

# ADNI Progress report

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## Part I

# Using HMMs to predict disease progression

Training set: randomly picked 1000 patients.  
Testing set: Remaining 398 patients.

## 1 Sanity Check

As a sanity check, the HMM was trained with the number of states  $k = 3$ .

Following are the temporal parameters, as learned by the HMM and contrasted with the ground truth.

$$\begin{aligned} gt.pi &= [ 0.3062 \quad 0.4667 \quad 0.2272 ] \\ model.pi &= [ 0.4630 \pm 0.0453 \quad 0.3479 \pm 0.0276 \quad 0.1891 \pm 0.0330 ] \\ gt.A &= \begin{bmatrix} 0.9416 & 0.0584 & 0 \\ 0.0264 & 0.8516 & 0.1220 \\ 0 & 0 & 1 \end{bmatrix} \\ model.A &= \begin{bmatrix} 0.975 \pm 0.013 & 0.019 \pm 0.013 & 0.006 \pm 0.005 \\ 0.000 \pm 0.000 & 0.977 \pm 0.005 & 0.023 \pm 0.005 \\ 0.000 \pm 0.000 & 0.000 \pm 0.000 & 1.000 \pm 0.000 \end{bmatrix} \end{aligned}$$

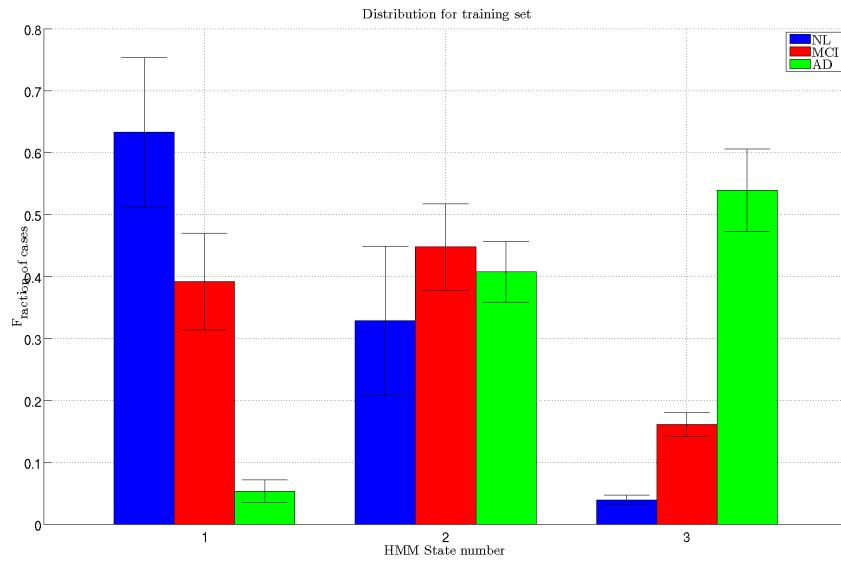


Figure 1: Distribution of states for training set

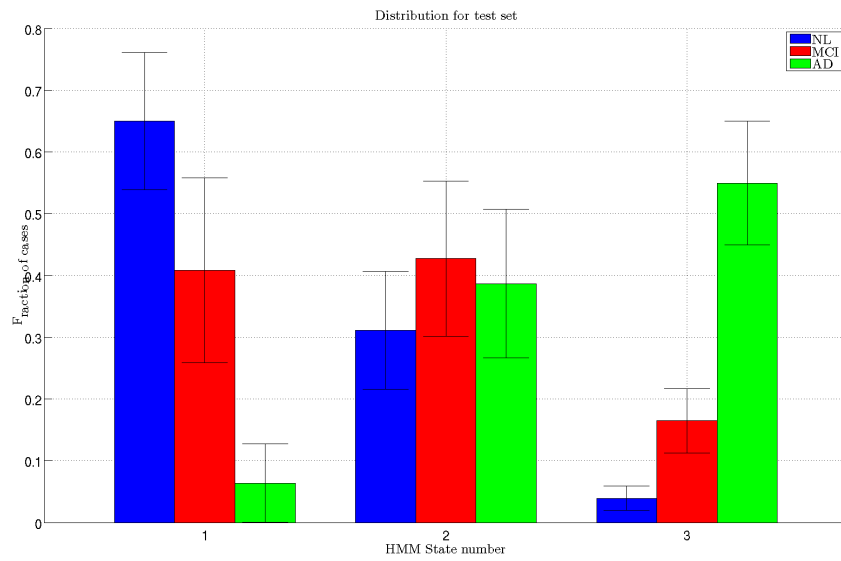


Figure 2: Distribution of states for testing set

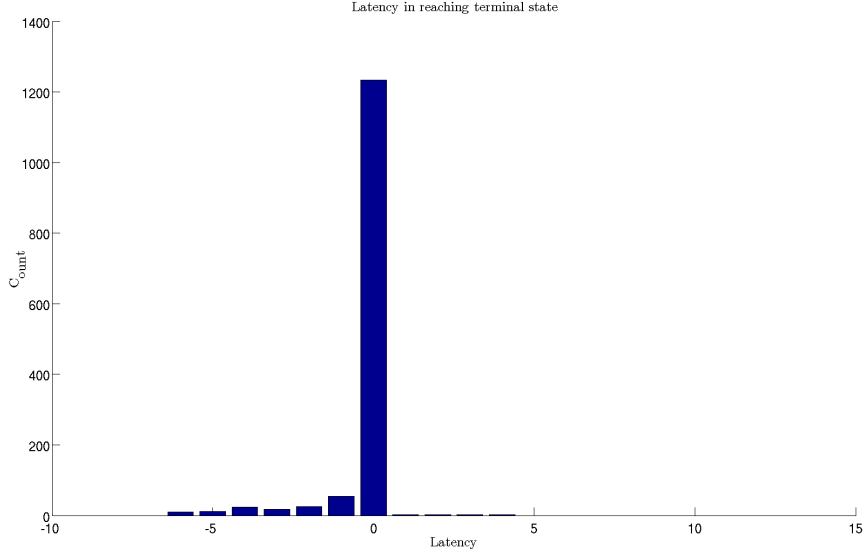


Figure 3: Distribution of latency

## 1.1 Analysing the transitions

## 1.2 K=3

Training set:

|                   | $NL \rightarrow NL$  | $MCI \rightarrow NL$ | $NL \rightarrow MCI$ |
|-------------------|----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.591 \pm 0.045$    | $0.479 \pm 0.127$    | $0.412 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.002 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.339 \pm 0.000$    | $0.375 \pm 0.000$    | $0.494 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.002 \pm 0.002$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.001 \pm 0.063$    | $0.000 \pm 0.054$    | $0.000 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.066 \pm 0.000$    | $0.146 \pm 0.000$    | $0.093 \pm 0.000$    |
