Energetic Profile-Based Protein Comparison: A New and Fast Approach for Structural and Evolutionary analysis

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|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Based** | **Method** | **Time** | **ARI** | | | | **Class Error** | | | |
| **3** | **4** | **5** | **6** | **3** | **4** | **5** | **6** |
| Sequence | **CPE** | **0.9 sec** | 0.50 | **0.95** | 0.94 | 0.92 | 0.22 | **0.08** | 0.1 | 0.11 |
| **TM Vec** | 89 sec | 0.16 | 0.48 | 0.87 | **0.86** | 0.34 | 0.22 | 0.12 | **0.14** |
| **MSA (ClustalW)** | 72 sec | 0.49 | 0.49 | 0.32 | 0.32 | 0.22 | 0.22 | 0.29 | 0.29 |
| Structure | **SPE** | **3 min** | **1** | **0.95** | 0.93 | 0.66 | **0** | **0.08** | 0.11 | 0.26 |
| **RMSD** | 70 min | 0.50 | 0.50 | 0.36 | **0.73** | 0.22 | 0.22 | 0.22 | **0.17** |
| **TM score** | 9.7 h | 0.50 | **0.56** | 0.40 | 0.40 | 0.22 | **0.17** | 0.24 | 0.24 |

Table S1. The results of clustering using the Adjusted Rand Index (ARI) and class error

