

# Resimulation of the Probability of Having Autistic Children using Hidden Markov Models as in [1]

EECE562 Project  
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## Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disability that related to age and sex, and it impedes people's ability to communicate and limits people's behavior or interests. Additionally, the medical cost for the children with ASD is about 6.2 times higher than those with Typical Development (TD). [2]

For the ASD children, it is important for them to have early diagnosis and treatments.

Several works have shown 80% of ASD children are inherited from their parents. [3].

Moreover, ASD boys are three to four times more than ASD girls. [4]

To have a more accurate estimation of the probability that children inherit ASD from their parents, many methods have been applied. One of the works is using Hidden Markov Model (HMM), by considering the ASD/TD children as hidden states and ASD/TD parents as observable states.

We are also interested to resimulate the HMM presented in [1].

## Implementation

HMM Parameters defined in [1]:

1. States
  - a. Two Hidden States:
    - TD: a Typical Girl/Boy
    - ASD: an ASD Girl/Boy
  - b. Two Observable States:
    - TP: Typical Parents
    - AP: ASD Parents

2. Initial Distribution:

Carvalho's paper used an ASD prevalence among children calculated from the ASD diagnosis data presented by  $\pi$ . From that diagnosis data, three important probabilities were calculated:

- 1) the children general ASD prevalence, regardless of gender ( $P(A) = 0.0125$ );
- 2) the ASD prevalence among girls ( $P(AG) = 0.005$ ); and
- 3) the ASD prevalence among boys ( $P(AB) = 0.0197$ ).

It is also proved by other research that generally, by gender, the ASD prevalence among boys and girls is 4:1.

From the probabilities and the hidden states previously defined, it was possible to determine our initial state distribution vectors ( $\pi$ ) for both girls ( $\pi_G$ ) and boys ( $\pi_B$ ).

$$\pi = \begin{matrix} & \text{TD} & \text{ASD} \\ \begin{bmatrix} 1 - P(\text{ASD}) & P(\text{ASD}) \end{bmatrix} \end{matrix}$$

$$\pi G = \begin{matrix} & \text{TG} & \text{AG} \\ \begin{bmatrix} 0.995 & 0.005 \end{bmatrix} \end{matrix}$$

$$\pi B = \begin{matrix} & \text{TB} & \text{AB} \\ \begin{bmatrix} 0.9803 & 0.0197 \end{bmatrix} \end{matrix}$$

These initial state distribution vectors were used for modeling all of our HMMs according to the respective children's gender.

### 3. Transition Matrix

Three transition matrices were created for each gender since the probabilities significantly changed according to the older sibling gender. Two of them, according to the older sibling gender, and the other one disregarding the older sibling gender. All transition probabilities presented in the following part were calculated according to the diagnostic data of the population studied by [5].

Sections (a), (b) and (c) are transition matrices for female births, given a male/female/regardless gender older sibling, respectively. Sections (d), (e) and (f) are transition matrices for male births, given a male/female/regardless gender older sibling, respectively.

#### a. Female births, given that there is an older brother

In Carvalho's paper, the following conditional probabilities were calculated:

1) a girl being autistic, given that she has an autistic older brother

$P(\text{AG}|\text{AB})=0.0422$ ;

2) a girl being autistic, given that she has a typical older brother

$P(\text{AG}|\text{TB})=0.0038$ ;

3) a girl being typical, given that she has an autistic older brother

$P(\text{TG}|\text{AB})=1-(\text{AG}|\text{AB})$ ;

and 4) a girl being typical, given that she has a typical older brother

$P(\text{TG}|\text{TB})=1-P(\text{AG}|\text{TB})$ .

These conditional probabilities constitute the transition matrix  $A(\text{MF})$ .

$$A(\text{MF}) = \begin{matrix} & \text{TG} & \text{AG} \\ \begin{bmatrix} P(\text{TG}|\text{TB}) & P(\text{AG}|\text{TB}) \\ P(\text{TG}|\text{AB}) & P(\text{AG}|\text{AB}) \end{bmatrix} & \begin{matrix} \text{TB} \\ \text{AB} \end{matrix} \end{matrix}$$

$$A(\text{MF}) = \begin{matrix} & \text{TG} & \text{AG} \\ \begin{bmatrix} 0.9962 & 0.0038 \\ 0.9578 & 0.0422 \end{bmatrix} & \begin{matrix} \text{TB} \\ \text{AB} \end{matrix} \end{matrix}$$

For clarification purposes, position  $\{A(\text{MF})\}=0.0038$  is the conditional probability value of  $P(\text{AG}|\text{TB})$ , which is the transition probability from the state TB to the state AG. In other words, it means the probability of a TD older brother having an ASD younger sister.