| <i>TotalCount</i> | $344.000 \pm 37.242$ | $16.000 \pm 1.000$   | $21.333 \pm 5.508$   |

|                   | $MCI \rightarrow MCI$ | $MCI \rightarrow AD$ | $AD \rightarrow AD$  |
|-------------------|-----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.333 \pm 0.036$     | $0.139 \pm 0.033$    | $0.026 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.003 \pm 0.000$     | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.466 \pm 0.000$     | $0.390 \pm 0.000$    | $0.384 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.001 \pm 0.000$     | $0.009 \pm 0.002$    | $0.004 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.002 \pm 0.061$     | $0.022 \pm 0.041$    | $0.010 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.196 \pm 0.000$     | $0.440 \pm 0.000$    | $0.576 \pm 0.000$    |
| <i>TotalCount</i> | $517.000 \pm 4.359$   | $74.000 \pm 3.606$   | $234.667 \pm 10.263$ |

Testing Set:

|                   | $NL \rightarrow NL$  | $MCI \rightarrow NL$ | $NL \rightarrow MCI$ |
|-------------------|----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.608 \pm 0.126$    | $0.532 \pm 0.122$    | $0.488 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.328 \pm 0.000$    | $0.337 \pm 0.000$    | $0.440 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.004 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.004 \pm 0.065$    | $0.000 \pm 0.089$    | $0.000 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.056 \pm 0.000$    | $0.131 \pm 0.000$    | $0.072 \pm 0.000$    |
| <i>TotalCount</i> | $172.000 \pm 37.242$ | $8.000 \pm 1.000$    | $10.667 \pm 5.508$   |

