Optimising Diffusion Models for Histopathology Image Synthesis

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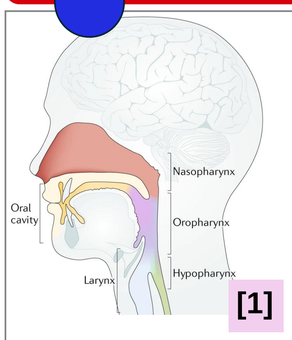
30 Second Summary

- Synthesis and classification of HPV-related cancerous tissue using **C**onditional **D**iffusion **M**odels (CDMs).
- Novel weighting schemes for the CDM training objective that capture relevant pathological markers.
- Feature representation improved by up to 10% over existing methods using classification metrics.

1. Overview

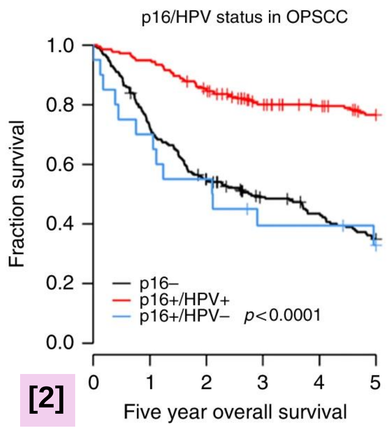


[1]

Oropharyngeal Squamous Cell Carcinoma (**OPSCC**) is a sub-type of head and neck cancer linked to *Human Papillomavirus* (**HPV**).

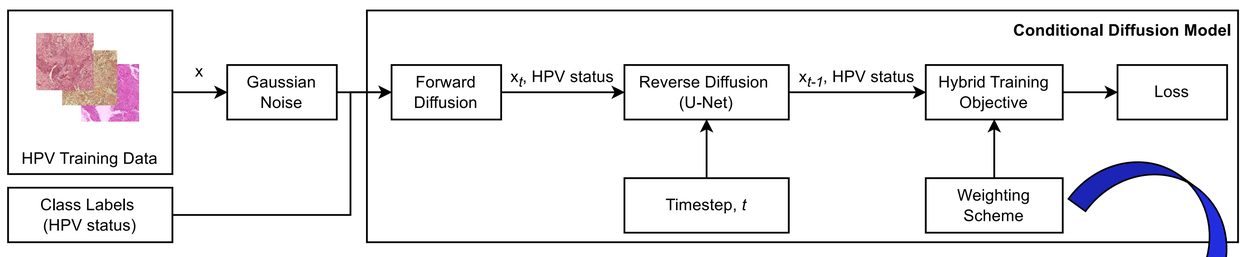
HPV+ OPSCC patients have an **improved prognosis** compared to HPV- OPSCC patients. The reason for this is **currently unknown [2]**.

Visualising the pathological differences of HPV status would be highly interpretable and may explain the **impact of HPV status** on OPSCC prognosis.



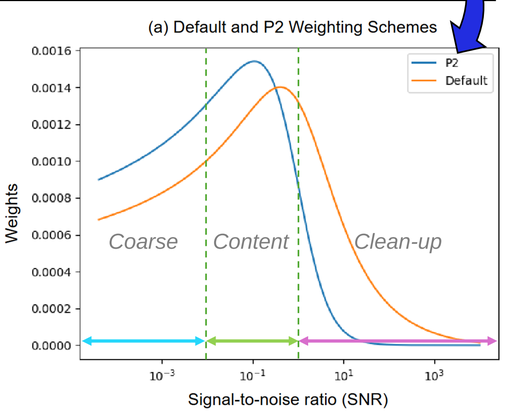
[2]

High-level Overview of the Training Pipeline



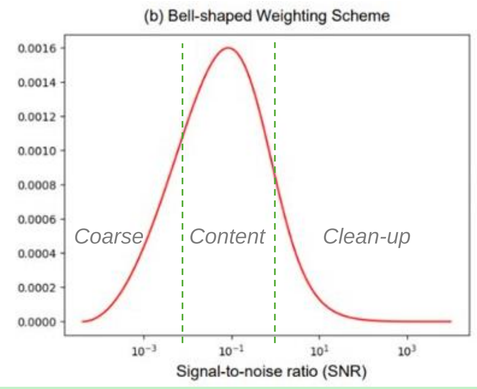
Prioritising certain noise levels over others during training improves CDM **[3]** performance on natural images **[4]**.

