

Prescient
Design

A Genentech Accelerator



Score-based 3D molecule generation with neural fields

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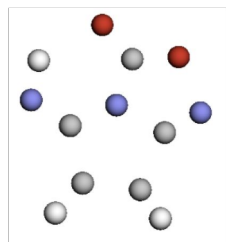
*: equal contribution

NeurIPS 2024

Genentech
A Member of the Roche Group

Generative models for 3D small molecules

3D point clouds



SE(3)-equivariant GNNs

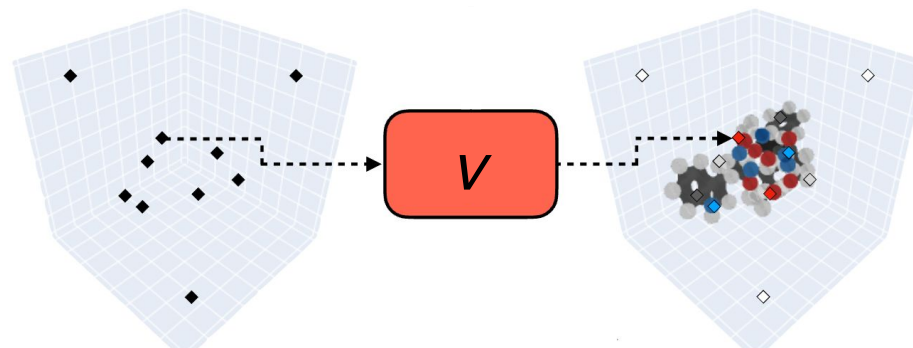
+: Built-in equivariance

-: Not scalable ($O(\text{atoms}^2)$)
Limited expressivity

[Hoogeboom et al., 2022](#),
[Schneuing et al. 2022](#)

Molecules as Images

Computer vision models + data augmentation



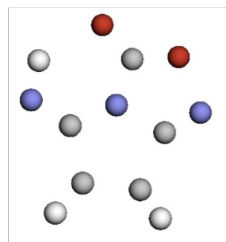
$$x \in \mathbb{R}^3$$

$$(v_C, v_H, v_N, v_O)(x) \in \mathbb{R}^n$$

[Li et al., 2014](#)

Generative models for 3D small molecules

3D point clouds



SE(3)-equivariant GNNs

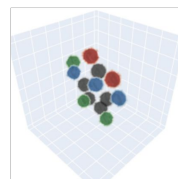
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[Hoogeboom et al., 2022](#),
[Schneuing et al. 2022](#)

Molecules as Images

Voxels



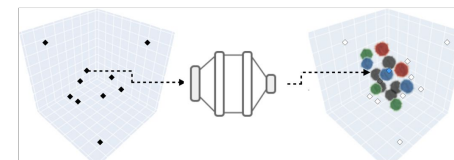
3D UNet

+: Expressive, state-of-the-art

-: Not scalable ($O(\text{grid}^3)$)

[Ragoza et al., 2017, 2022](#)
[Pinheiro et al. 2023 2024](#)

Fields



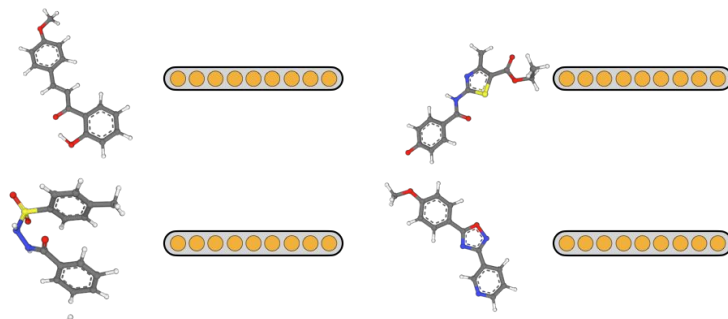
Neural Fields

+: Scalable, Expressive, Fast

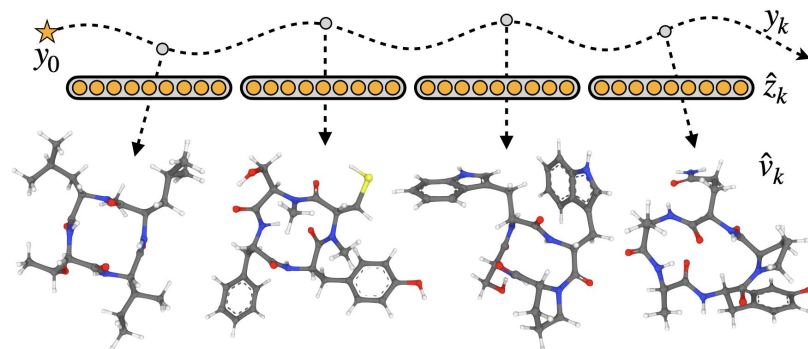
[FuncMol](#)