#### b. Female births, given that there is an older sister

From the diagnosis data, a girl being autistic, given that she has an autistic older sister ( $P(\text{AG}|\text{AG})=0.0759$ ); a girl being autistic, given that she has a typical older sister ( $P(\text{AG}|\text{TG})=0.0045$ ). Similar to the calculations above, we can constitute the transition matrix  $A(\text{FF})$ .

$$A(F) = \begin{array}{cc} & \begin{array}{cc} \text{TG} & \text{AG} \end{array} \\ \begin{array}{c} \text{TG} \\ \text{AG} \end{array} & \begin{bmatrix} P(\text{TG}|\text{TG}) & P(\text{AG}|\text{TG}) \\ P(\text{TG}|\text{AG}) & P(\text{AG}|\text{AG}) \end{bmatrix} \end{array}$$

$$A(F) = \begin{array}{cc} & \begin{array}{cc} \text{TG} & \text{AG} \end{array} \\ \begin{array}{c} \text{TG} \\ \text{AG} \end{array} & \begin{bmatrix} 0.9955 & 0.0045 \\ 0.9241 & 0.0759 \end{bmatrix} \end{array}$$

c. Female births, regardless the older sibling gender

From the diagnosis data, a girl being autistic, given that she has an autistic older sister ( $P(\text{AG}|\text{ASD})=0.0486$ ); a girl being autistic, given that she has a typical older sister ( $P(\text{AG}|\text{TD})=0.0041$ ). Similar to the calculations above, we can constitute the transition matrix  $A(XF)$ .

$$A(XF) = \begin{array}{cc} & \begin{array}{cc} \text{TG} & \text{AG} \end{array} \\ \begin{array}{c} \text{TD} \\ \text{ASD} \end{array} & \begin{bmatrix} P(\text{TG}|\text{TD}) & P(\text{AG}|\text{TD}) \\ P(\text{TG}|\text{ASD}) & P(\text{AG}|\text{ASD}) \end{bmatrix} \end{array}$$

$$A(XF) = \begin{array}{cc} & \begin{array}{cc} \text{TG} & \text{AG} \end{array} \\ \begin{array}{c} \text{TD} \\ \text{ASD} \end{array} & \begin{bmatrix} 0.9959 & 0.0041 \\ 0.9514 & 0.0486 \end{bmatrix} \end{array}$$

d. Male births, given that there is an older sister

From the diagnosis data, a boy being autistic, given that he has an autistic older sister ( $P(\text{AB}|\text{ASD})=0.1293$ ); a boy being autistic, given that he has a typical older sister ( $P(\text{AB}|\text{TD})=0.0154$ ). Similar to the calculations in part (a), we can constitute the transition matrix  $A(MM)$ .

$$A(MM) = \begin{array}{cc} & \begin{array}{cc} \text{TB} & \text{AB} \end{array} \\ \begin{array}{c} \text{TB} \\ \text{AB} \end{array} & \begin{bmatrix} P(\text{TB}|\text{TB}) & P(\text{AB}|\text{TB}) \\ P(\text{TB}|\text{AB}) & P(\text{AB}|\text{AB}) \end{bmatrix} \end{array}$$

$$A(MM) = \begin{array}{cc} & \begin{array}{cc} \text{TB} & \text{AB} \end{array} \\ \begin{array}{c} \text{TB} \\ \text{AB} \end{array} & \begin{bmatrix} 0.9846 & 0.0154 \\ 0.8707 & 0.1293 \end{bmatrix} \end{array}$$

e. Male births, given that there is an older brother

From the diagnosis data, a boy being autistic, given that he has an autistic older sister ( $P(\text{AB}|\text{ASD})=0.1681$ ); a boy being autistic, given that he has a typical older sister ( $P(\text{AB}|\text{TD})=0.0180$ ). Similar to the calculations in part (a), we can constitute the transition matrix  $A(FM)$ .

