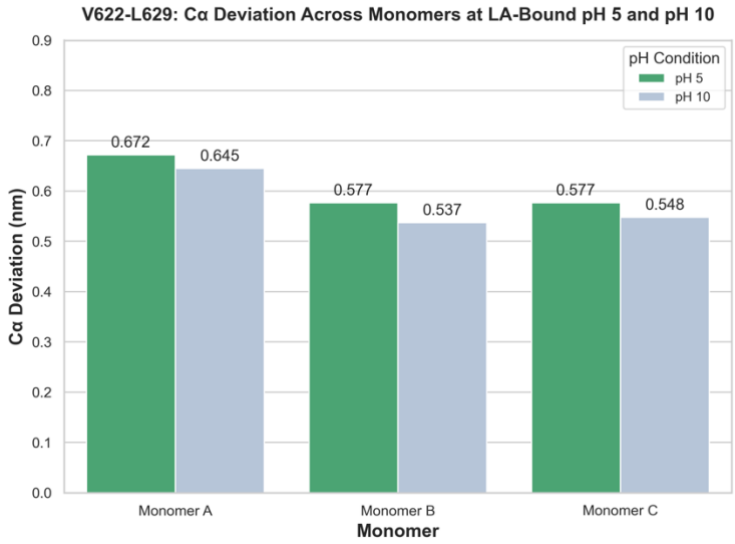

Figure 32 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's V622-L629 for LA-Bound Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5.5 D803-S813

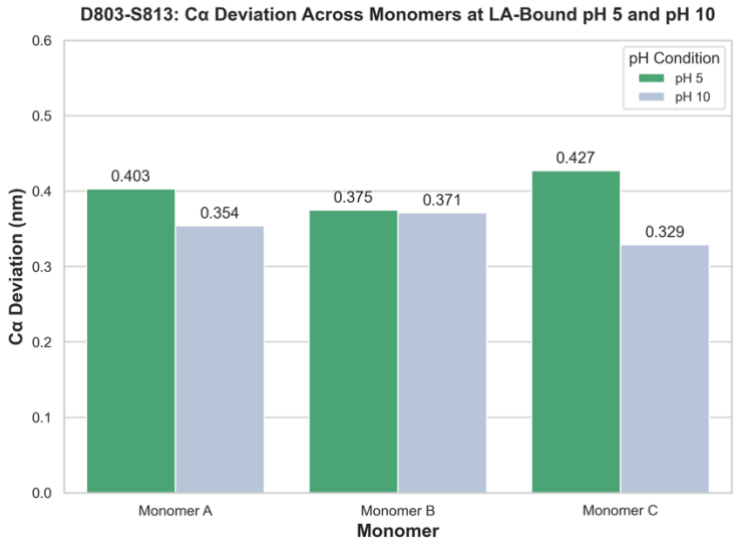

Figure 33 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's D808-S813 for LA-Bound Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

5.6 FPPR

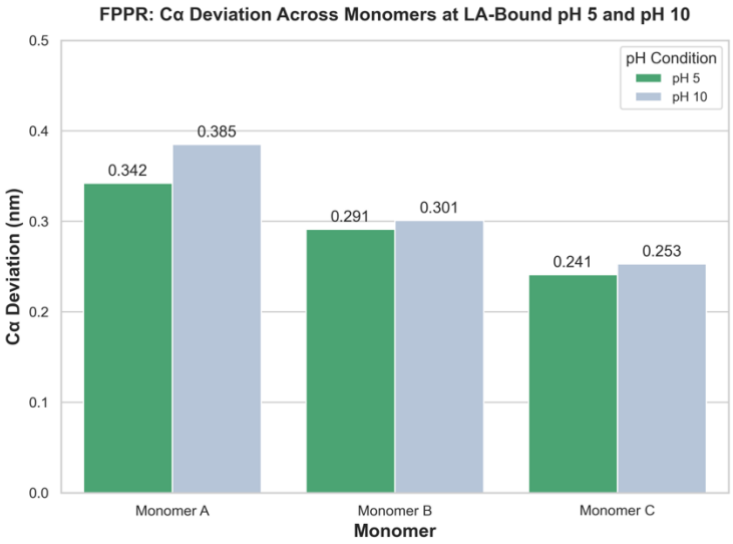

Figure 34 – Visual Comparative of the Deviation Response from Monomer A, Monomer B, and Monomer C's FPPR for LA-Bound Conditions. The y-axis represents the CA deviation in nanometres, nm and the x-axis refers to the Monomer. The numerical values above each bar represents the CA deviation. The green bars represent pH 5 and blue bars represent pH 10.