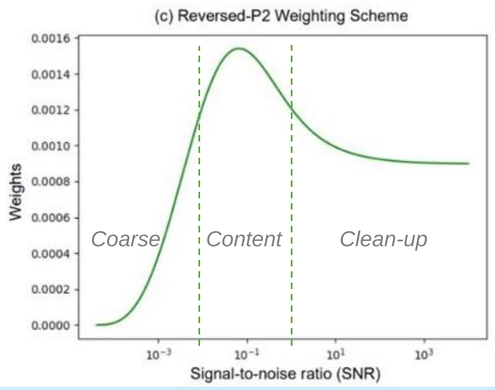
We take inspiration from this to determine **noise levels** that are **best suited** to the synthesis of **histopathology** images.



2. Methodology

We propose **two novel weighting schemes** for the training objective function which prioritise these **determined noise levels** during training.





Bell-Shaped$_t$ = ½ ∗ (−cos(2π ∗ t/T) + 1)

- ✓ Assigns higher weights to content and lower weights to coarse and clean-up.
- ✓ Perceptually discriminative content
- ✘ Colour and structural properties.

Reversed-P2$_t$ = λ_t/(k + SNR(T + 1 − t))$^\gamma$)

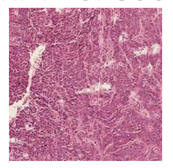
- ✓ Assigns higher weights to content and clean-up and lower weights to coarse.
- ✓ Imperceptible details.
- ✘ Colour and structural properties

3. Performance Evaluation

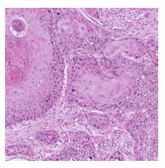
HPV Dataset

- 263 x 263 px tiles from whole slide images.
- 9438 HPV+ and 5790 HPV- training tiles.
- 4,578 HPV+ and 4,890 HPV- unseen testing tiles.

HPV+ OPSCC



HPV- OPSCC



Performance of CDMs on HPV Dataset

Model	Guidance	IS↑	FID↓	sFID↓
CDM-Default	☒	2.48	155.07	27.77
CDM-P2	☒	**3.09**	152.40	24.09
CDM-Reversed-P2	☒	2.92	191.56	31.15
CDM-Bell-Shaped	☒	2.93	**116.36**	**18.75**

The **Bell-Shaped** weighting scheme produces samples that best reflect the **spatial properties** of real HPV data.

Performance of GCDMs on HPV Dataset

Model	Guidance	IS↑	FID↓	sFID↓
CDM-Default	☑	2.50	152.35	27.34
CDM-P2	☑	**3.00**	146.37	23.11
CDM-Reversed-P2	☑	2.96	188.68	30.71
CDM-Bell-Shaped	☑	2.92	**115.90**	**18.45**

Classifier Guidance has a marginal effect on sample quality and is not worth the additional complexity.

4. Feature Representation Analysis

HPVNet **[5]** was used as an objective assessment of the models' ability to synthesise images that are representative of **class-significant features** (e.g., p16 expression) to enable successful classification.

HPV status Classification by HPVNet

Model	Guidance	Accuracy	F1	Precision	Recall
CDM-Default	☒	0.6606	0.6421	0.6798	0.6083
	☑	0.6850	0.6651	**0.7097**	0.6258
CDM-P2	☒	0.6665	0.7005	0.6338	0.7830
	☑	0.6983	0.7253	0.6662	0.7960
CDM-Reversed-P2	☒	0.6436	0.6776	0.6198	0.7472
	☑	0.6604	0.6917	0.6355	0.7589
CDM-Bell-Shaped	☒	0.6904	0.7229	0.6561	0.8049
	☑	**0.7102**	**0.7415**	0.6698	**0.8304**

The **Bell-Shaped** weighting scheme is the most effective at producing samples that exhibit the **HPV-related inter-class differences**.

Training & Evaluation Overview

Models trained for 250K steps.

50K synthetic samples for evaluation.

HPVNet cannot replace a pathologist's expertise!

5. Conclusion

- ✓ We propose the prioritisation of **spatial features** during training to encourage the CDM to **delineate** HPV-induced **pathological markers**.
- ✓ The resultant CDM is capable of **synthesising** distinguishing clinical and morphological **features** associated with HPV-related OPSCC tissue.
- ✓ We demonstrate that this approach improves the **performance** and **feature interpretability** of CDMs.

GitHub Repository

Acknowledgements

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[2] Craig et al. Recommendations for determining hpv status in patients with oropharyngeal cancers under tnm8 guidelines: a two-tier approach. British Journal of Cancer, 120(8):827–833 (2019).
[3] Dhariwal and Nichol. Diffusion models beat GANs on image synthesis. In Advances in Neural Information Processing Systems, volume 34, page 8780–8794, 2021.
[4] Choi et al. Perception prioritized training of diffusion models. In Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR), pages 11472–11481 (2022).
[5] Craig et al. A deep learning alternative to regional molecular testing for hpv status. AACR-AHNS Head and Neck Cancer Conference: Innovating through Basic, Clinical, and Translational Research (2023).