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Simulation based inference for MRI diffusion microstructure models

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Motivation & Introduction

Simulator:

Definition:
θ : Parameters vector of the simulator
x : Data vector generated by the simulator
x_o : Observation data acquired from experiment
$p(\theta)$: Prior distribution of the parameter
$p(x = x|\theta)$: Possibility of simulator generating data x given the prior θ

In many science fields, the mechanism under the observation is unknown. Therefore, we can use a simulator to approximate and analysis the mechanism under observation. Let's define the simulator as a generative model that can be used to simulate synthetic data x ~ p(x|θ) , where θ is the simulator parameters.

Simulation based inference (SBI):

Simulation based inference online(SBI) [1] is a machine learning field can be applied to fine tune the parameter and analysis the parameters correlation.

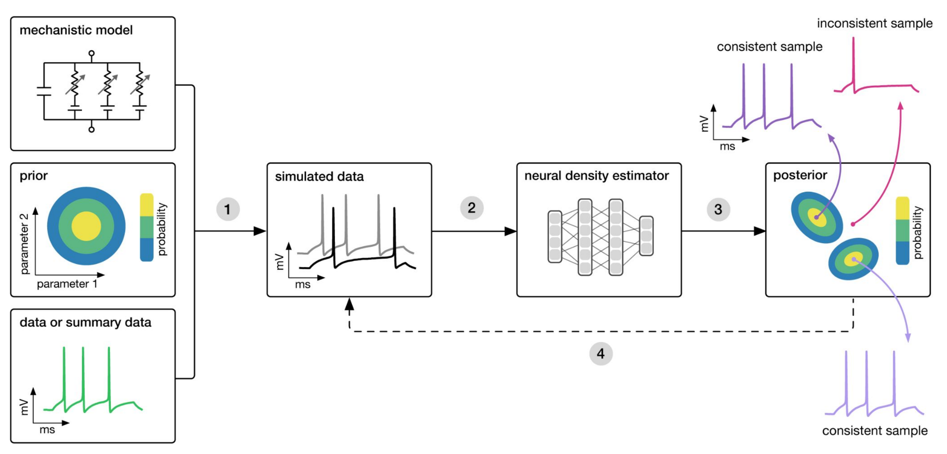


Fig 1: Basic simulation based inference

The basic SBI pipeline is defined in Fig 1. it contains such steps:. 1) Set biophysical prior parameters for a simulator, and generate some synthetic data. 2) Feed the synthetic data into a deep learning network. 3) Use the trained network to predict posterior parameters for the simulator. 4) Combine the observation data for fine tuning.

MRI diffusion microstructure model:

The MRI imaging theory is based on detecting the free water movement in the neuron cells. If the free water moves along the axons, it will move faster, if it moves perpendicular to the axon, it will move slower.

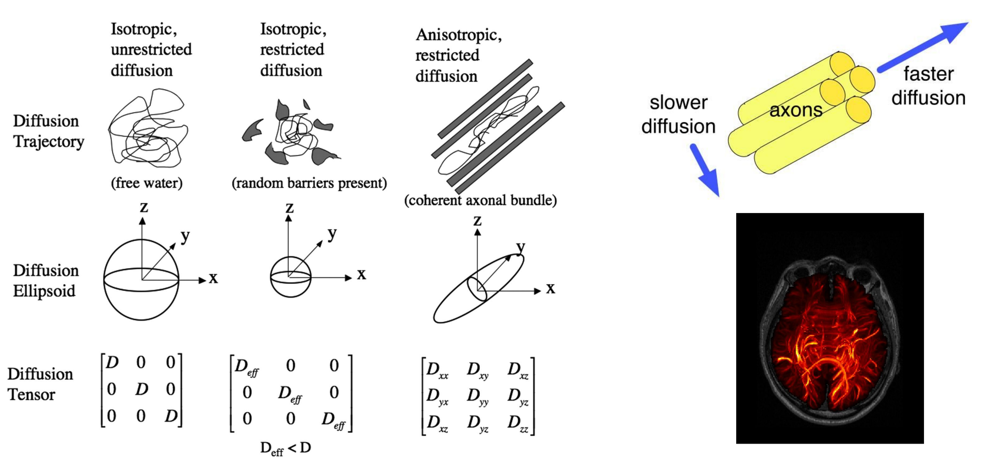


Fig 2: Basic MRI diffusion model

Fig 2 defines the basic pipeline of MRI diffusion model [2]. This paper use a tensor to describe the water movement in the brain. If this voxel is in the axons, the geometry looks like a ellipsoid, if it is in CSF, the it looks like a ball. Then we can get the eigen vector and eigen value of this tensor, which its eigen vector and value we can track the fiber orientation of the cells.