|                   | $MCI \rightarrow MCI$ | $MCI \rightarrow AD$ | $AD \rightarrow AD$  |
|-------------------|-----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.326 \pm 0.119$     | $0.134 \pm 0.039$    | $0.034 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.003 \pm 0.000$     | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.491 \pm 0.000$     | $0.434 \pm 0.000$    | $0.381 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.003 \pm 0.000$     | $0.010 \pm 0.002$    | $0.003 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.004 \pm 0.092$     | $0.008 \pm 0.095$    | $0.012 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.173 \pm 0.000$     | $0.413 \pm 0.000$    | $0.570 \pm 0.000$    |
| <i>TotalCount</i> | $258.000 \pm 4.359$   | $37.000 \pm 3.606$   | $117.333 \pm 10.263$ |

## 2 K=5

Training Set:

|                   | $NL \rightarrow NL$  | $MCI \rightarrow NL$ | $NL \rightarrow MCI$ |
|-------------------|----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.398 \pm 0.066$    | $0.394 \pm 0.079$    | $0.215 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.326 \pm 0.000$    | $0.291 \pm 0.000$    | $0.279 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.004 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.186 \pm 0.000$    | $0.170 \pm 0.000$    | $0.343 \pm 0.000$    |
| $1 \rightarrow 4$ | $0.000 \pm 0.081$    | $0.000 \pm 0.023$    | $0.000 \pm 0.000$    |
| $3 \rightarrow 4$ | $0.004 \pm 0.000$    | $0.000 \pm 0.000$    | $0.018 \pm 0.000$    |
| $4 \rightarrow 4$ | $0.049 \pm 0.000$    | $0.064 \pm 0.000$    | $0.116 \pm 0.000$    |
| $1 \rightarrow 5$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 5$ | $0.001 \pm 0.002$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $4 \rightarrow 5$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $5 \rightarrow 5$ | $0.032 \pm 0.035$    | $0.081 \pm 0.099$    | $0.030 \pm 0.000$    |
| <i>TotalCount</i> | $344.000 \pm 10.000$ | $16.000 \pm 1.000$   | $21.333 \pm 2.517$   |

|                   | $MCI \rightarrow MCI$ | $MCI \rightarrow AD$ | $AD \rightarrow AD$  |
|-------------------|-----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.200 \pm 0.050$     | $0.085 \pm 0.039$    | $0.015 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.000 \pm 0.000$     | $0.000 \pm 0.000$    | $0.001 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.243 \pm 0.000$     | $0.097 \pm 0.000$    | $0.051 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.003 \pm 0.000$     | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.001 \pm 0.000$     | $0.000 \pm 0.000$    | $0.002 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.294 \pm 0.000$     | $0.241 \pm 0.000$    | $0.212 \pm 0.000$    |
| $1 \rightarrow 4$ | $0.001 \pm 0.062$     | $0.000 \pm 0.105$    | $0.000 \pm 0.000$    |
| $3 \rightarrow 4$ | $0.004 \pm 0.000$     | $0.018 \pm 0.000$    | $0.011 \pm 0.000$    |
| $4 \rightarrow 4$ | $0.133 \pm 0.000$     | $0.249 \pm 0.000$    | $0.287 \pm 0.000$    |
| $1 \rightarrow 5$ | $0.001 \pm 0.000$     | $0.005 \pm 0.000$    | $0.003 \pm 0.000$    |
| $2 \rightarrow 5$ | $0.003 \pm 0.000$     | $0.014 \pm 0.001$    | $0.005 \pm 0.000$    |
| $4 \rightarrow 5$ | $0.000 \pm 0.000$     | $0.005 \pm 0.001$    | $0.001 \pm 0.000$    |
| $5 \rightarrow 5$ | $0.118 \pm 0.050$     | $0.287 \pm 0.063$    | $0.412 \pm 0.000$    |
| <i>TotalCount</i> | $517.333 \pm 8.737$   | $74.333 \pm 5.132$   | $235.000 \pm 18.520$ |

