

**Supplementary Table S9.** Benchmark results for the recall of CS prediction at four different tolerance windows. The bold value represents the highest recall among the predictors in a particular tolerance window. The SP type indicated with the symbol † represents SP types with limited training samples.

| Method/backbone   |        | Baseline    | Fine-tuning |              |              | Prompt Tuning |           |         | Adapter Tuning |              |              | LoRA         |           |              |
|-------------------|--------|-------------|-------------|--------------|--------------|---------------|-----------|---------|----------------|--------------|--------------|--------------|-----------|--------------|
| Organism          | window | SignalP 6.0 | ESM2-150M   | ESM2-650M    | ESM2-3B      | ESM2-150M     | ESM2-650M | ESM2-3B | ESM2-150M      | ESM2-650M    | ESM2-3B      | ESM2-150M    | ESM2-650M | ESM2-3B      |
| Archaea Sec/SPI   | ±0     | 0.575       | 0.547       | <b>0.640</b> | 0.570        | 0.490         | 0.575     | 0.575   | 0.612          | 0.625        | 0.611        | 0.603        | 0.531     | 0.612        |
|                   | ±1     | 0.632       | 0.623       | <b>0.697</b> | 0.651        | 0.557         | 0.642     | 0.651   | 0.688          | <b>0.697</b> | 0.673        | 0.642        | 0.618     | 0.679        |
|                   | ±2     | 0.632       | 0.632       | 0.697        | 0.651        | 0.557         | 0.642     | 0.651   | <b>0.706</b>   | 0.697        | 0.682        | 0.651        | 0.618     | 0.679        |
|                   | ±3     | 0.671       | 0.662       | 0.727        | 0.680        | 0.586         | 0.690     | 0.680   | <b>0.736</b>   | 0.727        | <b>0.736</b> | 0.690        | 0.647     | 0.708        |
| Archaea Sec/SPII  | ±0     | 0.806       | 0.806       | 0.861        | 0.861        | 0.706         | 0.875     | 0.667   | 0.875          | 0.778        | 0.806        | <b>0.917</b> | 0.875     | 0.764        |
|                   | ±1     | 0.806       | 0.806       | 0.861        | 0.861        | 0.706         | 0.875     | 0.667   | 0.875          | 0.778        | 0.806        | <b>0.917</b> | 0.875     | 0.764        |
|                   | ±2     | 0.806       | 0.806       | 0.861        | 0.861        | 0.706         | 0.875     | 0.667   | 0.875          | 0.778        | 0.806        | <b>0.917</b> | 0.875     | 0.764        |
|                   | ±3     | 0.806       | 0.806       | 0.861        | 0.861        | 0.706         | 0.875     | 0.708   | 0.875          | 0.778        | 0.806        | <b>0.917</b> | 0.875     | 0.764        |
| Archaea Sec/SPIII | ±0     | 0.500       | 0.417       | 0.389        | <b>0.861</b> | 0.278         | 0.528     | 0.500   | 0.556          | 0.750        | 0.500        | 0.389        | 0.389     | 0.417        |
|                   | ±1     | 0.500       | 0.417       | 0.389        | <b>0.861</b> | 0.278         | 0.528     | 0.500   | 0.667          | 0.750        | 0.500        | 0.444        | 0.417     | 0.472        |
|                   | ±2     | 0.500       | 0.417       | 0.389        | <b>0.861</b> | 0.278         | 0.528     | 0.500   | 0.750          | 0.750        | 0.500        | 0.444        | 0.417     | 0.611        |
|                   | ±3     | 0.500       | 0.417       | 0.389        | <b>0.861</b> | 0.278         | 0.528     | 0.500   | 0.750          | 0.750        | 0.500        | 0.444        | 0.417     | 0.611        |
| Archaea Tat/SPI   | ±0     | 0.292       | 0.333       | 0.292        | 0.226        | 0.155         | 0.226     | 0.286   | 0.220          | <b>0.351</b> | 0.268        | 0.310        | 0.310     | 0.268        |
|                   | ±1     | 0.363       | 0.405       | 0.339        | 0.274        | 0.179         | 0.274     | 0.405   | 0.315          | <b>0.446</b> | 0.315        | 0.405        | 0.405     | 0.292        |
