

ReG-SAM: Reference Graph-Driven SAM for 2D Foundational Vessel Segmentation

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Abstract

Vessel segmentation in medical images is essential for many clinical tasks, ranging from diagnosis to treatment planning. However, it remains challenging due to complex vascular morphology and diverse imaging conditions. Existing deep learning methods rarely aim at building a generalizable vessel segmentor across anatomies and modalities. While the Segment Anything Model (SAM) has shown promise for medical image segmentation, its original design does not fully exploit vascular morphology and struggles with fine-grained vascular structures, leading to suboptimal performance. In this paper, we propose ReG-SAM, a SAM-based framework tailored to 2D vessel segmentation that leverages reference graph set for enhancing vascular representations. Specifically, we introduce two modality-aware representations derived from the reference masks: graph prompt embeddings (GPEs) that encode global spatial features from graphs, and vascular prototype embeddings (VPEs) that capture fine-grained modality-specific vessel characteristics from multi-scale feature maps and vascular masks. Since both require vascular masks that are unavailable during inference and require robust modality-aware vascular feature representations, we construct a modality-wise vascular database and develop two reference graph-guided representation learning schemes for estimating GPEs and VPEs using samples from the database rather than ground-truth masks. Extensive experiments across 19 datasets demonstrate that ReG-SAM consistently outperforms existing baselines, even those using manual prompts, particularly on challenging thin vessels. The code and trained models will be made publicly available.

Introduction

Vessel segmentation, which extracts vascular structures from medical images, plays an important role in clinical diagnosis and treatment planning (Kock et al. 2024; Brugnara et al. 2023). It is considerably more challenging than organ segmentation due to the thin, elongated, and highly branching vascular morphology, large diameter variations, low contrast against surrounding tissues, and frequent discontinuities caused by imaging artifacts. Furthermore, vascular appearance varies substantially across anatomies and imaging modalities, making robust vessel segmentation particularly difficult. Traditional methods are essentially image

filters (Frangi et al. 1998) that rely on prior knowledge of vascular morphology. These modality-dependent approaches, although effective in specific scenarios, often struggle to generalize across diverse clinical settings. With the advent of deep learning, neural networks have demonstrated strong capability in modeling complex vascular patterns, leading to substantial performance improvements. Representative applications include fundus imaging (Wu et al. 2019; Wang et al. 2020; Ma and Li 2024; Luo et al. 2025), X-ray angiography (Iyer et al. 2021; Zhu et al. 2021; He et al. 2025), and optical coherence tomography angiography (Liu et al. 2022; Li et al. 2025). However, most are designed for individual datasets or modalities. Although foundation medical segmentation models have attracted increasing attention, they are not specifically tailored for vessels. Only few foundational methods (Song et al. 2025) have been proposed for 2D vessel segmentation across anatomies and modalities, leaving this area largely underexplored. In addition, these methods fail to capture discriminative vascular appearance features and model modality-specific vascular structures, such as distinct branching patterns.

The Segment Anything Model (SAM) (Kirillov et al. 2023), a foundation model originally proposed for natural image segmentation, has been successfully adapted to medical domains (Cheng et al. 2023; Ma et al. 2024a), making it a promising backbone for a general vessel segmentor. In SAM, the prompt encoder is an important component that provides high-level guidance to the mask decoder. However, its prompt types, such as points and bounding boxes, are inherently suboptimal for vessel segmentation. Unlike compact organs, vessels are elongated and highly branched tree-like structures, making point-based interaction unreliable, while randomly selected points may even degrade performance. Bounding boxes are also ineffective, as vessels often span large regions of the image, often covering nearly the entire field of view. In contrast, graphs naturally represent vascular morphology, making them a natural choice for vessel segmentation prompts. Besides, graph-derived prompt embeddings can include both vascular structural information and modality-specific characteristics, providing effective guidance across anatomies. Another limitation lies in the mask decoder, which was originally designed for generic object segmentation and hence struggles to preserve fine vascular details such as thin branches and vessel bifurcations.

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Substantial appearance variations across imaging modalities further exacerbate this problem, as the decoder block lacks explicit modality-aware vascular representations to guide fine-grained vessel recovery.

In this paper, we present **ReG-SAM**, a fully-automatic foundation model for 2D vessel segmentation built upon SAM and guided by modality-aware reference graph set. In particular, we introduce two modality-aware representations to enhance the prompt encoder and mask decoder. (1) A graph constructed from the vascular mask of an image is encoded into a graph prompt embedding (GPE), capturing modality-aware vascular morphology for guiding mask decoding. (2) An auxiliary convolutional neural network (CNN) is employed for extracting multi-scale image features that are used for computing a vascular prototype embedding (VPE) along with the vascular mask, yielding modality-specific vascular representations for fine-grained decoding.