6. Key Visual Illustrations Using Pymol

6.1 The RBM at High pH (pH 10) in the Presence of Linoleic Acid (LA)

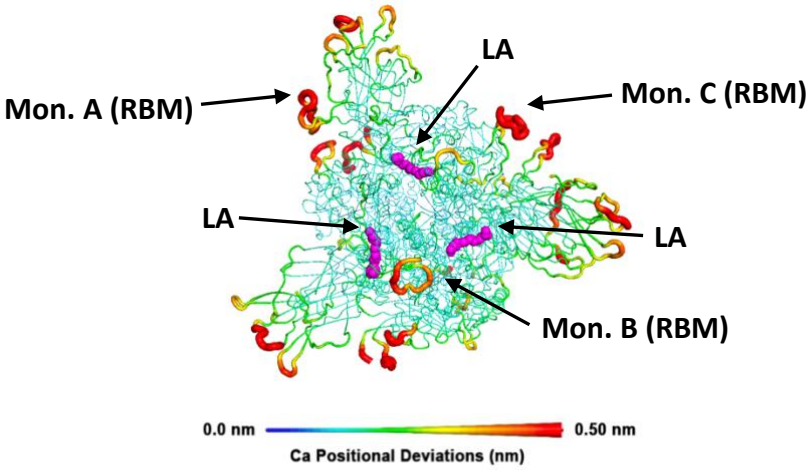

Figure 35 – Visual Illustration of the RBM at pH 10 for Monomers A (A), Monomer B (B), and Monomer C (C) at 10 ns whilst bound to LA. Linoleic Acid (LA) ligands are highlighted in purple spheres. The colour scale provides a scale for deviation up to 0.50 nm to facilitate visualisation, with regions of increasing deviations being illustrated with increasing thickness. Regions of deviations which are > 0.500 nm will therefore be the same colour and thickness. Note: Glycan chains are not included within these visualisations to enhance the visualisation of deviations for the SARS-CoV-2 spike. The deviations for the RBM within Monomer A was 0.539 nm, for Monomer B was 0.478 nm, and for Monomer C was 0.625 nm. Please zoom in for greater detail. This illustration was created using Pymol.

6.2 The FPPR at High pH (pH 10) in the Presence of Linoleic Acid (LA)

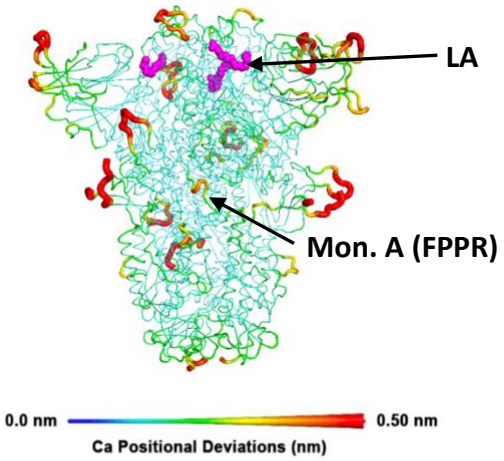

Figure 36 – Visual Illustration of the RBM at pH 10 for Monomer A at 10 ns whilst bound to LA. Linoleic Acid (LA) ligands are highlighted in purple spheres. The colour scale provides a scale for deviation up to 0.50 nm to facilitate visualisation, with regions of increasing deviations being illustrated with increasing thickness. Regions of deviations which are > 0.500 nm will therefore be the same colour and thickness. Note: Glycan chains are not included within these visualisations to enhance the visualisation of deviations for the SARS-CoV-2 spike. The deviation for the FPPR within Monomer A was 0.385 nm.

