# Fast Non-Markovian Diffusion Model for Weakly Supervised Anomaly Detection in Brain MR Images

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**Abstract.** In medical image analysis, anomaly detection in weakly supervised settings has gained significant interest due to the high cost associated with expert-annotated pixel-wise labeling. Current methods primarily rely on auto-encoders and flow-based healthy image reconstruction to detect anomalies. However, these methods have limitations in terms of high-fidelity generation and suffer from complicated training processes and low-quality reconstructions. Recent studies have shown promising results with diffusion models in image generation. However, their practical value in medical scenarios is restricted due to their weak detail-retaining ability and low inference speed. To address these limitations, we propose a fast non-Markovian diffusion model (FNDM) with hybrid-condition guidance to detect high-precision anomalies in the brain MR images. A non-Markovian diffusion process is designed to enable the efficient transfer of anatomical information across diffusion steps. Additionally, we introduce new hybrid pixel-wise conditions as more substantial guidance on hidden states, which enables the model to concentrate more efficiently on the anomaly regions. Furthermore, to reduce computational burden during clinical applications, we have accelerated the encoding and sampling procedures in our FNDM using multi-step ODE solvers. As a result, our proposed FNDM method outperforms the previous state-of-the-art diffusion model, achieving a 9.56% and 19.98% improvement in Dice scores on the BRATS 2020 and ISLES datasets, respectively, while requiring only six times less computational cost.

**Keywords:** Anomaly Detection · Diffusion Probabilistic Model · Medical Image Analysis

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## 1 Introduction

Weakly supervised anomaly detection holds significant potential in real-world clinical applications [27], particularly for new pandemic diseases where obtaining pixel-wise annotations from human experts is challenging or even impossible [16]. However, dominant anomaly detection methods based on the one-class classification paradigm [8,11] often overlook the binary labels of healthy and disease samples available in clinical centers, limiting their detection granularity. Traditional clustering techniques like z-score thresholding [15], PCA [14], and SVM [26] have limited clinical value as they mainly generate image-level anomaly results. To address this paradox, deep generative models leverage additional pixel-wise domain knowledge captured through adversarial training [1,12,24] or latent representation encoding [3,4,6,32]. While these approaches allow obtaining pixel-wise anomaly maps through Out-Of-Distribution (OOD) detection, they often fail to generate high-fidelity segmentation maps due to inadequate utilization of image conditions. Thus, the utilization of domain knowledge from weakly supervised data becomes a crucial factor in achieving high-quality anomaly detection.

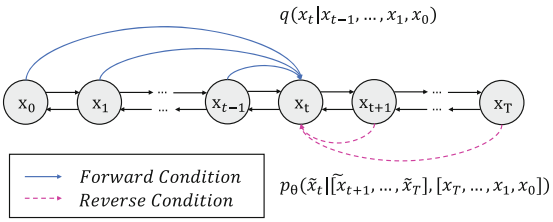


**Fig. 1. Non-Markovian Diffusion Framework**: To enhance information transfer, we make an assumption that the forward states and reverse states at the same time step $t$ follow different distributions. Based on this assumption, we introduce conditions in the forward process, where all previous states are used as conditions for the current state. This enables efficient information transfer between states. And the final state $x_T$ incorporates comprehensive information from the forward states. Similarly, the reverse process incorporates information from previous reverse states.

Moreover, traditional generative models, such as GANs [1,12] and normalizing flows [11], commonly used for pixel-wise anomaly detection, are constrained by one-step data projection in handling complex data distributions. This dilemma can be overcome by employing probabilistic diffusion models [13,25] that capture data knowledge through a series of step-by-step Markovian processes [5]. The high-fidelity generation proficiency, flexible network architecture, and stable training scheme of existing diffusion-based anomaly detection approaches have demonstrated promising performance in detecting anomaly regions [23,27–29]. However, diffusionnv-based approaches have high computational costs due to iterative evaluations. [20] explores the diffusion on the latent

space with smaller sizes instead of pixel space to reduce the computations. Moreover, all these methods still face challenges including the lack of fine-grained guidance and gradual loss of anatomical information in Markovian chains.