$$S_k = S_0 e^{-b g_k^T \mathbf{D} g_k} \qquad \text{eq 1}$$

Equation 1 defines the MRI signal decay according to this diffusion tensor. S_o is the initial MR signal, Sk is the decreased MR signal. All these can be detected from the MRI scanners. If we use a more complex model, then we can add more biophysical priors to it.

Related work

In our experiment we have use NODDI as simulating models [3], and tried different SBI methods on it. Finally we find SNPE-C [4] is most appropriate for our data.

Noddi:

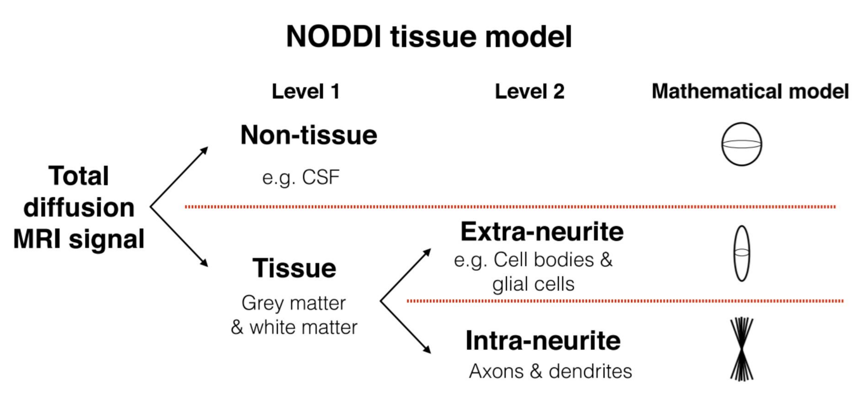


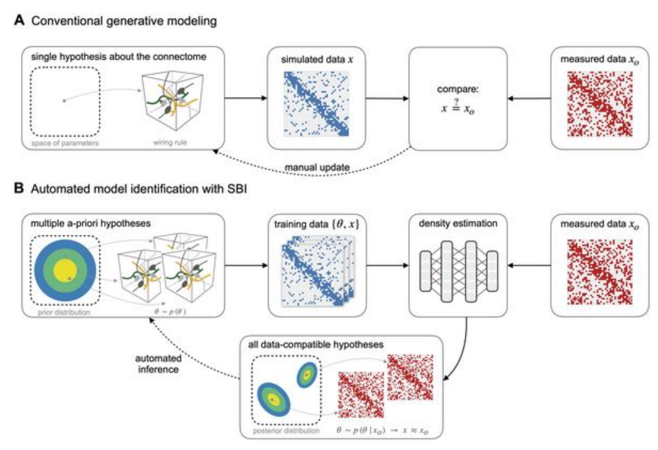
Fig 3: Noddi model

Fig 3 shows you the basic idea of the NODDI model. This model consists of three parts, CSF, grey matter and white matter. Each compartment has a signal function to describe the MRI signal decay in that brain tissue. And the merged signal A consists of all these three parts.. The according function is in equation 2.

$$A = (1 - v_{iso})\left(v_{ic} A_{ic} + (1 - v_{ic}) A_{ec}\right) + v_{iso} A_{iso} \qquad \text{eq 2}$$

SNPE-C (SBI):

Fig 4 shows you the pipeline of SNPE-C and compares it with the classical SBI. A is the pipeline of classical SBI, it needs to manually fit to the observation data. In SNPE-C, it has added a automatic pipeline to combine it with the real data. The following pseudo code is the algorithm for SNPE-C



Input: simulator with (implicit) density $p(x|\theta)$, data x_o, prior $p(\theta)$, density family q_ψ, neural network $F(x, \phi)$, simulations per round N, number of rounds R.