$$A(FM) = \begin{array}{cc} & \begin{array}{cc} \text{TB} & \text{AB} \end{array} \\ \begin{array}{c} \text{TG} \\ \text{AG} \end{array} & \begin{bmatrix} P(\text{TB}|\text{TG}) & P(\text{AB}|\text{TG}) \\ P(\text{TB}|\text{AG}) & P(\text{AB}|\text{AG}) \end{bmatrix} \end{array}$$

$$A(FM) = \begin{array}{cc} & \begin{array}{cc} \text{TB} & \text{AB} \end{array} \\ \begin{array}{c} \text{TG} \\ \text{AG} \end{array} & \begin{bmatrix} 0.9820 & 0.0180 \\ 0.8319 & 0.1681 \end{bmatrix} \end{array}$$

f. Male births, regardless the older sibling gender

From the diagnosis data, a boy being autistic, given that he has an autistic older

sister ( $P(AB|ASD)=0.1368$ ); a boy being autistic, given that he has a typical older sister ( $P(AB|TD)=0.0167$ ). Similar to the calculations in part (a), we can constitute the transition matrix  $A(XM)$ .

$$A(XM) = \begin{array}{cc} & \begin{array}{cc} TB & AB \end{array} \\ \begin{bmatrix} P(TB|TD) & P(AB|TD) \\ P(TB|ASD) & P(AB|ASD) \end{bmatrix} & \begin{array}{c} TD \\ ASD \end{array} \end{array}$$

$$A(XM) = \begin{array}{cc} & \begin{array}{cc} TD & ASD \end{array} \\ \begin{bmatrix} 0.9833 & 0.0167 \\ 0.8632 & 0.1368 \end{bmatrix} & \begin{array}{c} TD \\ ASD \end{array} \end{array}$$

#### 4. Emission Matrix

Because genetic factors are the ones with the highest ASD risk increase, the presence of ASD diagnosis/genes in parents was taken as the observable characteristic, which may allow predicting the probability of generating ASD children. By calculating the prevalence of TD and ASD children in the population, it can be found that population sex-ratio is 51.1% of boys ( $P(B)=0.511$ ), and 48.9% of girls ( $P(G)=0.489$ ).

A study conducted among siblings [5] has identified 14,516 children diagnosed with ASD. Such work studied 37570 twin pairs; 2642064 full sibling pairs; and 432281 maternal and 445531 paternal half-sibling pairs. This data was used for the determination of concordant and discordant sibling pairs, which allowed them to calculate ASD heritability. The best model was the one that used additive genetic and non-shared environmental parameters. The ASD heritability estimated was 83%. Thus, we have assumed that given an ASD child, there is a likelihood of 83% that its parents are also autistic ( $P(AP|ASD)=0.83$ ).

Two emission matrices were defined, one for boys ( $B(B)$ ) and one for girls ( $B(G)$ ). These two matrices were used for modeling all of our HMMs, according to the children's gender.

$$B(B) = \begin{array}{cc} & \begin{array}{cc} TP & AP \end{array} \\ \begin{bmatrix} 1 - P(AP|TB) & P(AP|TB) \\ 1 - P(AP|ASD) & P(AP|ASD) \end{bmatrix} & \begin{array}{c} TB \\ AB \end{array} \end{array}$$

$$B(B) = \begin{array}{cc} & \begin{array}{cc} TP & AP \end{array} \\ \begin{bmatrix} 0.9825 & 0.0175 \\ 0.1700 & 0.8300 \end{bmatrix} & \begin{array}{c} TB \\ AB \end{array} \end{array}$$