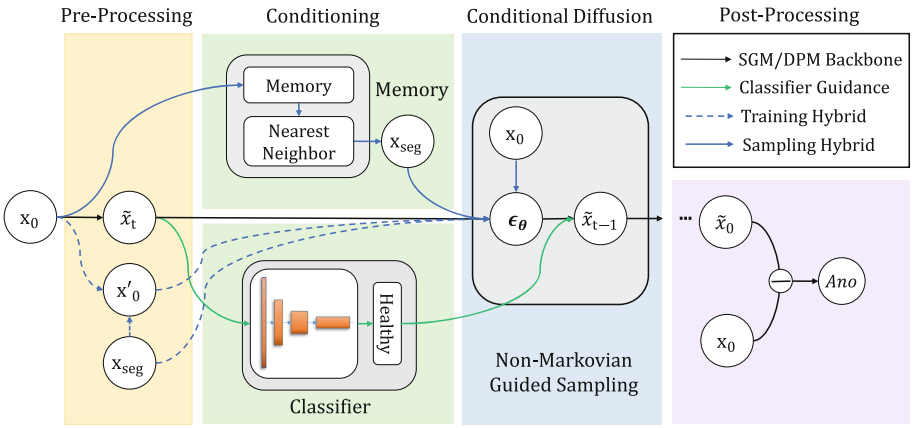


**Fig. 2. Overall Framework of FNDM**: The hybrid conditional noise prediction network $\epsilon_\theta$ and binary classifier are separately trained. FNDM combines image state $\tilde{x}_t$, original data $x_0$ and coarse segmentation map $x_{seg}$ into $\epsilon_\theta$, processing multi-step ODE sampling together with classifier gradient from current data. Finally, we obtain anomaly maps by subtraction.

To address these limitations, we propose a novel non-Markovian hybrid-conditioned diffusion model with fast samplers. Our approach utilizes strong hybrid image conditions that provide powerful sampling guidance by integrating coarse segmentation maps and original instance information based on the non-Markovian assumption (as shown in Fig. 1). Additionally, we modify the forward and reverse process as a higher-order deterministic Ordinary Differential Equation (ODE) sampler to accelerate inference. We validate our framework on two brain medical datasets, demonstrating the effectiveness of the framework components and showing more accurate detection results of anomaly regions.

## 2 Method

In this section, we present a fast non-Markovian diffusion model that utilizes pixel-wise strong conditions and encoding/sampling accelerator for anomaly segmentation to enhance generation fidelity and sampling speed. Section 2.1 introduces the non-Markonvian model and hybrid conditions for guided sampling. Section 2.2 proposes the acceleration approach for encoding and sampling.

### 2.1 Non-Markovian Diffusion Model with Hybrid Condition

Learning deterministic mappings between diseased and healthy samples sharing the same anatomical structures is essential to enhance inaccurate and time-consuming diffusion-based approaches, which require strong guidance during sampling. However, current diffusion-based models only provide insufficient conditions (such as binary classification results), leading to vague anomaly distributions. To achieve consistent and stable generation, we propose a hybrid conditional diffusion model dependent on the non-Markovian assumption. It injects noise into the original distribution sequentially using the Gaussian distribution and then reconstructs the original distribution by reverse sampling. Following the expression of [13], the Markovian-based diffusion framework is defined as:

$$q\left(\mathbf{x}_{1:T} \mid x_0\right) := \prod_{t=1}^{T} q\left(x_t \mid x_{t-1}\right), \quad p_\theta\left(\mathbf{x}_{0:T}\right) := p\left(x_T\right) \prod_{t=1}^{T} p_\theta\left(x_{t-1} \mid x_t\right), \tag{1}$$