Objective

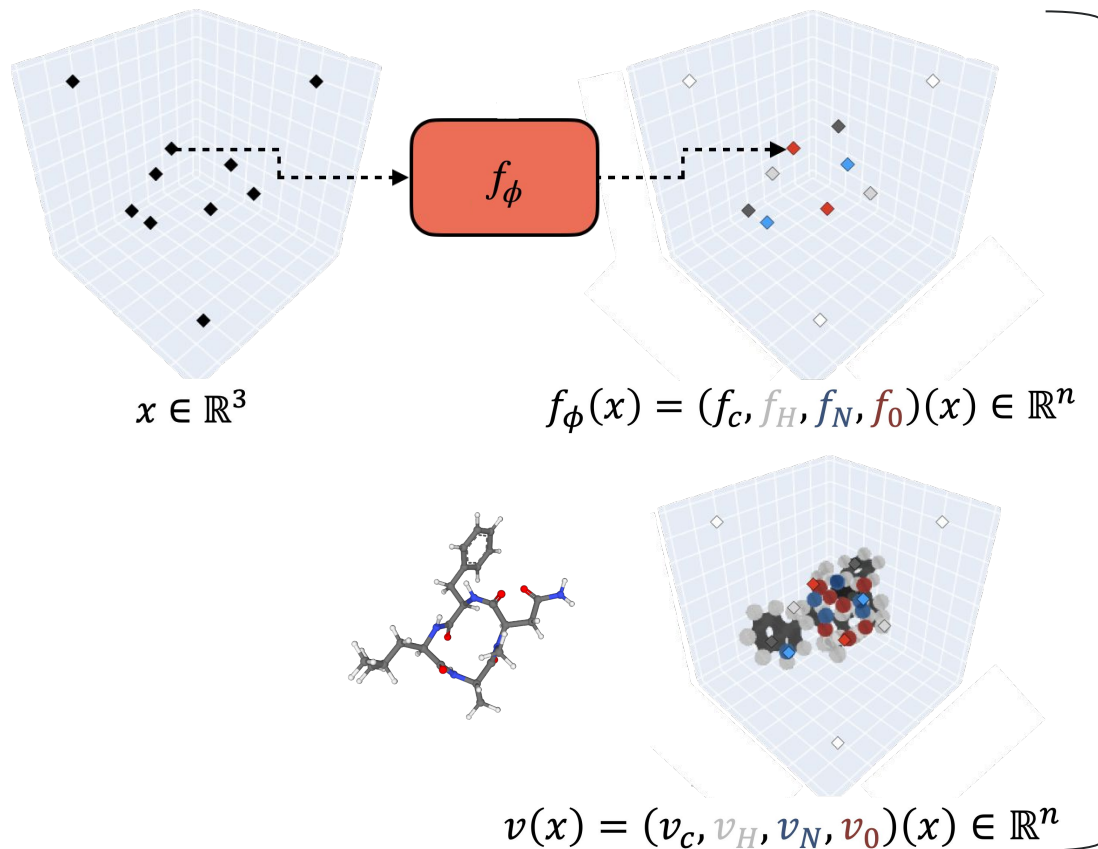
I. Learn a low-dimensional embedding of molecular fields