Table S2. The PDB IDs of spike proteins.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **pdbID** | **length** | **virus** | **pdbID** | **length** | **virus** | **pdbID** | **length** | **virus** | **pdbID** | **length** | **virus** |
| **6XM5A** | **1057** | **SARS-CoV-2** | **6CRZA** | **1068** | **SARS-CoV** | **6Q04B** | **1159** | **MERS-CoV** | **6ZGFC** | **1060** | **SARS-CoV-2** |
| **6ZP2A** | **1097** | **SARS-CoV-2** | **6CRWA** | **1068** | **SARS-CoV** | **6ACKB** | **1065** | **SARS-CoV** | **6ZGEC** | **1098** | **SARS-CoV-2** |
| **6ZP1A** | **1017** | **SARS-CoV-2** | **5W9JA** | **463** | **MERS-CoV** | **6ACJB** | **1065** | **SARS-CoV** | **6Z97C** | **991** | **SARS-CoV-2** |
| **6ZP0A** | **1030** | **SARS-CoV-2** | **5XLRA** | **1022** | **SARS-CoV** | **6ACGB** | **1065** | **SARS-CoV** | **7BYRC** | **973** | **SARS-CoV-2** |
| **6ZOZA** | **1069** | **SARS-CoV-2** | **5X5FA** | **1141** | **MERS-CoV** | **6ACDB** | **1065** | **SARS-CoV** | **6X6PC** | **1017** | **SARS-CoV-2** |
| **6ZOYA** | **1021** | **SARS-CoV-2** | **5X58A** | **1054** | **SARS-CoV** | **6ACCB** | **1065** | **SARS-CoV** | **6Z43C** | **991** | **SARS-CoV-2** |
| **6ZOXA** | **1017** | **SARS-CoV-2** | **5WRGA** | **736** | **SARS-CoV** | **5W9OD** | **463** | **MERS-CoV** | **6X2CC** | **971** | **SARS-CoV-2** |
| **6XEYA** | **1034** | **SARS-CoV-2** | **6ZP7B** | **930** | **SARS-CoV-2** | **5W9ND** | **463** | **MERS-CoV** | **6X2AC** | **961** | **SARS-CoV-2** |
| **6ZGIA** | **1098** | **SARS-CoV-2** | **6ZP5B** | **943** | **SARS-CoV-2** | **5W9MD** | **457** | **MERS-CoV** | **6X29C** | **972** | **SARS-CoV-2** |
| **6ZGGA** | **1069** | **SARS-CoV-2** | **6ZOWB** | **930** | **SARS-CoV-2** | **5W9LB** | **726** | **MERS-CoV** | **6WPTC** | **952** | **SARS-CoV-2** |
| **6ZGFA** | **1060** | **SARS-CoV-2** | **6ZHDB** | **992** | **SARS-CoV-2** | **5W9KD** | **462** | **MERS-CoV** | **6WPSE** | **955** | **SARS-CoV-2** |
| **6ZGEA** | **1098** | **SARS-CoV-2** | **6XM5B** | **1056** | **SARS-CoV-2** | **5W9JD** | **463** | **MERS-CoV** | **6VYBC** | **960** | **SARS-CoV-2** |
| **6Z97A** | **995** | **SARS-CoV-2** | **6ZP2B** | **1097** | **SARS-CoV-2** | **5W9HD** | **463** | **MERS-CoV** | **6VXXC** | **972** | **SARS-CoV-2** |
| **6XCMA** | **966** | **SARS-CoV-2** | **6ZP1B** | **1017** | **SARS-CoV-2** | **5XLRB** | **1022** | **SARS-CoV** | **6VSBC** | **973** | **SARS-CoV-2** |
| **6X6PA** | **1017** | **SARS-CoV-2** | **6ZP0B** | **1030** | **SARS-CoV-2** | **5X5FB** | **1141** | **MERS-CoV** | **6Q07C** | **1159** | **MERS-CoV** |
| **6X2CA** | **971** | **SARS-CoV-2** | **6ZOZB** | **1069** | **SARS-CoV-2** | **5X5CB** | **1141** | **MERS-CoV** | **6Q06C** | **1159** | **MERS-CoV** |
| **6X2BA** | **963** | **SARS-CoV-2** | **6ZOYB** | **1021** | **SARS-CoV-2** | **5X5BB** | **1053** | **SARS-CoV** | **6Q05C** | **1159** | **MERS-CoV** |
| **6X2AA** | **966** | **SARS-CoV-2** | **6ZOXB** | **1017** | **SARS-CoV-2** | **5X58B** | **1053** | **SARS-CoV** | **6Q04C** | **1159** | **MERS-CoV** |
| **6X29A** | **972** | **SARS-CoV-2** | **6XEYB** | **1034** | **SARS-CoV-2** | **5WRGB** | **736** | **SARS-CoV** | **6NB3C** | **1169** | **MERS-CoV** |
| **6WPTA** | **945** | **SARS-CoV-2** | **6XKLB** | **976** | **SARS-CoV-2** | **6ZP7C** | **943** | **SARS-CoV-2** | **6ACCC** | **1065** | **SARS-CoV** |
| **6WPSA** | **955** | **SARS-CoV-2** | **7C2LB** | **1055** | **SARS-CoV-2** | **6ZP5C** | **930** | **SARS-CoV-2** | **6CS1C** | **1068** | **SARS-CoV** |
| **6VYBA** | **966** | **SARS-CoV-2** | **6ZGIB** | **1098** | **SARS-CoV-2** | **6ZOWC** | **943** | **SARS-CoV-2** | **6CS0C** | **1069** | **SARS-CoV** |
| **6VXXA** | **972** | **SARS-CoV-2** | **6ZGHB** | **1077** | **SARS-CoV-2** | **6ZHDC** | **990** | **SARS-CoV-2** | **6CRZC** | **1069** | **SARS-CoV** |
| **6Q07A** | **1159** | **MERS-CoV** | **6ZGFB** | **1060** | **SARS-CoV-2** | **6XM5C** | **1036** | **SARS-CoV-2** | **6CRXC** | **1069** | **SARS-CoV** |
| **6Q06A** | **1159** | **MERS-CoV** | **6ZGEB** | **1098** | **SARS-CoV-2** | **6ZP2C** | **1097** | **SARS-CoV-2** | **6CRWC** | **1068** | **SARS-CoV** |
| **6Q05A** | **1159** | **MERS-CoV** | **7BYRB** | **998** | **SARS-CoV-2** | **6ZP1C** | **1017** | **SARS-CoV-2** | **5W9OG** | **463** | **MERS-CoV** |
| **6Q04A** | **1159** | **MERS-CoV** | **6X6PB** | **1017** | **SARS-CoV-2** | **6ZP0C** | **1030** | **SARS-CoV-2** | **5W9NG** | **457** | **MERS-CoV** |
| **6NB6A** | **1052** | **SARS-CoV** | **6Z43B** | **992** | **SARS-CoV-2** | **6ZOZC** | **1070** | **SARS-CoV-2** | **5W9ME** | **726** | **MERS-CoV** |
| **6NB4A** | **1169** | **MERS-CoV** | **6X2CB** | **971** | **SARS-CoV-2** | **6ZOYC** | **1021** | **SARS-CoV-2** | **5W9LC** | **726** | **MERS-CoV** |
| **6NB3A** | **1169** | **MERS-CoV** | **6X29B** | **972** | **SARS-CoV-2** | **6ZOXC** | **1017** | **SARS-CoV-2** | **5W9JG** | **463** | **MERS-CoV** |
| **6ACKA** | **1065** | **SARS-CoV** | **6WPSB** | **955** | **SARS-CoV-2** | **6XEYC** | **1030** | **SARS-CoV-2** | **5W9HG** | **463** | **MERS-CoV** |
| **6ACJA** | **1065** | **SARS-CoV** | **6VXXB** | **972** | **SARS-CoV-2** | **6XKLC** | **976** | **SARS-CoV-2** | **5XLRC** | **1022** | **SARS-CoV** |
| **6ACGA** | **1065** | **SARS-CoV** | **6VSBB** | **973** | **SARS-CoV-2** | **7C2LC** | **1049** | **SARS-CoV-2** | **5X5BC** | **1053** | **SARS-CoV** |
| **6ACDA** | **1065** | **SARS-CoV** | **6Q07B** | **1159** | **MERS-CoV** | **6ZGIC** | **1098** | **SARS-CoV-2** | **5X58C** | **1052** | **SARS-CoV** |
| **6ACCA** | **1065** | **SARS-CoV** | **6Q06B** | **1159** | **MERS-CoV** | **6ZGHC** | **1080** | **SARS-CoV-2** | **5WRGC** | **736** | **SARS-CoV** |
| **6CS0A** | **1068** | **SARS-CoV** | **6Q05B** | **1159** | **MERS-CoV** | **6ZGGC** | **1067** | **SARS-CoV-2** |  |  |  |