|                   | ±2     | 0.363       | 0.405       | 0.363        | 0.274        | 0.250         | 0.345     | 0.405   | 0.315          | <b>0.446</b> | 0.315        | 0.405        | 0.429     | 0.339        |
|                   | ±3     | 0.429       | 0.470       | 0.446        | 0.339        | 0.292         | 0.387     | 0.488   | 0.423          | <b>0.571</b> | 0.381        | 0.488        | 0.512     | 0.405        |
| Archaea Tat/SPII  | ±0     | 0.688       | 0.812       | <b>1.000</b> | 0.875        | 0.312         | 0.438     | 0.250   | 0.625          | <b>1.000</b> | 0.812        | 0.750        | 0.812     | <b>1.000</b> |
|                   | ±1     | 0.812       | 0.812       | <b>1.000</b> | 0.875        | 0.312         | 0.438     | 0.250   | 0.625          | <b>1.000</b> | 0.812        | 0.750        | 0.812     | <b>1.000</b> |
|                   | ±2     | 0.812       | 0.812       | <b>1.000</b> | 0.875        | 0.312         | 0.438     | 0.250   | 0.625          | <b>1.000</b> | 0.812        | 0.750        | 0.812     | <b>1.000</b> |
|                   | ±3     | 0.812       | 0.812       | <b>1.000</b> | 0.875        | 0.312         | 0.438     | 0.250   | 0.625          | <b>1.000</b> | 0.812        | 0.750        | 0.875     | <b>1.000</b> |
| Eukarya Sec/SPI   | ±0     | 0.817       | 0.825       | 0.839        | 0.835        | 0.825         | 0.828     | 0.835   | 0.826          | 0.827        | <b>0.846</b> | 0.821        | 0.776     | 0.827        |
|                   | ±1     | 0.858       | 0.860       | 0.877        | 0.873        | 0.861         | 0.861     | 0.867   | 0.866          | 0.864        | <b>0.882</b> | 0.858        | 0.830     | 0.866        |
|                   | ±2     | 0.900       | 0.887       | 0.910        | 0.904        | 0.891         | 0.888     | 0.894   | 0.897          | 0.894        | <b>0.910</b> | 0.889        | 0.881     | 0.901        |
|                   | ±3     | 0.920       | 0.904       | 0.925        | 0.920        | 0.907         | 0.902     | 0.908   | 0.917          | 0.909        | <b>0.926</b> | 0.905        | 0.904     | 0.920        |
| Negative Sec/SPI  | ±0     | 0.855       | 0.789       | 0.847        | 0.873        | 0.790         | 0.774     | 0.819   | 0.862          | 0.889        | <b>0.894</b> | 0.839        | 0.850     | 0.858        |
|                   | ±1     | 0.886       | 0.830       | 0.875        | 0.906        | 0.819         | 0.793     | 0.840   | 0.904          | 0.912        | <b>0.925</b> | 0.872        | 0.889     | 0.895        |
|                   | ±2     | 0.892       | 0.841       | 0.887        | 0.921        | 0.826         | 0.798     | 0.847   | 0.911          | 0.915        | <b>0.933</b> | 0.885        | 0.904     | 0.900        |
|                   | ±3     | 0.898       | 0.849       | 0.895        | 0.928        | 0.828         | 0.802     | 0.850   | 0.921          | 0.920        | <b>0.938</b> | 0.892        | 0.909     | 0.908        |
| Negative Sec/SPII | ±0     | 0.935       | 0.947       | 0.948        | 0.947        | 0.885         | 0.945     | 0.925   | 0.938          | 0.949        | 0.947        | <b>0.954</b> | 0.944     | 0.951        |
|                   | ±1     | 0.936       | 0.947       | 0.948        | 0.947        | 0.885         | 0.945     | 0.927   | 0.938          | 0.949        | 0.947        | <b>0.955</b> | 0.944     | 0.951        |
|                   | ±2     | 0.936       | 0.947       | 0.948        | 0.947        | 0.885         | 0.945     | 0.927   | 0.938          | 0.949        | 0.947        | <b>0.955</b> | 0.945     | 0.951        |
|                   | ±3     | 0.937       | 0.947       | 0.949        | 0.948        | 0.885         | 0.946     | 0.929   | 0.939          | 0.950        | 0.948        | <b>0.956</b> | 0.945     | 0.952        |