Testing Set:

|                   | $NL \rightarrow NL$  | $MCI \rightarrow NL$ | $NL \rightarrow MCI$ |
|-------------------|----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.418 \pm 0.111$    | $0.304 \pm 0.313$    | $0.230 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.296 \pm 0.000$    | $0.290 \pm 0.000$    | $0.221 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.002 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.184 \pm 0.000$    | $0.333 \pm 0.000$    | $0.410 \pm 0.000$    |
| $3 \rightarrow 4$ | $0.002 \pm 0.118$    | $0.000 \pm 0.042$    | $0.000 \pm 0.000$    |
| $4 \rightarrow 4$ | $0.053 \pm 0.000$    | $0.000 \pm 0.000$    | $0.114 \pm 0.000$    |
| $1 \rightarrow 5$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 5$ | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $4 \rightarrow 5$ | $0.000 \pm 0.004$    | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $5 \rightarrow 5$ | $0.044 \pm 0.000$    | $0.074 \pm 0.000$    | $0.026 \pm 0.000$    |
| <i>TotalCount</i> | $172.000 \pm 10.000$ | $8.000 \pm 1.000$    | $10.667 \pm 2.517$   |

|                   | $MCI \rightarrow MCI$ | $MCI \rightarrow AD$ | $AD \rightarrow AD$  |
|-------------------|-----------------------|----------------------|----------------------|
| $1 \rightarrow 1$ | $0.223 \pm 0.144$     | $0.061 \pm 0.031$    | $0.013 \pm 0.000$    |
| $1 \rightarrow 2$ | $0.003 \pm 0.000$     | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 2$ | $0.219 \pm 0.000$     | $0.159 \pm 0.000$    | $0.033 \pm 0.000$    |
| $1 \rightarrow 3$ | $0.001 \pm 0.000$     | $0.000 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 3$ | $0.001 \pm 0.000$     | $0.008 \pm 0.000$    | $0.002 \pm 0.000$    |
| $3 \rightarrow 3$ | $0.285 \pm 0.000$     | $0.226 \pm 0.002$    | $0.198 \pm 0.000$    |
| $3 \rightarrow 4$ | $0.007 \pm 0.035$     | $0.011 \pm 0.118$    | $0.006 \pm 0.000$    |
| $4 \rightarrow 4$ | $0.128 \pm 0.000$     | $0.193 \pm 0.000$    | $0.303 \pm 0.000$    |
| $1 \rightarrow 5$ | $0.000 \pm 0.000$     | $0.009 \pm 0.000$    | $0.000 \pm 0.000$    |
| $2 \rightarrow 5$ | $0.006 \pm 0.000$     | $0.011 \pm 0.000$    | $0.011 \pm 0.000$    |
| $4 \rightarrow 5$ | $0.001 \pm 0.000$     | $0.000 \pm 0.002$    | $0.000 \pm 0.000$    |
| $5 \rightarrow 5$ | $0.126 \pm 0.000$     | $0.322 \pm 0.002$    | $0.435 \pm 0.000$    |
| <i>TotalCount</i> | $257.667 \pm 8.737$   | $36.667 \pm 5.132$   | $117.000 \pm 18.520$ |

### 3 HMM with larger state space

$$model.pi = \begin{bmatrix} 0.2481 \pm 0.0425 & 0.2863 \pm 0.0224 & 0.2109 \pm 0.0186 & 0.1039 \pm 0.0060 & 0.1508 \pm 0.0060 \end{bmatrix}$$

$$model.A = \begin{bmatrix} 0.981 \pm 0.006 & 0.006 \pm 0.010 & 0.009 \pm 0.011 & 0.002 \pm 0.003 & 0.002 \pm 0.003 \\ 0.001 \pm 0.001 & 0.962 \pm 0.004 & 0.016 \pm 0.002 & 0.003 \pm 0.005 & 0.018 \pm 0.009 \\ 0.000 \pm 0.000 & 0.000 \pm 0.000 & 0.951 \pm 0.020 & 0.049 \pm 0.020 & 0.000 \pm 0.000 \\ 0.000 \pm 0.000 & 0.000 \pm 0.000 & 0.000 \pm 0.000 & 0.992 \pm 0.011 & 0.008 \pm 0.011 \\ 0.000 \pm 0.000 & 0.000 \pm 0.000 & 0.000 \pm 0.000 & 0.000 \pm 0.000 & 1.000 \pm 0.000 \end{bmatrix}$$