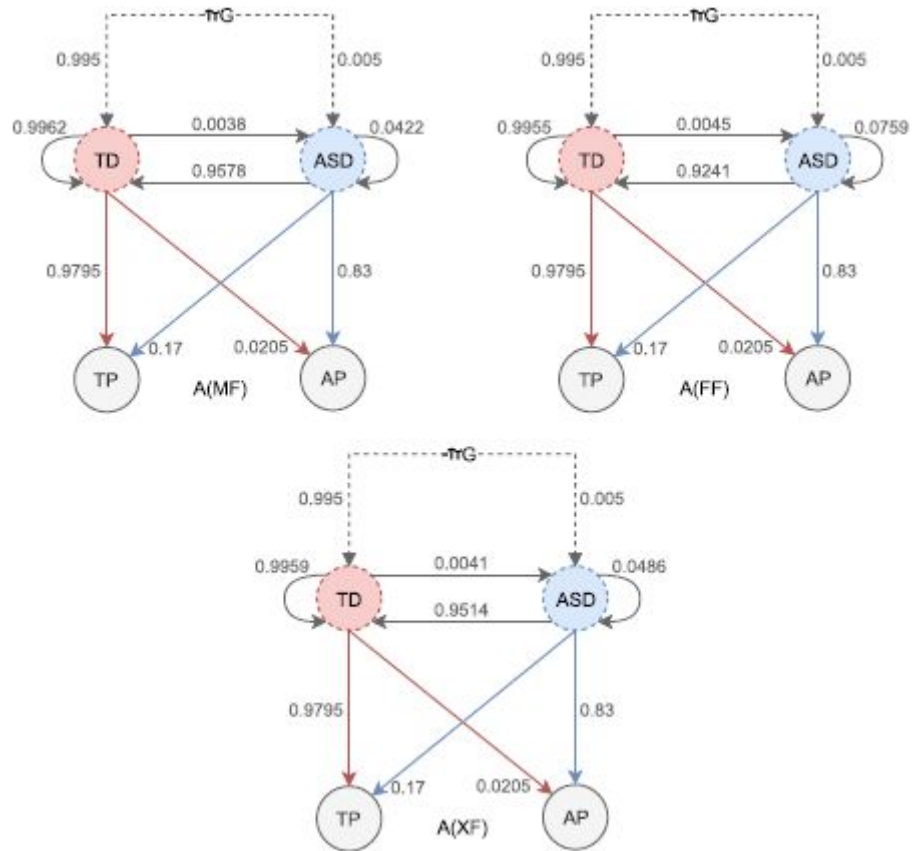
$$B(G) = \begin{array}{cc} & \begin{array}{cc} TP & AP \end{array} \\ \begin{bmatrix} 1 - P(AP|TG) & P(AP|TG) \\ 1 - P(AP|ASD) & P(AP|ASD) \end{bmatrix} & \begin{array}{c} TG \\ AG \end{array} \end{array}$$

$$B(G) = \begin{array}{cc} & \begin{array}{cc} TP & AP \end{array} \\ \begin{bmatrix} 0.9795 & 0.0205 \\ 0.1700 & 0.8300 \end{bmatrix} & \begin{array}{c} TG \\ AG \end{array} \end{array}$$