| Method/backbone    |        | Baseline     | Fine-tuning  |              |              | Prompt Tuning |              |         | Adapter Tuning |              |              | LoRA         |           |              |
|--------------------|--------|--------------|--------------|--------------|--------------|---------------|--------------|---------|----------------|--------------|--------------|--------------|-----------|--------------|
| Organism           | window | SignalP 6.0  | ESM2-150M    | ESM2-650M    | ESM2-3B      | ESM2-150M     | ESM2-650M    | ESM2-3B | ESM2-150M      | ESM2-650M    | ESM2-3B      | ESM2-150M    | ESM2-650M | ESM2-3B      |
| Negative Sec/SPIII | ±0     | 0.842        | 0.993        | 0.952        | 0.959        | 0.928         | 0.978        | 0.964   | <b>1.000</b>   | <b>1.000</b> | 0.899        | 0.816        | 0.391     | 0.739        |
|                    | ±1     | 0.842        | 0.993        | 0.952        | 0.959        | 0.928         | 0.978        | 0.964   | <b>1.000</b>   | <b>1.000</b> | 0.899        | 0.859        | 0.591     | 0.739        |
|                    | ±2     | 0.842        | 0.993        | 0.952        | 0.993        | 0.928         | 0.978        | 0.964   | <b>1.000</b>   | <b>1.000</b> | 0.899        | 0.859        | 0.765     | 0.739        |
|                    | ±3     | 0.842        | 0.993        | 0.952        | 0.993        | 0.928         | 0.978        | 0.964   | <b>1.000</b>   | <b>1.000</b> | 0.899        | 0.859        | 0.859     | 0.900        |
| Negative Tat/SPI   | ±0     | 0.782        | 0.788        | 0.781        | 0.716        | 0.656         | 0.772        | 0.649   | 0.776          | 0.792        | 0.712        | <b>0.805</b> | 0.771     | 0.711        |
|                    | ±1     | 0.839        | 0.833        | 0.828        | 0.773        | 0.698         | 0.817        | 0.703   | 0.816          | 0.847        | 0.763        | <b>0.852</b> | 0.815     | 0.764        |
|                    | ±2     | 0.892        | 0.882        | 0.879        | 0.816        | 0.732         | 0.867        | 0.738   | 0.865          | 0.891        | 0.802        | <b>0.904</b> | 0.886     | 0.878        |
|                    | ±3     | 0.914        | 0.906        | 0.891        | 0.828        | 0.754         | 0.878        | 0.752   | 0.894          | 0.913        | 0.815        | <b>0.916</b> | 0.902     | 0.904        |
| Negative Tat/SPII  | ±0     | 0.431        | 0.505        | 0.523        | 0.458        | 0.097         | 0.347        | 0.375   | 0.375          | <b>0.542</b> | 0.486        | 0.306        | 0.500     | <b>0.542</b> |
|                    | ±1     | 0.523        | 0.505        | 0.523        | 0.458        | 0.097         | 0.347        | 0.375   | 0.375          | <b>0.542</b> | 0.486        | 0.306        | 0.500     | <b>0.542</b> |
|                    | ±2     | 0.523        | 0.505        | 0.523        | 0.458        | 0.097         | 0.384        | 0.375   | 0.375          | <b>0.542</b> | 0.486        | 0.306        | 0.500     | <b>0.542</b> |
|                    | ±3     | 0.523        | 0.505        | 0.523        | 0.458        | 0.097         | 0.384        | 0.375   | 0.375          | <b>0.542</b> | 0.486        | 0.306        | 0.500     | <b>0.542</b> |
| Positive Sec/SPI   | ±0     | 0.766        | 0.807        | <b>0.820</b> | 0.809        | 0.745         | 0.671        | 0.752   | 0.803          | 0.814        | 0.816        | 0.785        | 0.732     | 0.813        |
|                    | ±1     | 0.779        | 0.818        | 0.830        | 0.826        | 0.750         | 0.679        | 0.763   | 0.819          | <b>0.838</b> | 0.838        | 0.796        | 0.741     | 0.832        |
|                    | ±2     | 0.794        | 0.833        | 0.848        | 0.841        | 0.769         | 0.692        | 0.772   | 0.834          | <b>0.855</b> | 0.853        | 0.816        | 0.756     | 0.852        |