## 4 Trellis plots

### 4.1 K=3

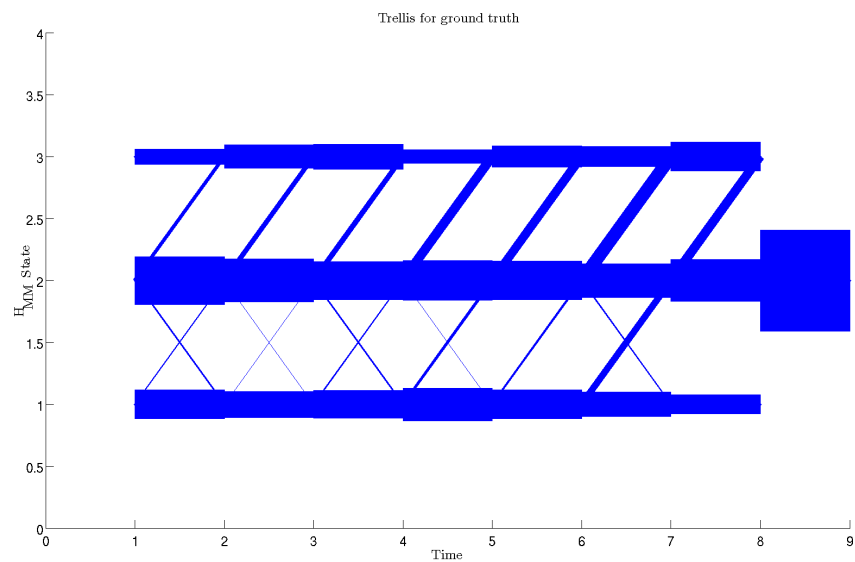


Figure 4: Trellis for ground truth

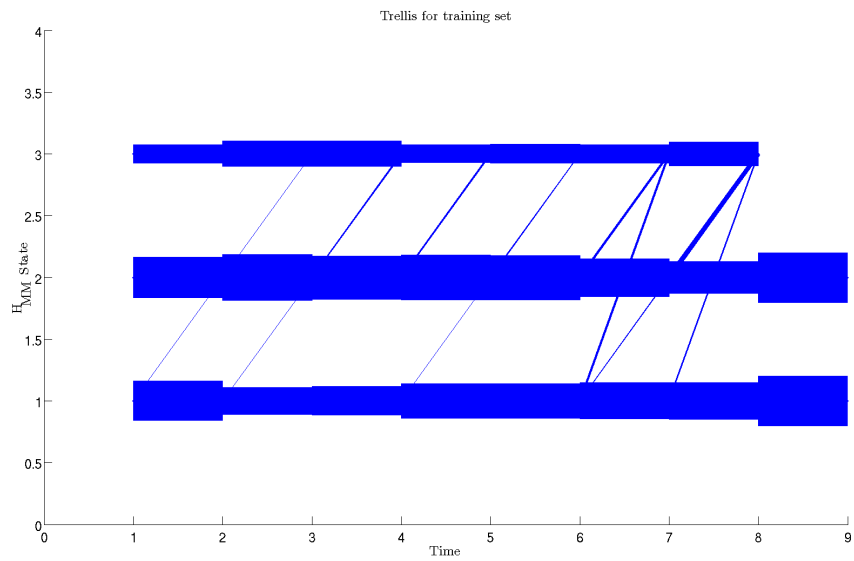


Figure 5: Trellis for training set

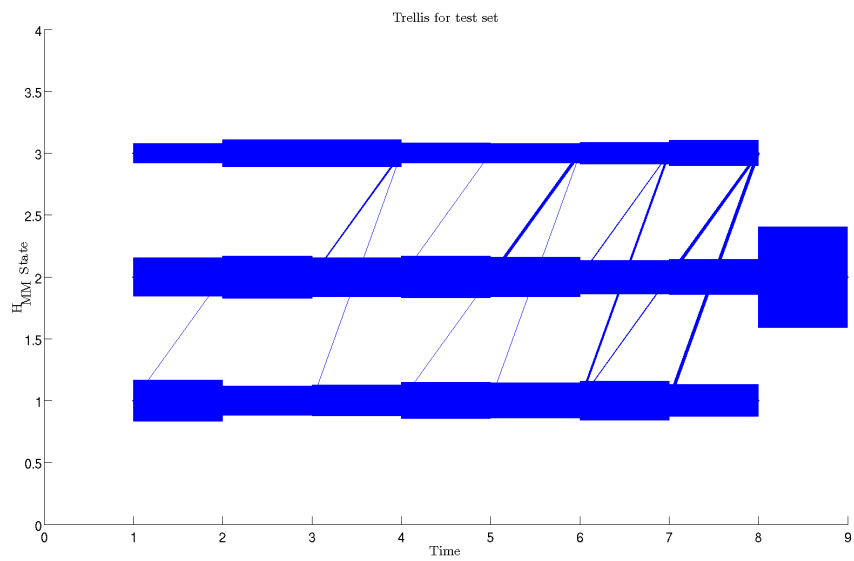