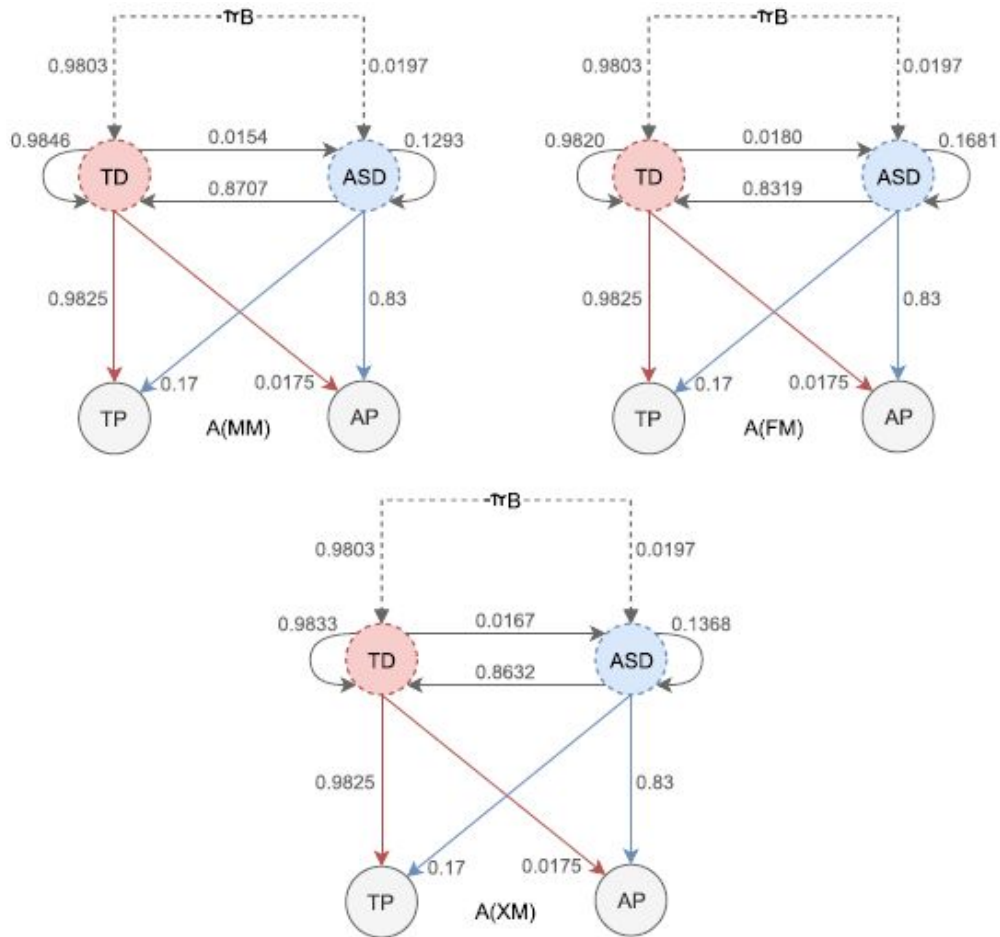
#### HMMs structure

The HMMs presented in Figure 1 and Figure 2 show our proposing HMMs structures and probabilities for female and male births, respectively. There are HMMs groups divided by gender because of the difference in statistical data regarding the prevalence and genetic inheritance of autism between male and female children.

The sources of initial state distributions, transition matrices and emission matrices were discussed in above sections.



**FIGURE 1. HMMs for predicting the probability of having ASD girls. A(MF): transition data given that the older sibling is a boy; A(FF): transition data given that the older sibling is a girl; A(XF): transition data regardless of the older sibling gender.**



**FIGURE 2. HMMs for predicting the probability of having ASD boys. A(MM): transition data, given that the older sibling is a boy; A(FM): transition data, given that the older sibling is a girl; A(XM): transition data regardless of the older sibling gender.**

## Simulation

Matlab was used for developing our HMM models. We implemented six HMM models as defined in the last section. The Hidden Markov Model (HMM) Toolbox was used to validate our self-built HMM model.

For each HMM set (boys and girls) and parents states/proles (TP and AP), we simulated the birth of male/female children, maintaining the pattern of two children per couple presented by [5].

## Results

We summarize our results in the following two tables.

**Table 1. Probabilities of TD parents generating TD/ASD boys**

	TB(%)	AB(%)
MM	100	0
FM	100	0
XM	100	0

**Table 2. Probabilities of ASD parents generating TD/ASD boys**

	TB(%)	AB(%)
MM	19.94	80.06
FM	5.24	94.76
XM	19.93	80.07

#### Paper Results

**Table 3. Probabilities of TD parents generating TD/ASD boys, provided in [1]**

	TB(%)	AB(%)
MM	99.7051	0.2949
FM	99.6855	0.3145
XM	99.6938	0.3062

**Table 4. Probabilities of ASD parents generating TD/ASD boys, provided in [1]**

	TB(%)	AB(%)
MM	21.014	78.986
FM	17.6446	82.3554
XM	20.3818	79.6182

#### Discussion

We have completed the resimulations for both probabilities of TD parents generating TD/ASD boys and ASD parents generating TD/ASD boys. Comparing the results as in the paper, our resimulation results are almost similar as theirs. The slight differences might be caused by the small number of data we used, which is only 100,000, compared with their 3,121,074 data. The prevalence of ASD is extremely small (0.0197%) and the probabilities of a younger ASD child birth given a TD older siblings are also small (0.0038), so with the size of data in our simulation, it's normal to have a small group of TD parents generating ASD boys.

## Bibliography

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- [4] J. Baio et al., "Prevalence of autism spectrum disorder among children aged 8 yearsAutism and developmental disabilities monitoring network, 11 sites, United States, 2014," *MMWR Surveill. Summaries*, vol. 67, no. 6, pp. 123, 2018.
- [5] N. Palmer, A. Beam, D. Agniel, A. Eran, A. Manrai, C. Spettell, G. Steinberg, K. Mandl, K. Fox, S. F. Nelson, and I. Kohane, "Association of sex with recurrence of autism spectrum disorder among siblings," *JAMA Pediatrics*, vol. 171, no. 11, pp. 11071112, 2017.
- [5] S. Sandin, P. Lichtenstein, R. Kuja-Halkola, C. Hultman, H. Larsson, and A. Reichenberg, "The heritability of autism spectrum disorder," *Jama*, vol. 318, no. 12, pp. 11821184, 2017.