where the discrete states $\{x_t\}_{t=0}^{T}$ are from step 0 to $T$, forward step $q$ and trained reverse step $p_\theta$ have one-to-one mapping. Denoting $\{\alpha_t\}_{t=0}^{T}$ and $\{\sigma_t\}_{t=0}^{T}$ as variance scales for noise perturbation, the Gaussian transition kernels are:

$$\begin{aligned} q\left(x_t \mid x_{t-1}\right) &:= \mathcal{N}\left(x_t; \sqrt{\alpha_t} x_{t-1}, (1-\alpha_t)\mathbf{I}\right) \\ p_\theta\left(x_{t-1} \mid x_t\right) &:= \mathcal{N}\left(x_{t-1}; \boldsymbol{\mu}_\theta\left(x_t, t\right), \boldsymbol{\sigma}_t\right). \end{aligned} \tag{2}$$

To keep the anatomical information across states, the proposed non-Markovian anatomy structure mappings are built by adding previous-state information into forward and reverse states, which preserves distribution prior for high-quality reconstruction. Denoting all accumulated states from the forward process as $c$ and the state in the backward step $t$ as $\tilde{x}_t$, we formulate the Generalized Non-Markovian Diffusion Framework (GNDF) as:

$$q(\mathbf{x}_{0:T}) := q(x_0) \prod_{t=1}^{T} q(x_t|x_{i<t}), \quad p_\theta\left(\tilde{\mathbf{x}}_{0:T}|c\right) := p(\tilde{x}_T|c) \prod_{t=T}^{1} p_\theta(\tilde{x}_{t-1}|\tilde{x}_{i\geq t}, c) \tag{3}$$

Similar to vanilla DDPM [13], our conditional noise prediction network is trained according to the negative log-likelihood (NLL) lower bound minimization of generated distributions. It is further transformed into the L2 loss between the estimated conditional noise and the ground-truth Gaussian noise as:

$$\begin{aligned} \mathcal{L} &:= \mathbb{E}\left[-\log p_\theta\left(x_0\right)\right] \\ &\leq \mathbb{E}_{x_0,t}\left[\mathcal{KL}(p_\theta(\tilde{x}_{t-1}|\tilde{x}_t, c)|q(x_{t-1}|x_t, x_{t-2}, ..., x_0))\right] \\ &= \mathbb{E}_{x_0,\epsilon,t}\left[\omega(t)\left\|\epsilon_\theta\left(\tilde{x}_t, t, c\right) - \epsilon\right\|_2^2\right]. \end{aligned} \tag{4}$$

To enable the diffusion model to effectively differentiate between anatomical and anomaly information from previous states, we introduce a hybrid condition that includes the input state $x_0$, coarse segmentation maps, and classifier

gradients derived from healthy labels. In order to simplify the computational complexity and leverage the rich information contained in $x_0$, we replace the forward state conditions $c$ with the original state $x_0$.

Regarding hybrid condition implementation, we train a binary classifier with healthy and diseased images to provide further guidance on anomaly regions independently, following class-conditional methods [10,27]. A memory bank [21] is applied to store representative features of healthy samples, which enables quick generation of coarse segmentation maps $x_{seg}$ during the testing phase, addressing the issue of knowledge forgetting in original diffusion models. To keep the active segmentation map as a condition in the diffusion model training, a health image $x_0$ is transformed into a diseased image $x_0^n$ based on a random $x_{seg}$.

Overall, we train our non-Markovian diffusion model depending on the current states, the coarse segmentation maps, image labels, and the original data during the diffusion process with healthy and diseased images. The training objective is given by:

$$\min_{\theta} \mathbb{E}_{x_0,\epsilon,t}\left[\omega(t)\left\|\epsilon_\theta\left(\tilde{x}_t^{'}, t, y\right)-\epsilon\right\|_2^2\right], \tag{5}$$

where $\tilde{x}_t^{'}$ is the concatenation of $\tilde{x}_t$, $x_0^n$, and $x_{seg}$. $y$ denotes the corresponding binary label for each data. $\omega(t)$ is a weighted function for providing dynamic weights to explore density regions. In this work, we simply set $\omega(t)$ as 1. The full framework of our model is shown in Fig. 2.