Figure 6: Trellis for test set



## 4.2 K=5

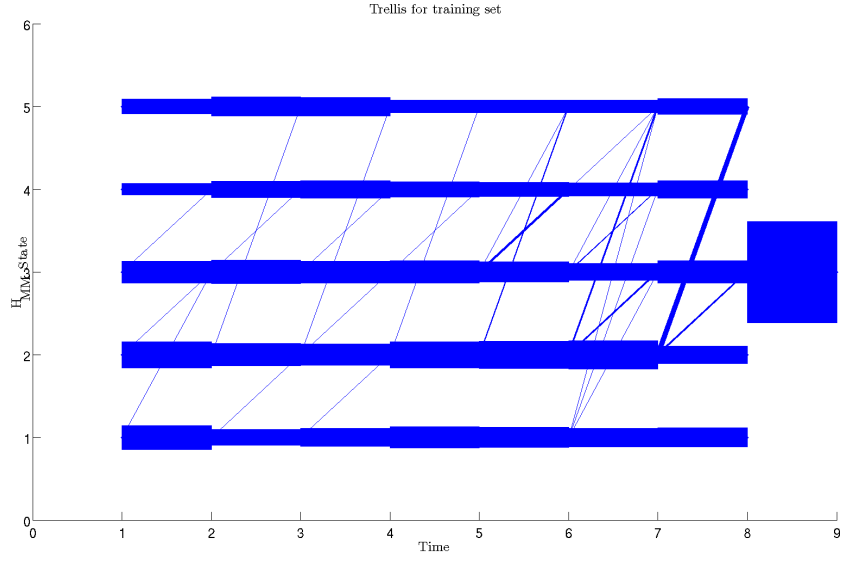


Figure 7: Trellis for training set

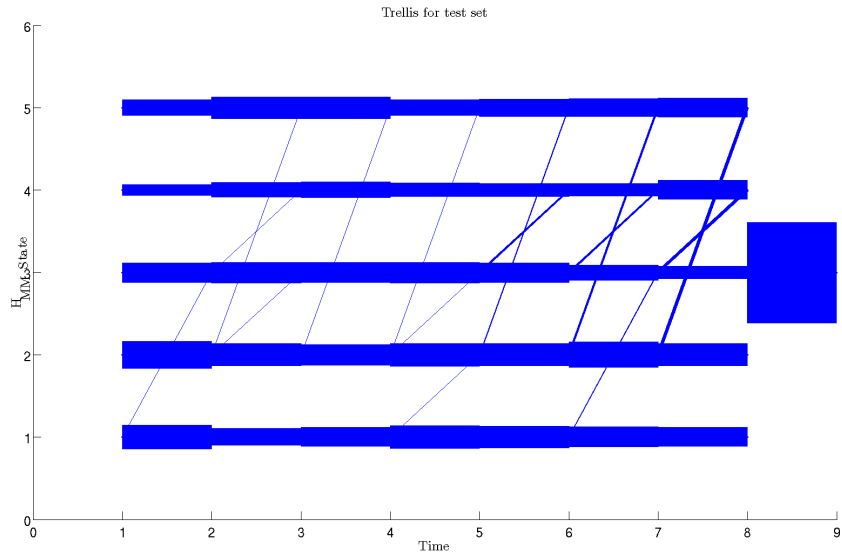


Figure 8: Trellis for test set