Table S3. The results of 1-NN classification on SARS Proteome using CPE.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SARS\_Proteome | ac | pr | re | f1 |
| E\_protein | 99.68 | 100 | 96.55 | 98 |
| N\_C-terminaldomain | 99.68 | 100 | 100 | 100 |
| N\_N-terminaldomain | 99.68 | 99.82 | 100 | 100 |
| NSP1\_protein | 99.68 | 100 | 95.83 | 98 |
| NSP10\_protein | 99.68 | 100 | 100 | 100 |
| NSP12\_protein | 99.68 | 100 | 100 | 100 |
| NSP13\_protein | 99.68 | 100 | 100 | 100 |
| NSP14\_protein | 99.68 | 100 | 100 | 100 |
| NSP15\_protein | 99.68 | 100 | 100 | 100 |
| NSP16\_protein | 99.68 | 99.61 | 100 | 100 |
| NSP2\_protein | 99.68 | 100 | 100 | 100 |
| NSP3\_cd21525\_SUD\_C\_SARS-CoV\_Nsp3 | 99.68 | 99.2 | 100 | 100 |
| NSP3\_cd21557\_Macro\_X\_Nsp3-like | 99.68 | 99.19 | 99.19 | 99 |
| NSP3\_cd21717\_TM\_Y\_SARS-CoV-like\_Nsp3\_C | 99.68 | 100 | 99.19 | 100 |
| NSP3\_cd21732\_betaCoV\_PLPro | 99.68 | 99.18 | 100 | 100 |
| NSP3\_cd21822\_SARS-CoV-like\_Nsp3\_NAB | 99.68 | 98.33 | 99.16 | 99 |
| NSP3\_cl00019\_Macro\_SF | 99.68 | 100 | 97.62 | 99 |
| NSP3\_cl13138\_SUD-M | 99.68 | 99.17 | 95.97 | 98 |
| NSP3\_cl13772\_DUF3655 | 99.68 | 100 | 100 | 100 |
| NSP5\_protein | 99.68 | 100 | 99.59 | 100 |
| NSP7\_protein | 99.68 | 100 | 100 | 100 |
| NSP8\_protein | 99.68 | 99.5 | 100 | 100 |
| NSP9\_protein | 99.68 | 98.21 | 99.4 | 99 |
| orf3a\_protein | 99.68 | 100 | 100 | 100 |
| orf7a\_protein | 99.68 | 100 | 100 | 100 |
| orf8\_protein | 99.68 | 100 | 100 | 100 |
| orf9b\_protein | 99.68 | 91.3 | 100 | 95 |
| S\_protein | 99.68 | 100 | 100 | 100 |
| 29 | 99.68 | 99.4110714 | 99.375 | 99.4642857 |