$\tilde{p}_1(\theta) := p(\theta)$
for $r = 1$ **to** R **do**
  for $j = 1$ **to** N **do**
    Sample $\theta_{r,j} \sim \tilde{p}_r(\theta)$
    Simulate $x_{r,j} \sim p(x|\theta_{r,j})$
  end for
  $\phi \leftarrow \underset{\phi}{\operatorname{argmin}} \sum_{i=1}^{r} \sum_{j=1}^{N} -\log \tilde{q}_{x_{i,j},\phi}(\theta_{i,j})$
  $\tilde{p}_{r+1}(\theta) := q_{F(x_o,\phi)}(\theta)$
end for
return $q_{F(x_o,\phi)}(\theta)$

Fig 4: Pipeline of SNPE-C

Experiment & Result

Data preprocessing: Denoise & Normalization

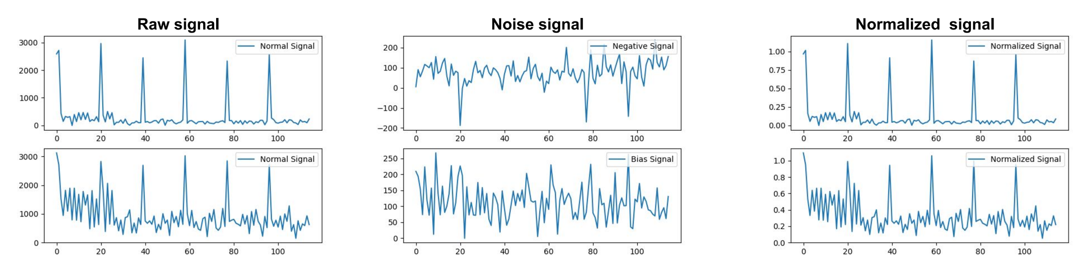


Fig 5: Signal analysis

Fig 5 shows you the data preprocessing. The raw signal can have noise like negative value. We delete all the voxels with negative value. Then normalize the signal by dividing the average of the b0.

MRI Diffusion model initialization:

We have set 7 free parameters from the NODDI model, they are [theta, phi] to describe the orientation of the voxels, we have also set the Orientation Dispersion Index(ODI), Intra-Cellular Volume Fraction(ICVF), Isotropic Volume Fraction(ISOVF) and Non-Isotropic Volume Fraction(anISOVF) as the free parameters. We have added noise also as a free parameter for the model. All the other parameters are fixed value.

Simulation based inference setup:

Here we selected SNPE-C as the SBI inference model, generating 30000 samplings for the training. The simulator if the initialized Noddi model.

Experiment result (SNPE-C):

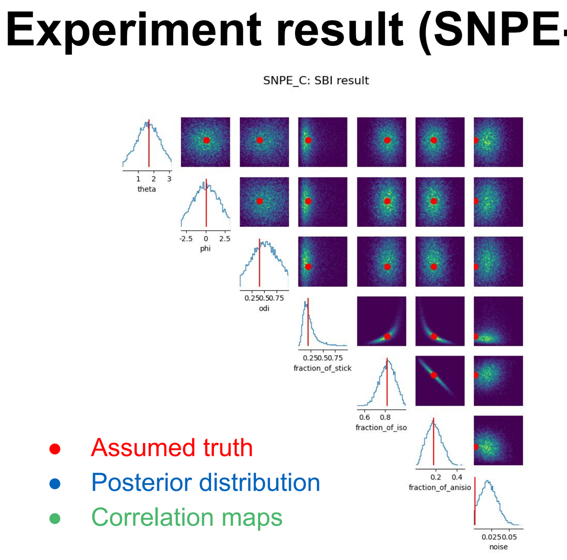


Fig 6: Training result for one voxel

Here is the training result of SNPE-C for one voxel. At first, we set assumed true values of the 7 free parameters. The SNPE-C network will generate posterior for these 7 free parameters. We pair plot the correlation maps of the different parameters. The result is in fig 6. The result for this voxel looks good, because the prediction is close to the assumed groundtruth.

After the training, then we need to fit the model to our real data. Fig 7 shows you the result of the fitting. The blue line is the real data, the yellow line the the generating sample from our simulating model.