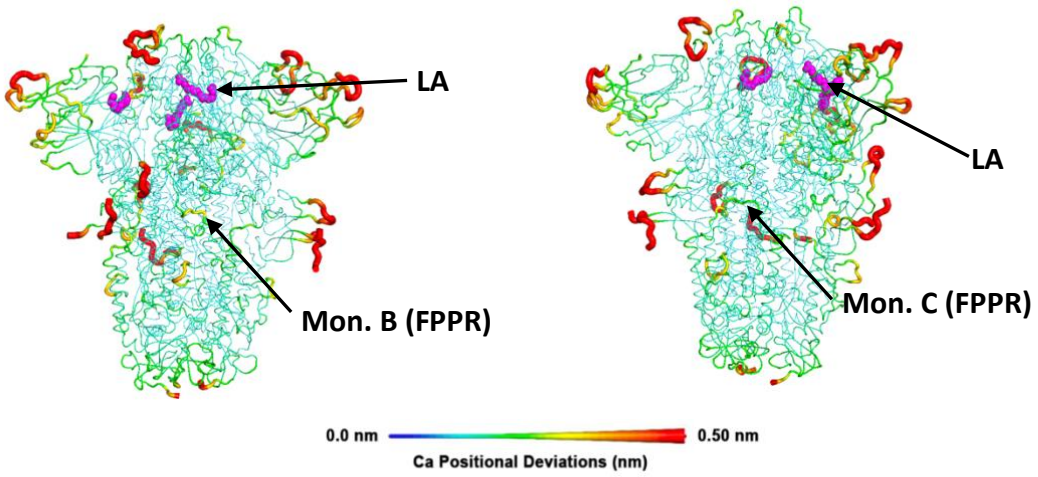

Figure 37 – Visual Illustration of the FPPR at pH 10 for Monomer B (Mon. B, left) and C (Mon. C, right) at 10 ns whilst bound to LA. Linoleic Acid (LA) ligands are highlighted in purple spheres. The colour scale provides a scale for deviation up to 0.50 nm to facilitate visualisation, with regions of increasing deviations being illustrated with increasing thickness. Regions of deviations which are > 0.500 nm will therefore be the same colour and thickness. Note: Glycan chains are not included within these visualisations to enhance the visualisation of deviations for the SARS-CoV-2 spike. The deviation for the FPPR within Monomer B was 0.301 nm and for Monomer C was 0.253 nm.

6.3 The V622-L629 at Low pH (pH 5) in the Presence of Linoleic Acid (LA)

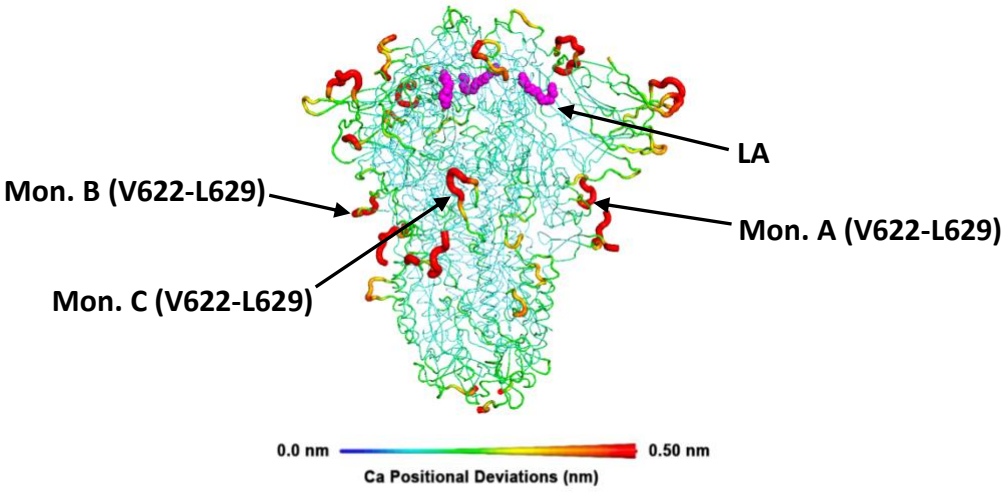

Figure 38 – Visual Illustration of the V622-L629 segment at pH 5 for Monomers A (Mon. A), Monomer B (Mon. B), and Monomer C (Mon. C) at 10 ns whilst bound to LA. Linoleic Acid (LA) ligands are highlighted in purple spheres. The colour scale provides a scale for deviation up to 0.50 nm to facilitate visualisation, with regions of increasing deviations being illustrated with increasing thickness. Regions of deviations which are > 0.500 nm will therefore be the same colour and thickness. Note: Glycan chains are not included within these visualisations to enhance the visualisation of deviations for the SARS-CoV-2 spike. The deviation for Monomer A was 0.672 nm, for Monomer B and for Monomer C the deviation was 0.577 nm. Please zoom in for greater detail. This illustration was created using Pymol.