Table S4. The results of 1-NN classification on SARS Proteome using SPE.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Proteom | ac | pr | re | f1 |
| E\_protein | 99.73 | 100 | 96.55 | 98 |
| N\_C-terminaldomain | 99.73 | 100 | 99.82 | 100 |
| N\_N-terminaldomain | 99.73 | 100 | 100 | 100 |
| NSP1\_protein | 99.73 | 100 | 95.83 | 98 |
| NSP10\_protein | 99.73 | 99.55 | 100 | 100 |
| NSP12\_protein | 99.73 | 100 | 100 | 100 |
| NSP13\_protein | 99.73 | 100 | 100 | 100 |
| NSP14\_protein | 99.73 | 100 | 100 | 100 |
| NSP15\_protein | 99.73 | 100 | 100 | 100 |
| NSP16\_protein | 99.73 | 100 | 100 | 100 |
| NSP2\_protein | 99.73 | 100 | 100 | 100 |
| NSP3\_cd21525\_SUD\_C\_SARS-CoV\_Nsp3 | 99.73 | 96.88 | 100 | 98 |
| NSP3\_cd21557\_Macro\_X\_Nsp3-like | 99.73 | 100 | 100 | 100 |
| NSP3\_cd21717\_TM\_Y\_SARS-CoV-like\_Nsp3\_C | 99.73 | 100 | 100 | 100 |
| NSP3\_cd21732\_betaCoV\_PLPro | 99.73 | 100 | 100 | 100 |
| NSP3\_cd21822\_SARS-CoV-like\_Nsp3\_NAB | 99.73 | 98.35 | 100 | 99 |
| NSP3\_cl00019\_Macro\_SF | 99.73 | 97.22 | 83.33 | 90 |
| NSP3\_cl13138\_SUD-M | 99.73 | 100 | 99.19 | 100 |
| NSP3\_cl13772\_DUF3655 | 99.73 | 100 | 100 | 100 |
| NSP5\_protein | 99.73 | 100 | 100 | 100 |
| NSP7\_protein | 99.73 | 100 | 100 | 100 |
| NSP8\_protein | 99.73 | 100 | 100 | 100 |
| NSP9\_protein | 99.73 | 98.81 | 100 | 99 |
| orf3a\_protein | 99.73 | 100 | 100 | 100 |
| orf7a\_protein | 99.73 | 96.3 | 100 | 98 |
| orf8\_protein | 99.73 | 95 | 100 | 97 |
| orf9b\_protein | 99.73 | 100 | 100 | 100 |
| S\_protein | 99.73 | 100 | 100 | 100 |