II. Perform generative modelling on this space

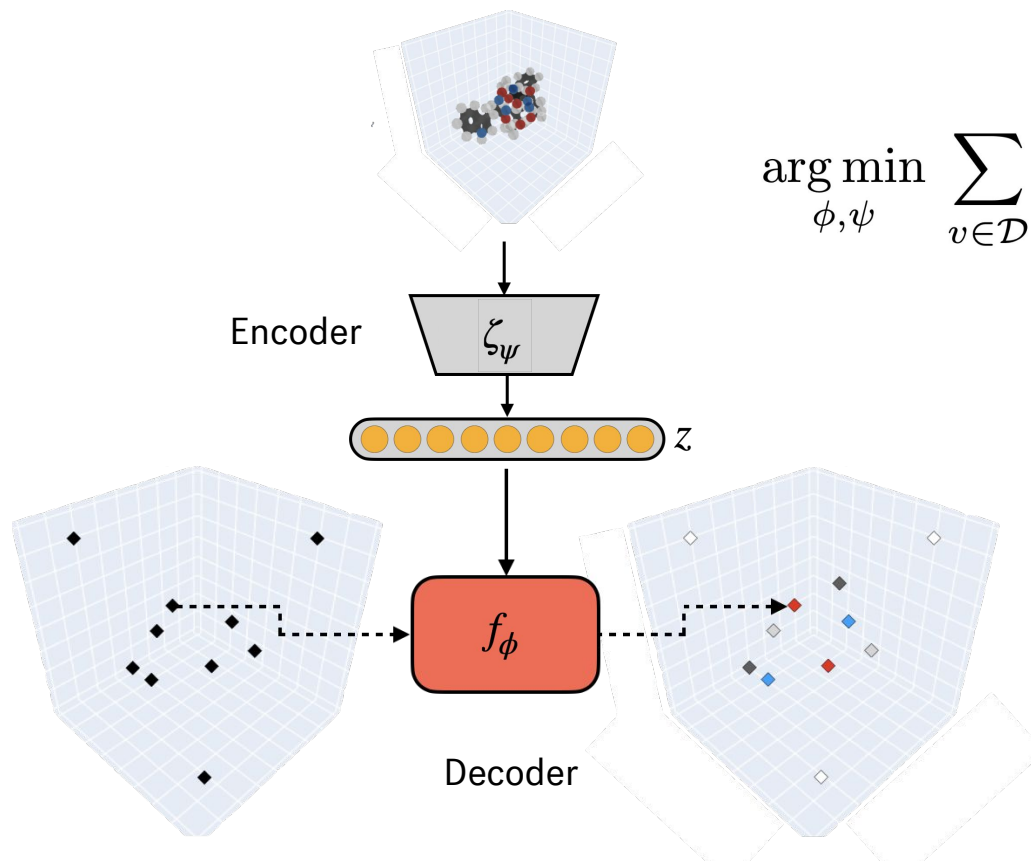


What is a neural field ?