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```
% HMM_for_MM
clear all
close all
clc
% Generate Data
    %TB      AB
P=[0.9846,0.0154; %TB
    0.8707,0.1293];%AB
N=100000;
U1 = rand;
if U1<0.9803
    X(1)=1;
else
    X(1)=-1;
end

for ii = 1:1:N-1
    if X(ii) == 1
        U1 = rand;
        if U1<P(1,1)
            X(ii+1)=1;
        else
            X(ii+1)=-1;
        end
    end

    if X(ii) == -1
        U1 = rand;
        if U1<P(2,2)
            X(ii+1)=-1;
        else
            X(ii+1)=1;
        end
    end
end

%TP      AP
Pb = [0.9825, 0.0175 %TB
    0.17,    0.83]; %AB

for ii = 1:1:N
    if X(ii)==1 %TP
        U1 = rand;
        if U1<Pb(1,1)
            y(ii)=1; %TP
        else
            y(ii)=-1; %AP
        end
    end
end
```

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```

        if X(ii) == -1 %ASD
            U1 = rand;
            if U1<Pb(2,1)
                y(ii)=1; %TP
            else
                y(ii)=-1; %AP
            end
        end
    end
end

for ii = 1:1:N
    U1 = rand;
    if U1<0.2
        y(ii)=1; %TP
    else
        y(ii)=-1; %AP
    end
end

end

% Estimation---HMM Model
Pi(1,1:2) = [0.9803, 0.0197];

for ii = 1:1:N-1
    Pi(ii+1, 1) = ((y(ii+1)==1)*Pb(1,1)+(y(ii
+1)==-1)*Pb(1,2))*Pi(ii,:)*P(:, 1);
    Pi(ii+1, 2) = ((y(ii+1)==1)*Pb(2,1)+(y(ii
+1)==-1)*Pb(2,2))*Pi(ii,:)*P(:, 2);

    sum = Pi(ii+1, 1)+Pi(ii+1, 2);

    Pi(ii+1, 1) = Pi(ii+1, 1)./sum;
    Pi(ii+1, 2) = Pi(ii+1, 2)./sum;
end

[M,I] = max(Pi,[],2);

I_1 = find(I==1);
I_2 = find(I==2);

new_I = zeros(1,N);

new_I(I_1)=1;
new_I(I_2)=-1;

% observation is parents, state is children
I11 = find(y==1&new_I==1);
I22 = find(y==1);

AP_AB = length(I11)/length(I22)
AP_TB = 1-AP_AB

```

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```
I11 = find(y==1&new_I==-1);  
I22 = find(y==1);  
  
TP_AB = length(I11)/length(I22)  
TP_TB = 1-TP_AB
```

```
AP_AB =  
  
    0.8000
```

```
AP_TB =  
  
    0.2000
```

```
TP_AB =  
  
    0
```

```
TP_TB =  
  
    1
```

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```
% HMM_for_FM

clear all
close all
clc
% Generate Data
%TB      AB
P=[0.9820,0.0180; %TG
   0.8319,0.1681];%AG
N=100000;
U1 = rand;
if U1<0.9803
    X(1)=1;
else
    X(1)=-1;
end

for ii = 1:1:N-1
    if X(ii) == 1
        U1 = rand;
        if U1<P(1,1)
            X(ii+1)=1;
        else
            X(ii+1)=-1;
        end
    end

    if X(ii) == -1
        U1 = rand;
        if U1<P(2,2)
            X(ii+1)=-1;
        else
            X(ii+1)=1;
        end
    end
end

%TP      AP
Pb = [0.9825, 0.0175 %TB
      0.17,   0.83]; %AB

for ii = 1:1:N
    if X(ii)==1 %TP
        U1 = rand;
        if U1<Pb(1,1)
            y(ii)=1; %TP
        else
            y(ii)=-1; %AP
        end
    end
end
```

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```

        end
        if X(ii) == -1 %ASD
            U1 = rand;
            if U1<Pb(2,1)
                y(ii)=1; %TP
            else
                y(ii)=-1; %AP
            end
        end
    end
end

for ii = 1:1:N
    U1 = rand;
    if U1<0.2
        y(ii)=1; %TP
    else
        y(ii)=-1; %AP
    end
end