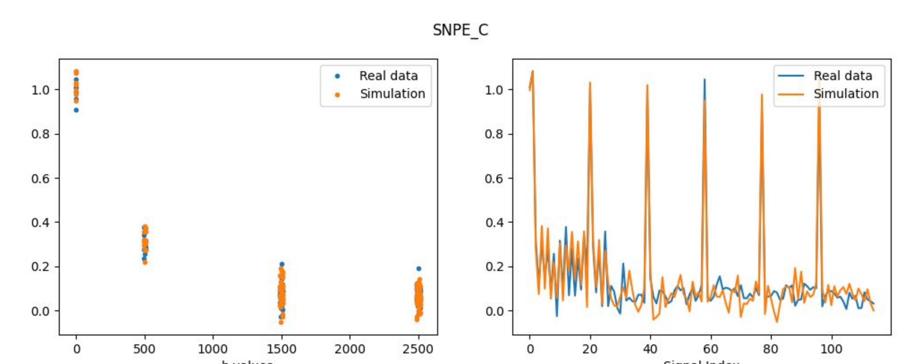


Fig 7: Comparison of the simulation and real data

The result looks good. The simulated signal from the Noddi model after training looks similar to the real data. But this is only for one voxels, to make sure the result is also good for most case, we random selected 500 voxels from real data, predict the posterior for these 7 free parameters, then calculate the difference of the assumed truth and the predicted posterior, we use a histogram in fig 8 to show this prediction bias.

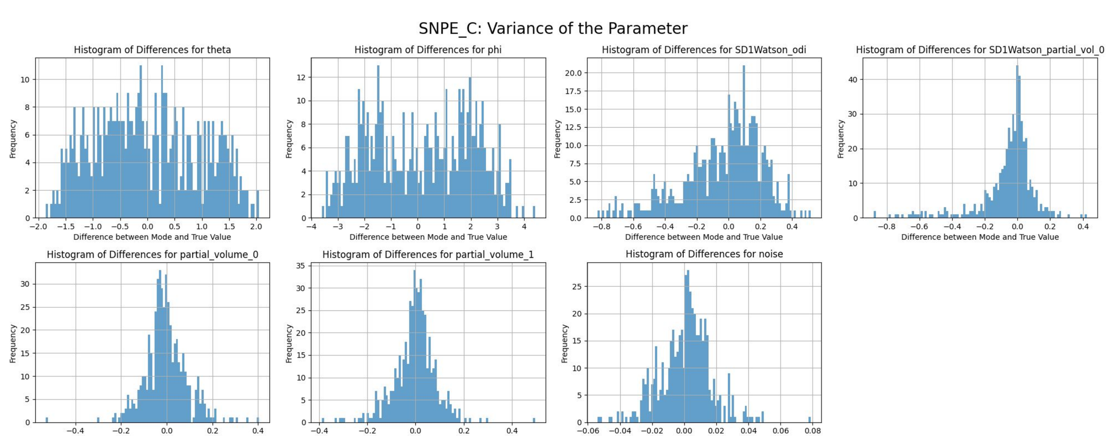


Fig 8: Prediction bias of SNPE-C

If the result is good, the peak of the histogram shoule be close to 0. The training result of ODI, ICVF, ISOVF, anISOVF are converge to 0, that means the results for these parameters are good. But the result for theta and phi are not converge. That is because we have set all parameters as uniform distribution, but if we use angle to describe the orientation, the theta and phi are not uniform distributed.

Comparison of SBI methods:

All the metrics we have mentioned before are for one SBI algorithm, we have tested the following algorithms [5][6][7][8][9][10][11], compare there performance and finally selected the SNPE-C for our real data.

Methods	Converge epochs	Fitting time for one voxel/ms	Prediction bias	Robust
SNPE-A	163	7380	✓	✖
SNPE-C	**84**	**203**	✓	✓
SNLE	196	168034	✓	✖
SNLE-V	123	622375	None	None
SNRE	56	51500	None	None
SNRE-V	73	5743218	None	None
BNRE	110	None	None	None
MNLE	134	None	None	None

Table 1: Comparison of different SBI methods

Table 1 compares the performance of difference SBI algorithm. We compare the epochs for the SBI to converge, and the time for prediction of one voxel. The prediction bias is like fig 8, If the bias converge to 0, it means this algorithm for the real data. The robust is shown in fig 9, the algorithm should not ignore too much voxels. This table shows that only SNPE-C works for our real data.

Robust:

As mentioned in the section MRI diffusion model initialization, we have set the noise as a threshold. We set the noise also as a uniform distribution from 0 to the threshold value. Different maximum threshold will cause different result. If the maximum threshold is high, it result is robust and ignore less voxel, if the threshold is low, the result is accurate and ignore more voxel. So we need to get a balance of the accuracy and robust. Finally we selected 0.1 as the miximum threshold of noise. Fig 9 shows you the comparison of different threshold.