However, GPEs and VPEs face two key challenges. The first is their dependence on ground-truth vascular masks that are unavailable during inference. In particular, GPE construction requires graphs derived from ground-truth masks. Existing alternatives construct graphs by partitioning images into patches and treating each patch as a node (Li et al. 2026; Jalali, Fateh, and Rezvani 2024), or by generating coarse masks using auxiliary modules (Mishra et al. 2021; Shin et al. 2019). However, such graphs often fail to faithfully represent global vascular structures and generalize poorly across anatomies. Second, the learned representations should accurately capture modality-aware spatial and semantic information while remaining robust to variations in anatomy and imaging modality.

To address these challenges, we propose two reference graph-guided representation learning schemes for GPEs and VPEs. (3) We build a modality-aware vascular database containing mask-derived graphs. During training, reference graphs are randomly sampled from the database and encoded into embeddings, which are encouraged to align with the embedding representation of a query image through dedicated loss functions. Consequently, robust GPEs and VPEs with corresponding modality priors can be estimated from the database during inference without ground-truth masks. (4) We establish a comprehensive benchmark comprising 19 public datasets across anatomies and modalities. Extensive experiments demonstrate that ReG-SAM outperforms existing SAM-based foundational methods for 2D vessel segmentation, even those augmented with manual prompts.

Related Work

Domain-Specific Vessel Segmentation

Early methods (Frangi et al. 1998; Staal et al. 2004) rely on handcrafted vascular priors, such as matched filtering, ridge detection, and Hessian-based vessel filtering to enhance curvilinear structures, but require careful parameter tuning and generalize poorly across anatomies and imaging modalities. Although deep learning has substantially improved vessel segmentation performance, most existing methods (Wu et al. 2019; Wang et al. 2020; Ma and Li 2024; Luo et al. 2025; Iyer et al. 2021; Zhu et al. 2021; He et al. 2025; Liu et al.

2022; Li et al. 2025) remain domain-specific, being trained and evaluated on individual datasets or modalities. To address the sparsity of vascular annotations in the area, some approaches focus on data synthesis (Ma et al. 2021; Kim, Oh, and Ye 2022; Lin et al. 2023; Zhang et al. 2024b; Kreitner et al. 2024; Zhang et al. 2024a; Liang et al. 2026; Hao et al. 2026), scaling up training data with synthesized ones, for achieving better segmentation results. Some works incorporate graph information either by constructing graphs from intermediate segmentation masks (Shin et al. 2019; Mishra et al. 2021) or by building graph structures directly within feature representations (Xu and Wu 2024; Ahmed et al. 2026) or from the input image via patch-based partitioning (Jalali, Fateh, and Rezvani 2024; Li et al. 2026).

Foundational Medical Image Segmentation

Foundational medical image segmentation methods typically build upon SAM and adapt it to medical domains through fine-tuning. SAM-Med2D (Cheng et al. 2023) and MedSAM (Ma et al. 2024a) are two pioneering medical image segmentors in this direction. Subsequent works have focused on improving specific aspects, such as parameter-efficient adaptation using adapters (Wu et al. 2025b; Tejero et al. 2025) and enhancing computational efficiency (Ma et al. 2024b; Lyu, Gao, and Staring 2024). Despite recent advances, foundational 2D vessel segmentation remains largely underexplored. OVS-Net (Song et al. 2025) represents the current state-of-the-art general vessel segmentor, employing a hybrid encoder that combines a SAM backbone with a convolutional branch. However, it remains a semi-automatic framework that relies on conventional point prompts and lacks dedicated modeling of vascular morphology.

Methodology

In this section, we present the ReG-SAM for foundational 2D vessel segmentation, as illustrated in Figure 1. Graph prompt embeddings (GPEs) and vascular prototype embeddings (VPEs) are employed to enhance the segmentation performance. To eliminate their need for ground-truth masks during inference and ensure robust representation learning, we construct a modality-organized vascular database and propose two reference-guided representation learning schemes. Given a query image, k reference graphs are randomly sampled from the database based on the modality of the query image. They are encoded into combined embeddings for aligning with the embedding representations of the query image. During inference, the GPE and VPE are estimated directly from the database without relying on annotated masks, enabling fully automatic and enhanced vessel segmentation.

Graph Set Sampling from Vascular Database

Annotated vascular images are much scarcer than other medical images (Ma et al. 2024a), making effective use of available data crucial. Moreover, images from the same modality share consistent semantic and imaging characteristics, allowing segmentation to benefit from same-modality references. We therefore construct a modality-organized vascular