% Estimation---HMM Model
Pi(1,1:2) = [0.9803, 0.0197];

for ii = 1:1:N-1
    Pi(ii+1, 1) = ((y(ii+1)==1)*Pb(1,1)+(y(ii
+1)==-1)*Pb(1,2))*Pi(ii,:)*P(:, 1);
    Pi(ii+1, 2) = ((y(ii+1)==1)*Pb(2,1)+(y(ii
+1)==-1)*Pb(2,2))*Pi(ii,:)*P(:, 2);

    sum = Pi(ii+1, 1)+Pi(ii+1, 2);

    Pi(ii+1, 1) = Pi(ii+1, 1)./sum;
    Pi(ii+1, 2) = Pi(ii+1, 2)./sum;
end

[M,I] = max(Pi,[],2);

I_1 = find(I==1);
I_2 = find(I==2);

new_I = zeros(1,N);

new_I(I_1)=1;
new_I(I_2)=-1;

% observation is parents, state is children
I11 = find(y==1&new_I==1);
I22 = find(y==1);

AP_AB = length(I11)/length(I22)
AP_TB = 1-AP_AB

```

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```
I11 = find(y==1&new_I==-1);  
I22 = find(y==1);  
  
TP_AB = length(I11)/length(I22)  
TP_TB = 1-TP_AB
```

```
AP_AB =  
  
    0.9489
```

```
AP_TB =  
  
    0.0511
```

```
TP_AB =  
  
    0
```

```
TP_TB =  
  
    1
```

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```
% HMM_for_XM
clear all
close all
clc
% Generate Data
    %TB      AB
P=[0.9833,0.0167; %TD
    0.8632,0.1368];%ASD
N=100000;
U1 = rand;
if U1<0.9803
    X(1)=1;
else
    X(1)=-1;
end

for ii = 1:1:N-1
    if X(ii) == 1
        U1 = rand;
        if U1<P(1,1)
            X(ii+1)=1;
        else
            X(ii+1)=-1;
        end
    end

    if X(ii) == -1
        U1 = rand;
        if U1<P(2,2)
            X(ii+1)=-1;
        else
            X(ii+1)=1;
        end
    end
end

end

    %TP      AP
Pb = [0.9825, 0.0175 %TB
    0.17,    0.83]; %AB

for ii = 1:1:N
    if X(ii)==1 %TP
        U1 = rand;
        if U1<Pb(1,1)
            y(ii)=1; %TP
        else
            y(ii)=-1; %AP
        end
    end
end
```

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```

        if X(ii) == -1 %ASD
            U1 = rand;
            if U1<Pb(2,1)
                y(ii)=1; %TP
            else
                y(ii)=-1; %AP
            end
        end
    end
end

for ii = 1:1:N
    U1 = rand;
    if U1<0.2
        y(ii)=1; %TP
    else
        y(ii)=-1; %AP
    end
end

end

% Estimation---HMM Model
Pi(1,1:2) = [0.9803, 0.0197];

for ii = 1:1:N-1
    Pi(ii+1, 1) = ((y(ii+1)==1)*Pb(1,1)+(y(ii
+1)==-1)*Pb(1,2))*Pi(ii,:)*P(:, 1);
    Pi(ii+1, 2) = ((y(ii+1)==1)*Pb(2,1)+(y(ii
+1)==-1)*Pb(2,2))*Pi(ii,:)*P(:, 2);

    sum = Pi(ii+1, 1)+Pi(ii+1, 2);

    Pi(ii+1, 1) = Pi(ii+1, 1)./sum;
    Pi(ii+1, 2) = Pi(ii+1, 2)./sum;
end

[M,I] = max(Pi,[],2);

I_1 = find(I==1);
I_2 = find(I==2);

new_I = zeros(1,N);

new_I(I_1)=1;
new_I(I_2)=-1;

% observation is parents, state is children
I11 = find(y==1&new_I==1);
I22 = find(y==1);

AP_AB = length(I11)/length(I22)
AP_TB = 1-AP_AB

```

---



---

```
I11 = find(y==1&new_I==-1);  
I22 = find(y==1);  
  
TP_AB = length(I11)/length(I22)  
TP_TB = 1-TP_AB
```

```
AP_AB =  
  
    0.8010
```

```
AP_TB =  
  
    0.1990
```

```
TP_AB =  
  
    0
```

```
TP_TB =  
  
    1
```

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