Table S5. The results of 1-NN classification on SARS Proteome using TM-Vec.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | ac | pr | re | f1 |
| Average | 99.66 | 99.4157143 | 99.1167857 | 99.25 |
| E\_protein | 99.66 | 98.31 | 100 | 99 |
| N\_C-terminaldomain | 99.66 | 100 | 99.82 | 100 |
| N\_N-terminaldomain | 99.66 | 100 | 100 | 100 |
| NSP1\_protein | 99.66 | 100 | 95.83 | 98 |
| NSP10\_protein | 99.66 | 100 | 99.55 | 100 |
| NSP12\_protein | 99.66 | 100 | 100 | 100 |
| NSP13\_protein | 99.66 | 100 | 100 | 100 |
| NSP14\_protein | 99.66 | 100 | 100 | 100 |
| NSP15\_protein | 99.66 | 100 | 100 | 100 |
| NSP16\_protein | 99.66 | 100 | 100 | 100 |
| NSP2\_protein | 99.66 | 100 | 100 | 100 |
| NSP3\_cd21525\_SUD\_C\_SARS-CoV\_Nsp3 | 99.66 | 94.62 | 99.19 | 97 |
| NSP3\_cd21557\_Macro\_X\_Nsp3-like | 99.66 | 100 | 100 | 100 |
| NSP3\_cd21717\_TM\_Y\_SARS-CoV-like\_Nsp3\_C | 99.66 | 100 | 99.19 | 100 |
| NSP3\_cd21732\_betaCoV\_PLPro | 99.66 | 100 | 100 | 100 |
| NSP3\_cd21822\_SARS-CoV-like\_Nsp3\_NAB | 99.66 | 98.32 | 98.32 | 98 |
| NSP3\_cl00019\_Macro\_SF | 99.66 | 100 | 97.62 | 99 |
| NSP3\_cl13138\_SUD-M | 99.66 | 99.17 | 96.77 | 98 |
| NSP3\_cl13772\_DUF3655 | 99.66 | 100 | 100 | 100 |
| NSP5\_protein | 99.66 | 100 | 100 | 100 |
| NSP7\_protein | 99.66 | 100 | 100 | 100 |
| NSP8\_protein | 99.66 | 100 | 100 | 100 |
| NSP9\_protein | 99.66 | 98.22 | 100 | 99 |
| orf3a\_protein | 99.66 | 100 | 96.67 | 98 |
| orf7a\_protein | 99.66 | 100 | 92.31 | 96 |
| orf8\_protein | 99.66 | 95 | 100 | 97 |
| orf9b\_protein | 99.66 | 100 | 100 | 100 |
| S\_protein | 99.66 | 100 | 100 | 100 |

Fig. S1. Corr210



**Fig. S2|** The Clustering analysis of spike glycoprotein structures from SARS-CoV, SARS-CoV-2, and MERS-CoV based on CPE method.



**Fig. S3|** The Clustering analysis of spike glycoprotein structures from SARS-CoV, SARS-CoV-2, and MERS-CoV based on SPE method.



**Fig. S4|** The Clustering analysis of spike glycoprotein structures from SARS-CoV, SARS-CoV-2, and MERS-CoV based on TM-Vec method.



**Fig. S5|** The Clustering analysis of spike glycoprotein structures from SARS-CoV, SARS-CoV-2, and MERS-CoV based on MSA method.



**Fig. S6|** **UMAP Visualization of Energy Profiles in Large-Scale SARS-Cov2 data set.** The UMAP projection of Structural Energy Profiles (SPE) on 28 protein families with a total of 4,405 protein models. UMAP plot was generated using parameters n\_neighbors = 150 and min\_dist = 0.1.



**Fig. S7|** **UMAP Visualization of Energy Profiles in Large-Scale SARS-Cov2 data set.** The UMAP projection of Compositional Energy Profiles (CPE) on 28 protein families with a total of 4,405 protein models. UMAP plot was generated using parameters n\_neighbors = 150 and min\_dist = 0.1.



**Fig. S8|** **UMAP Visualization of Energy Profiles in Large-Scale SARS-Cov2 data set.** The UMAP projection of TM-Vec on 28 protein families with a total of 4,405 protein models. UMAP plot was generated using parameters n\_neighbors = 150 and min\_dist = 0.1.