|                    | ±3     | 0.812        | 0.839        | 0.854        | 0.859        | 0.777         | 0.698        | 0.778   | 0.840          | <b>0.861</b> | 0.859        | 0.825        | 0.774     | 0.860        |
| Positive Sec/SPII  | ±0     | 0.870        | 0.901        | 0.911        | 0.890        | 0.800         | 0.872        | 0.866   | 0.912          | 0.881        | 0.898        | <b>0.929</b> | 0.903     | 0.921        |
|                    | ±1     | 0.870        | 0.901        | 0.911        | 0.890        | 0.802         | 0.872        | 0.866   | 0.912          | 0.881        | 0.898        | <b>0.929</b> | 0.903     | 0.921        |
|                    | ±2     | 0.871        | 0.901        | 0.911        | 0.890        | 0.802         | 0.872        | 0.866   | 0.912          | 0.881        | 0.898        | <b>0.929</b> | 0.903     | 0.921        |
|                    | ±3     | 0.871        | 0.901        | 0.911        | 0.890        | 0.802         | 0.872        | 0.866   | 0.912          | 0.881        | 0.898        | <b>0.929</b> | 0.903     | 0.921        |
| Positive Sec/SPIII | ±0     | <b>1.000</b> | <b>1.000</b> | 0.917        | <b>1.000</b> | 0.833         | <b>1.000</b> | 0.750   | <b>1.000</b>   | <b>1.000</b> | <b>1.000</b> | 0.750        | 0.500     | 0.833        |
|                    | ±1     | <b>1.000</b> | <b>1.000</b> | 0.917        | <b>1.000</b> | 0.833         | <b>1.000</b> | 0.750   | <b>1.000</b>   | <b>1.000</b> | <b>1.000</b> | 0.917        | 0.667     | 0.833        |
|                    | ±2     | <b>1.000</b> | <b>1.000</b> | 0.917        | <b>1.000</b> | 0.833         | <b>1.000</b> | 0.750   | <b>1.000</b>   | <b>1.000</b> | <b>1.000</b> | 0.917        | 0.833     | 0.833        |
|                    | ±3     | <b>1.000</b> | <b>1.000</b> | 0.917        | <b>1.000</b> | 0.833         | <b>1.000</b> | 0.750   | <b>1.000</b>   | <b>1.000</b> | <b>1.000</b> | 0.917        | 0.833     | <b>1.000</b> |
| Positive Tat/SPI   | ±0     | 0.396        | 0.526        | 0.485        | 0.411        | 0.406         | 0.430        | 0.265   | 0.389          | 0.494        | 0.387        | 0.444        | 0.511     | <b>0.550</b> |
|                    | ±1     | 0.457        | 0.526        | 0.507        | 0.411        | 0.406         | 0.450        | 0.285   | 0.400          | 0.494        | 0.415        | 0.465        | 0.533     | <b>0.550</b> |
|                    | ±2     | 0.669        | 0.741        | 0.672        | 0.576        | 0.506         | 0.633        | 0.431   | 0.633          | 0.641        | 0.611        | 0.691        | 0.733     | <b>0.765</b> |
|                    | ±3     | 0.669        | 0.741        | 0.700        | 0.604        | 0.543         | 0.633        | 0.431   | 0.633          | 0.641        | 0.611        | 0.691        | 0.733     | <b>0.765</b> |
| Positive Tat/SPII  | ±0     | <b>1.000</b> | 0.861        | 0.972        | 0.972        | 0.361         | 0.194        | 0.194   | 0.722          | 0.694        | <b>1.000</b> | 0.611        | 0.667     | 0.972        |
|                    | ±1     | <b>1.000</b> | 0.889        | 0.972        | 0.972        | 0.361         | 0.194        | 0.194   | 0.722          | 0.694        | <b>1.000</b> | 0.611        | 0.667     | 0.972        |
|                    | ±2     | <b>1.000</b> | 0.889        | 0.972        | 0.972        | 0.361         | 0.194        | 0.194   | 0.722          | 0.694        | <b>1.000</b> | 0.611        | 0.667     | 0.972        |
|                    | ±3     | <b>1.000</b> | 0.889        | 0.972        | 0.972        | 0.361         | 0.194        | 0.194   | 0.722          | 0.694        | <b>1.000</b> | 0.611        | 0.667     | 0.972        |
| mean               |        | 0.761        | 0.768        | 0.785        | 0.792        | 0.599         | 0.679        | 0.630   | 0.755          | <b>0.799</b> | 0.767        | 0.729        | 0.716     | 0.775        |