$$\arg \min_{\phi} \int \|f_\phi(x) - v(x)\|_2^2 dx$$

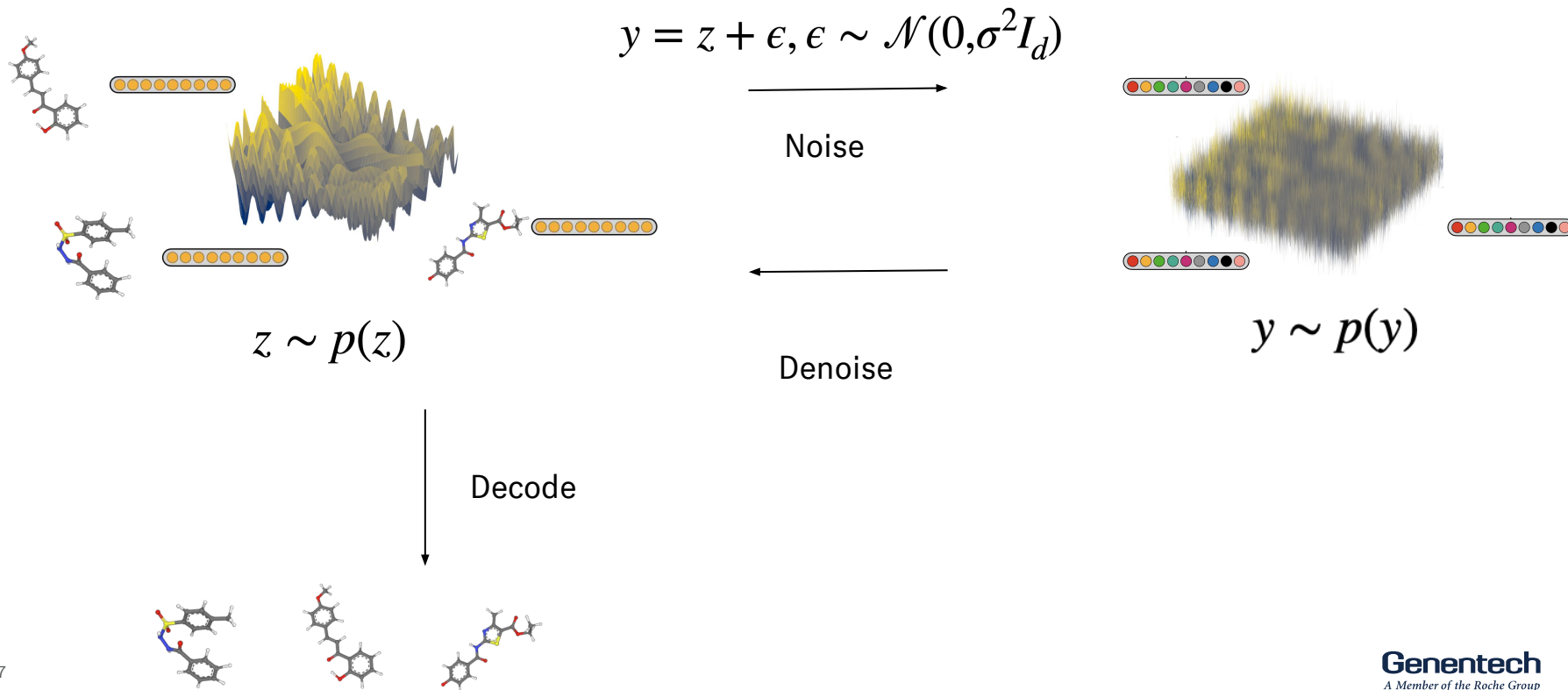
Neural-field based auto-encoder



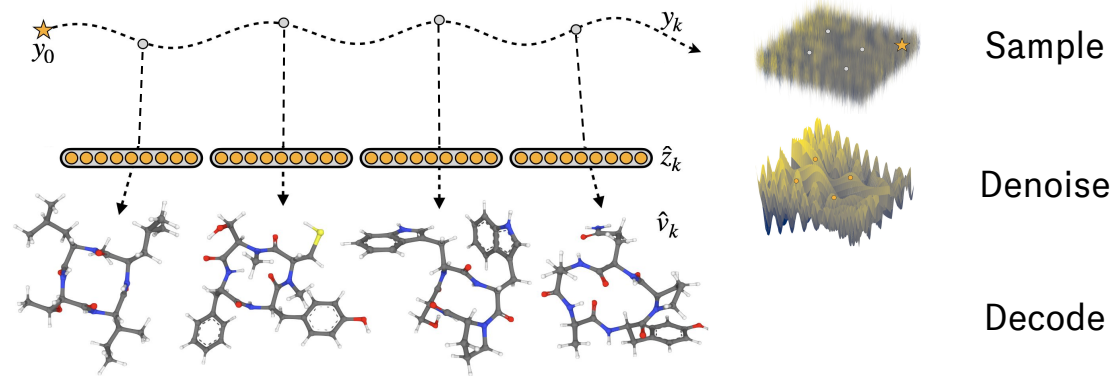
$$\arg \min_{\phi, \psi} \sum_{v \in \mathcal{D}} \int \|f_\phi(x, \zeta_\psi(v)) - v(x)\|_2^2 dx$$

[[Mescheder et al. 2019 CVPR](#)]

Latent “Walk-Jump Sampling” [Saremi & Hyvärinen, 2019 JMLR]



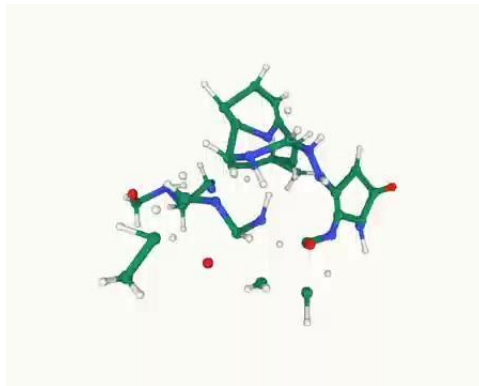
Sampling via Langevin MCMC



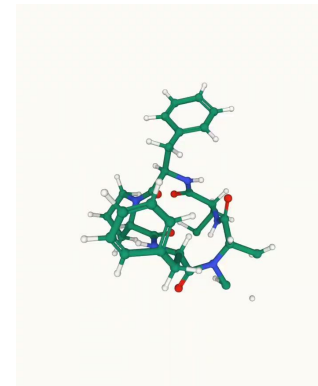
QM9 (small molecule)



GEOM-drugs (small molecule)



[CREMP](#) (macro cyclic peptides)



A new representation for 3D molecules

- All-atom 3D generation using neural fields
- Close to SOTA on unconditional 3D molecule generation
- One order faster sampling time.
- Scales to larger 3D molecules e.g. macro-cyclic peptides
- General framework
 - Usable across data modalities
 - Applicable to other “fields”: electron density, surface, orbitals, etc.