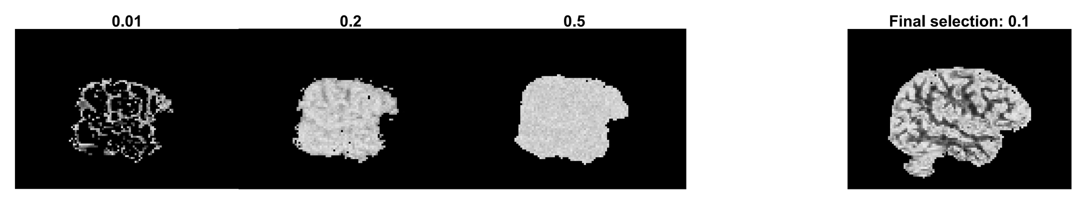


Fig 9a: Result of different noise threshold

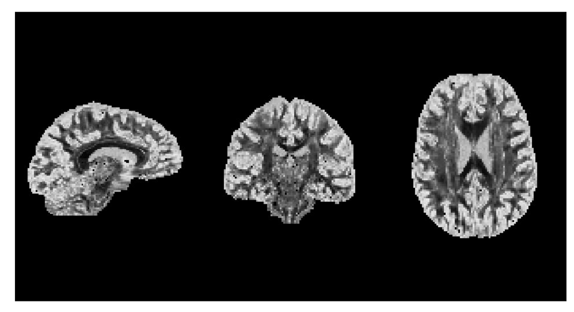


Fig 9b: ODI with 0.1 noise

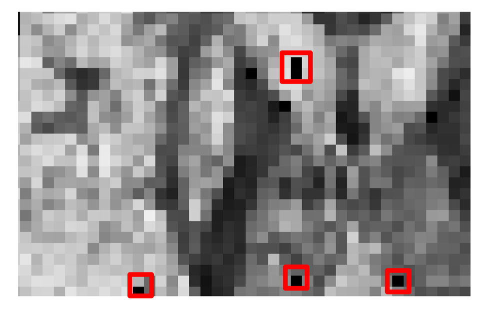


Fig 9c: Ignored voxel of ODI with 0.1 noise

Reconstruction & Visulization:

After the training and precessing the bias, now we can reconstruct and visuliza the final result for all the voxels. Asmentioned, SNPE-C is applied for all the voxels in a brain, so we can get the index of the voxel and reconstruct the 3D images of all the brain. Fig 10 is the result ODI, ISOVF and ICVF by SNPE-C. We have also use a classical deep learning network Brute2fine [12] to predict such index and compare the result in fig 10.