6.4 D803-S813 (FS) at Low pH (pH 5) in the Presence of Linoleic Acid (LA)

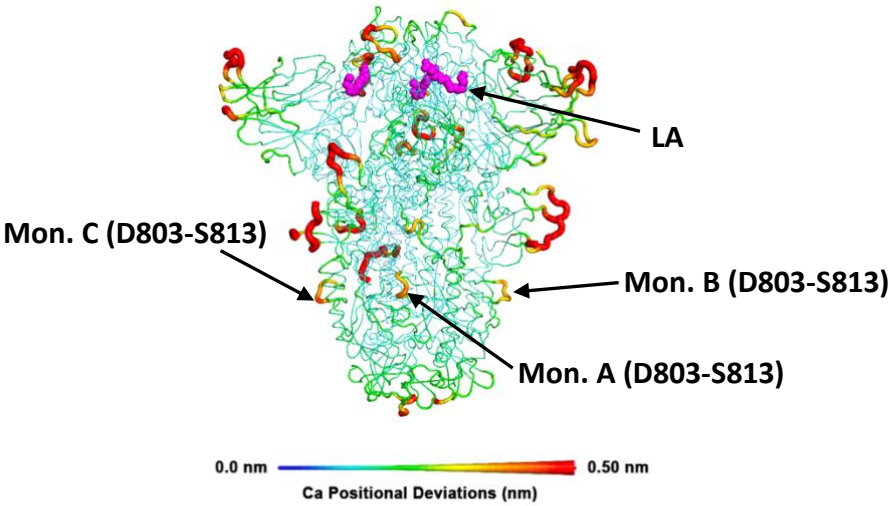

Figure 39 – Visual Illustration of the D803-S813 segment at pH 5 for Monomers A (Mon. A), Monomer B (Mon. B), and Monomer C (Mon. C) at 10 ns whilst bound to LA. Linoleic Acid (LA) ligands are highlighted in purple spheres. The colour scale provides a scale for deviation up to 0.50 nm to facilitate visualisation, with regions of increasing deviations being illustrated with increasing thickness. Regions of deviations which are > 0.500 nm will therefore be the same colour and thickness. Note: Glycan chains are not included within these visualisations to enhance the visualisation of deviations for the SARS-CoV-2 spike. The deviation for Monomer A was 0.403 nm, for Monomer B was 0.375 nm, and for Monomer C the deviation was 0.427 nm. Please zoom in for greater detail. This illustration was created using Pymol.

6.5 The Furin Cleavage Site (FS) at Low pH (pH 5) in the Presence of Linoleic Acid (LA)

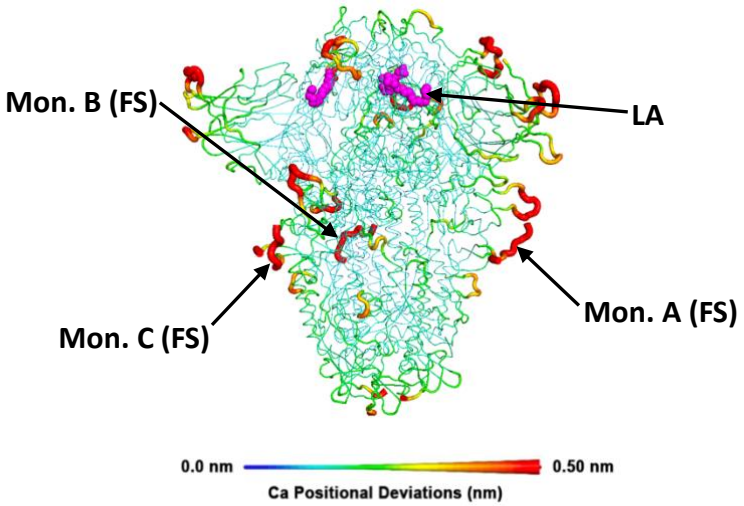

Figure 40 – Visual Illustration of the FS at pH 5 for Monomers A (Mon. A), Monomer B (Mon. B), and Monomer C (Mon. C) at 10 ns whilst bound to LA. Linoleic Acid (LA) ligands are highlighted in purple spheres. The colour scale provides a scale for deviation up to 0.50 nm to facilitate visualisation, with regions of increasing deviations being illustrated with increasing thickness. Regions of deviations which are > 0.500 nm will therefore be the same colour and thickness. Note: Glycan chains are not included within these visualisations to enhance the visualisation of deviations for the SARS-CoV-2 spike. The deviation for Monomer C was 1.576 nm, for Monomer B was 1.113 nm, and for Monomer A the deviation was 1.110 nm. Please zoom in for greater detail. This illustration was created using Pymol.