### 2.2 Accelerated Encoding and Sampling

Diffusion acceleration, which is equivalent to reconstruction error minimization [7], is implemented by balancing the trade-off between sample quality and computation cost. Existing diffusion-based anomaly detectors [27] require a significant number of evaluation steps for encoding and sampling, which makes them impractical for clinical applications. To address this paradox, we adapt an Ordinary Differential Equation solver [17] for fast and stable encoding & sampling independent of the complex trade-off.

Following the setting of continuous-time Ito stochastic differential equation, where the drift coefficient, the diffusion coefficient, and the Wiener process are denoted as $\mathbf{f}(x,t)$, $g(t)$, $\mathbf{w}$, we have our forward process and probability flow ODE sampling [25] as:

$$\mathrm{d}x = \mathbf{f}(x,t)\mathrm{d}t + g(t)\mathrm{d}\mathbf{w}, \quad \frac{\mathrm{d}x}{\mathrm{d}t} = \mathbf{f}(x,t) - g(t)^2\nabla_x \log p_t(x). \tag{6}$$

By decomposing the conditional sampling scheme according to Bayes Theorem, the guided diffusion process can be achieved by mixture guidance composed of conditional noise prediction model and classifier gradient:

$$p_{\theta,\phi}(\tilde{x}_{t-1}, y|\tilde{x}_t, x_0) \propto p_\theta(\tilde{x}_{t-1}|\tilde{x}_t, x_0)p_\phi(y|\tilde{x}_t). \tag{7}$$

Denote the classifier as $\mathcal{C}$, the binary label as $y$, the signal-to-noise coefficient as $\lambda$, and the conditional noise prediction network as $\boldsymbol{\epsilon}_\theta\left(\tilde{x}^{'}, \lambda, y\right)$, we further have the hybrid conditional diffusion network $\hat{\boldsymbol{\epsilon}}_\theta$ as:

$$\hat{\boldsymbol{\epsilon}}_\theta(\tilde{x}^{'}, \lambda, y) := \boldsymbol{\epsilon}_\theta(\tilde{x}^{'}, \lambda, y) + s \cdot \mathcal{C}(\tilde{x}_t, t, y). \tag{8}$$

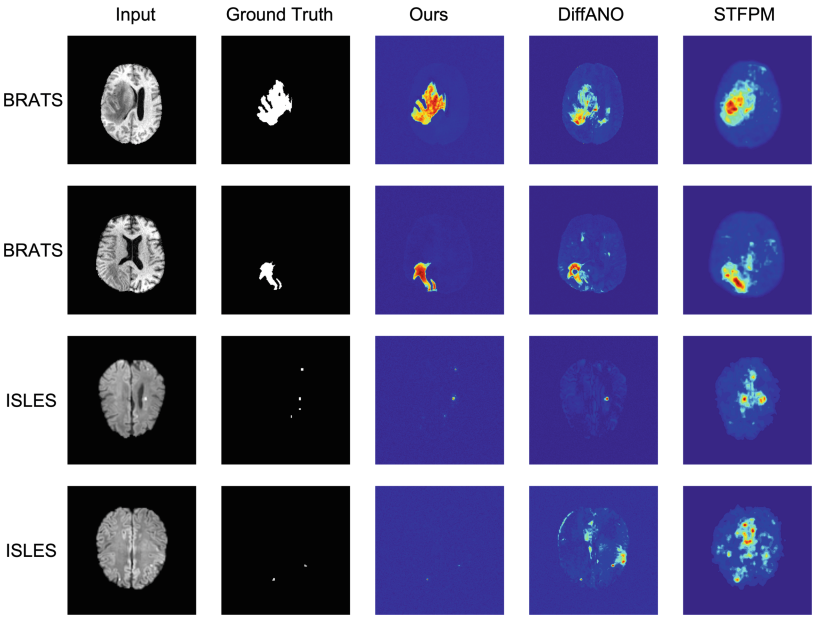


**Fig. 3.** Qualitative comparisons on BRATS and ISLES datasets. The lesions in ISLES are small, zooming in this figure to get better visualization. Thanks to the pixel-wise hybrid guidance, our results have few noise.