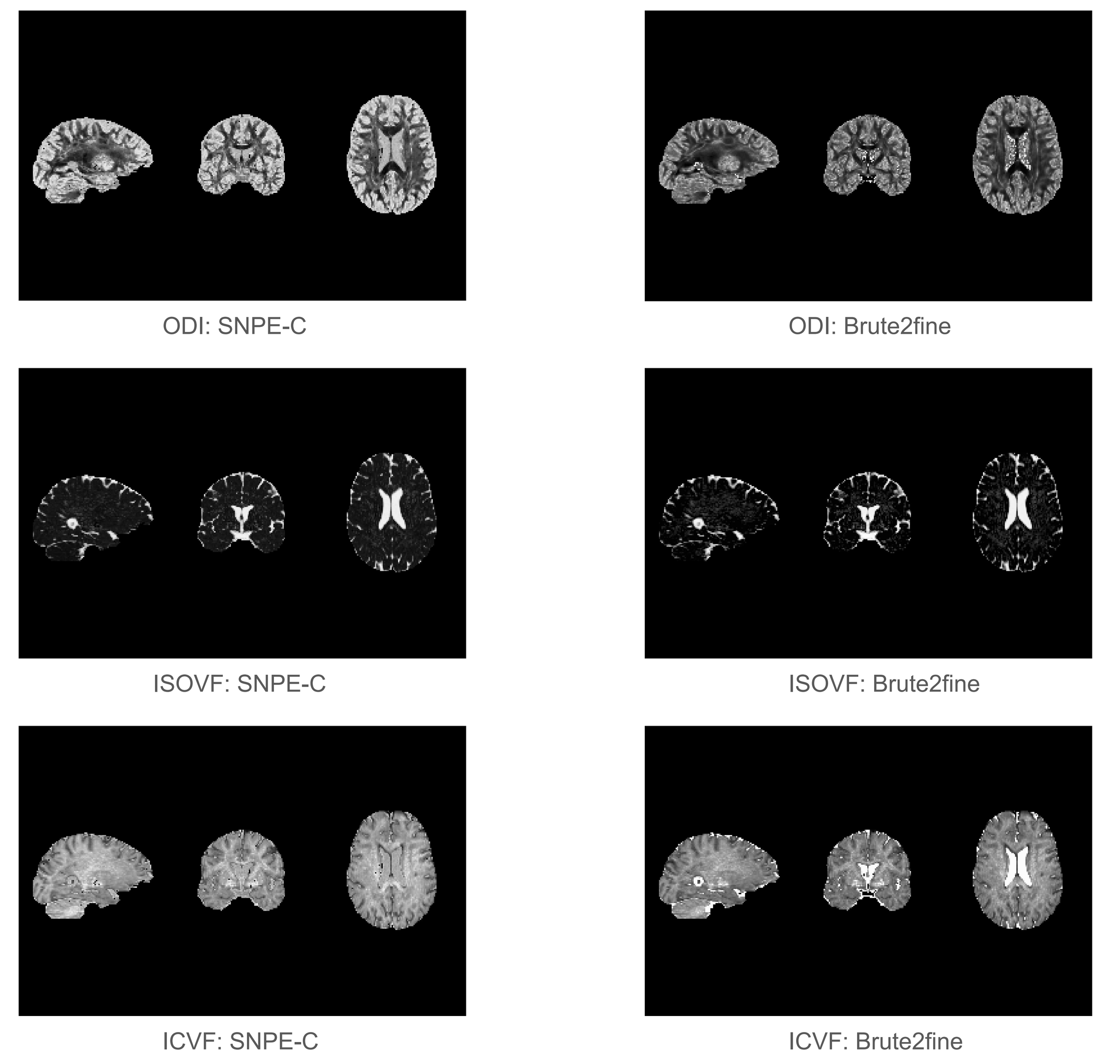


Fig 10: Compare the result of SNPE-C and Brute2fine

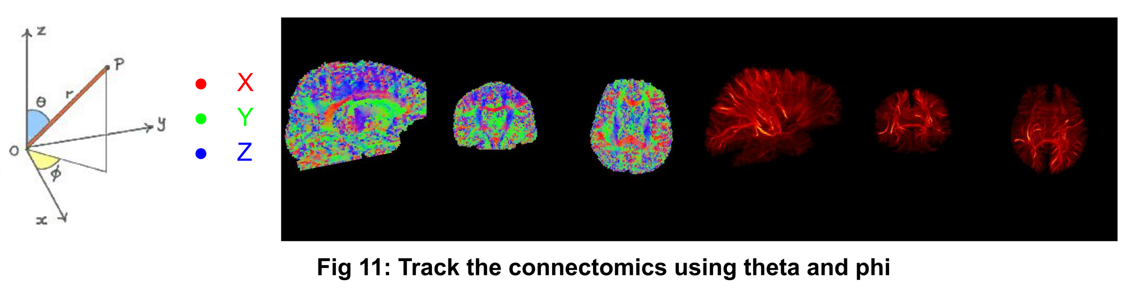


Fig 11: Track the connectomics using theta and phi

In fig 11 we use the theta and phi to track the connectomics in the human brain. Because the X, Y, Z coordinate are fixed, so we only need two angle to describe the orientation of the neuron fibers. But the result I shown here is not the result from SBI, but the result of BedpostX and Tractography from FSL [13].

Conclusion

In theory, simulation based inference can improve the accuracy of the prediction, because it can add the related prior knowledge to the simulator. While the other classical deep learning network only focus on the images. But our experiment shows that simulation based inference is too sensitive to the noise data, when the noise of real data is too high, the rejection function of SBI will deney this sample. To balance the robust and accuracy we have modified to algorithm, the SBI will return a blank sample when the noise is too high. What more, the SBI package is still in developing, it does not support CUDA to accelerate the training.

In summary, SBI should have higher accuracy comparing with the classical deep learning methods. But it is a new tool in developing, we still need time to enhance their performance.

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