The semi-linear probability flow ODE is solved reversely with second-order multi-step numerical methods [18]. Then, we apply hybrid conditional sampling to noisy data $\tilde{x}_t$ to reproduce a healthy one with the same anatomy structure by conditional data prediction network and the binary classifier [10]. Following the symbol of [17,18], the conditional sampling is:

$$\frac{x_t}{\alpha_t} = \frac{x_s}{\alpha_s} - \int_{\lambda_s}^{\lambda_t} e^{-\lambda} \hat{\boldsymbol{\epsilon}}_\theta\left(\tilde{x}^{'}, \lambda, y\right) \mathrm{d}\lambda. \tag{9}$$

Finally, we post-process the reconstructed samples by subtracting original inputs and performing Otsu's threshold to obtain the anomaly segmentation map.

**Table 1.** Comparison with state-of-the-art anomaly detection methods. The best performances are bolded. The second-best performances are underlined.

| | | BRATS 2020 | | | ISLES | |
|---|---|---|---|---|---|---|
| Method | Dice↑ | HDis↓ | VSim↑ | Dice↑ | HDis↓ | VSim↑ |
| PadimCore [8] | 36.76 | 5.78 | 57.83 | 4.89 | 8.35 | 4.89 |
| CFlow [11] | 38.95 | 5.41 | 58.40 | 3.68 | 9.08 | 3.38 |
| CSFlow [22] | 22.33 | 7.05 | 44.09 | 7.52 | 6.02 | 12.53 |
| FastFlow [31] | 32.34 | 7.86 | 35.93 | 5.55 | 8.27 | 5.65 |
| RevDis [9] | 34.46 | 7.46 | 36.77 | 17.87 | 6.17 | 20.8 |
| STFPM [33] | 53.83 | 4.82 | 72.20 | 10.32 | 6.75 | 12.12 |
| PatchCore [21] | 51.78 | <u>4.29</u> | 62.83 | 5.83 | 7.91 | 5.83 |
| DiffANO [27] | <u>66.65</u> | 4.82 | <u>81.74</u> | <u>34.46</u> | <u>3.38</u> | <u>48.68</u> |
| FNDM(Ours) | **76.21** | **3.80** | **82.28** | **54.44** | **1.99** | **75.41** |

## 3 Experiment

### 3.1 Dataset and Evaluation Metric

BRATS 2020 [2] is a brain tumor segmentation dataset containing the MR sequences of T1, T1Gd, T2, and FLAIR. Following the preprocessing approach of [27], we concatenate all image modalities along the channel dimension, prune the upper and lower axial slices, and pad each slice into $256 \times 256$. All tumor classes are merged into a single class in the segmentation mask. The training set contains 10,410 slices with tumors and 5,809 healthy slices. The testing set includes 1,316 images with tumors. ISLES 2022 [19] is an MR image dataset for stroke lesions segmentation. It contains ischemic strokes of various sizes and from different disease stages. We extract the axial slices from DWI sequence and resize them into $256 \times 256$. The training set includes 2,707 healthy slices and 1,483 slices with lesions. The testing set contains 282 slices with lesions. Note that only the image-level binary labels are used in our training. The evaluation metrics include Dice, Volumetric Similarity, and Hausdorff Distance, which are calculated in slice level and volume level for BRATS and ISLES, respectively.

### 3.2 Implementation Details

To fairly compare with previous state-of-the-art diffusion models, we use the same network architectures as DiffANO [27]. We set the batch sizes of diffusion model and classifier as 3 and 10, respectively. The Adam optimizer with a learning rate of 0.0001 is used to train the diffusion model for 130,000 iterations and train the classifier for 150,000 iterations. The training diffusion step is 1000. The forward encoding and sampling steps are both set to 50 in the inference. We randomly generate the lesion masks as [30] and corrupt the corresponding regions on the conditioning images in the training phase.

### 3.3 Comparison with State-of-the-Art Methods

To compare the performance, we choose the anomaly detection methods including memory-based methods (such as PatchCore [8] and PadimCore [8]), normalizing flow based methods (such as CSFlow [22] and FastFlow [31]), distillation-based methods (such as Reverse Distillation [9] and STFPM [33]), and a diffusion-based method (DiffANO [27]) which also utilizes image-level binary labels. We train them on BRATS2020 and ISLES datasets. Table 1 shows the segmentation results. Our FNDM outperforms the existing methods in all metrics on both datasets. Diffusion methods have a more powerful generation ability than non-diffusion methods, and our method outperforms the best non-diffusion methods over 20% Dice. FNDM also outperforms the previous state-of-the-art diffusion method, DiffANO, by a large gap of +9.56% Dice, –0.98% HDis, and +0.54% VSim on BRATS dataset, and +19.98% Dice, –1.39% HDis, and +26.73% VSim on ISLES dataset, revealing that our FNDM is effective to reconstruct the healthy image from diseased to detect the anomaly regions in brain MR images. Thanks to non-Markovian procedure and pixel-wise hybrid guidance, the performance improvement of our method is larger on the ISLES dataset where stroke lesions are more challenging due to smaller sizes and irregular shapes.

**Table 2.** Ablation study on the hybrid guidance in our method.

| | Modules | | | BRATS | |
|---|---|---|---|---|---|
| CG | NM | MB | Dice | HDis | VSim |
| √ | | | 63.26 | 4.83 | 79.25 |
| √ | √ | | 73.87 | 3.82 | 79.80 |
| √ | √ | √ | 76.26 | 3.75 | 81.16 |

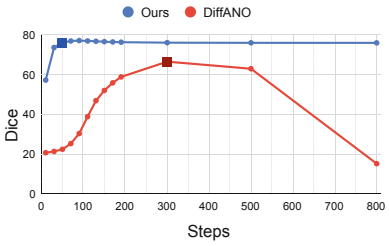


**Fig. 4.** Ablation on steps. We use the same step value in encoding and sampling.

### 3.4 Ablation Study

We conduct ablation studies for hybrid conditions and the steps of encoding and sampling procedures. From Table 2, we decompose the overall pixel-wise hybrid condition into classifier gradient (CG), Non-Markovian (NM), and Memory Bank (MB), comparing all possible combinations on BRATS2020 dataset. We observe that combinations with more components achieve better performance, and NM module achieves a higher increase than MB module. In Fig. 4, we further evaluate the segmentation performance of DiffANO [27] and ours across diverse steps on BRATS2020 dataset. DiffANO performs best at 300 steps, concluding that it is the optima where anomaly information vanishes and anatomy information

preserves partly. Our method only needs 50 steps which achieve 6-time acceleration compared to DiffANO when both approaches reach the best Dice scores. Besides, our method performs stably as the step amount exceeds 50 since non-Markovain strong guidance ensures high-quality information transition along the timeline, independent of the loss of anatomy structure.

## 4 Conclusion and Discussion

We propose a Fast Non-Markovian Diffusion Model (FNDM) for weakly supervised anomaly detection. FNDM first encodes the images into noisy ones, then applies hybrid conditional generation to reconstructed original images without anomalies. FNDM achieves high-fidelity generation on weak labels by leveraging non-Markovian modeling and pixel-wise hybrid conditions. Besides, FNDM conducts ODE fast solver for encoding and sampling to reach 6-time acceleration. Extensive experiments on two brain datasets reveal the effectiveness and superiority of our approach for anomaly detection. The limitation of our method is that, as a diffusion-based method, it still needs more evaluation steps than GANs. In the future, we could investigate the knowledge distillation techniques to further reduce the sampling steps and apply FNDM in other modalities.

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