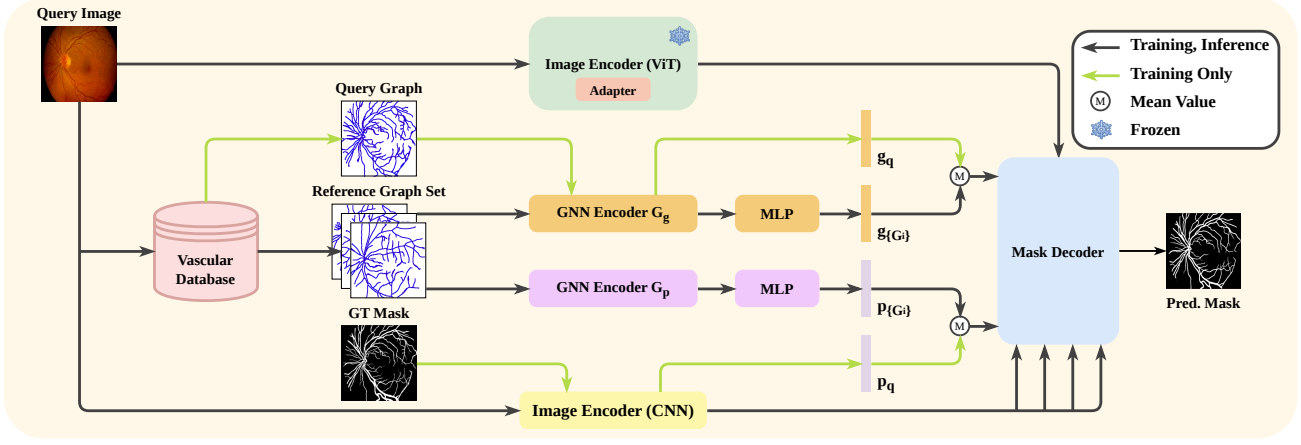


Figure 1: An overview of the proposed ReG-SAM. Given a query image, reference graphs are randomly sampled from a vascular database, and their combined embeddings are aligned with the embedding representations of the query image during training.

database containing graphs and their modality labels. A vascular graph $G_i = \{V_i, E_i\}$ is constructed from the mask $M_i \in \{0, 1\}^{h \times w}$, where V_i and E_i denote the node and edge sets, respectively, and h and w are spatial dimensions. Specifically, the mask is first skeletonized (Zhang and Suen 1984; Soille et al. 1999; Lee, Kashyap, and Chu 1994) and pruned to remove short, noisy branches. Skeleton pixels are then treated as nodes, local neighborhood connections as edges, and pixel coordinates as node features, preserving vessel geometry and topology for graph-based representation learning. Although same-modality images share common imaging characteristics, their anatomical details may vary substantially. Thus, rather than selecting only the most similar samples, which may reduce diversity and limit generalization, we randomly sample references to learn robust modality-level priors. Given a query image $I_q \in \mathbb{R}^{3 \times h \times w}$ with modality m_q , we define the corresponding modality-specific candidate set as S_{m_q} . This set contains the indices of the graphs with the same modality m_q except for the graph of the query image itself. Consequently, we randomly sample k indices from S_{m_q} :

$$N_q = \text{RANDOM}_k(S_{m_q}). \quad (1)$$

Finally, the reference graph set $\{G_i \mid i \in N_q\}$ is constructed for the query image.

Reference-Guided Graph-Prompt Learning

Since encoding of vascular graphs into embeddings can provide complementary structural information for vessel segmentation, we introduce graph prompt embeddings (GPEs) for capturing modality-aware vascular morphology. As illustrated in Figure 1, given a query image, its graph is encoded into an embedding to aid the mask decoder, similarly to the sparse prompt embedding in the original SAM. However, the graphs rely on annotated vascular masks that are unavailable during inference. Therefore, we propose a reference-guided graph-prompt learning (RGPL) scheme. We employ a shared graph encoder $\mathcal{G}_g$ to encode both the graph G_q of the query image and the sampled graph set $\{G_i \mid i \in N_q\}$. The encoder is a transformer-based graph neural network

(GNN) comprising an input projection layer and multiple TransformerConv (Shi et al. 2020) blocks to model local and global vascular structures. Node embeddings are refined by linear layers with dropout and aggregated via global average pooling (GAP) to produce an embedding $\mathbf{g}_q \in \mathbb{R}^{c_g}$,

$$\mathbf{g}_q = \text{GAP}(\mathcal{G}_g(G_q)). \quad (2)$$

For the sampled graph set, the individual embeddings are concatenated and passed through a multi-layer perceptron (MLP) $\mathcal{H}_g$ to yield a fused embedding $\mathbf{g}_{\{G_i\}} \in \mathbb{R}^{c_g}$:

$$\mathbf{g}_{\{G_i\}} = \mathcal{H}_g(\text{CONCAT}(\{\mathbf{g}_i \mid i \in N_q\})). \quad (3)$$

Since both $\mathbf{g}_q$ and $\mathbf{g}_{\{G_i\}}$ are available during training, we average them to obtain the GPE $\mathbf{g}_{\text{train}} \in \mathbb{R}^{c_g}$, allowing both representations to participate in optimization while facilitating their alignment:

$$\mathbf{g}_{\text{train}} = \frac{1}{2} (\mathbf{g}_q + \mathbf{g}_{\{G_i\}}). \quad (4)$$

During inference, since the graph G_q cannot be constructed without the unavailable ground-truth vascular mask, the fused embedding $\mathbf{g}_{\{G_i\}}$ is directly used as the GPE.

Reference-Guided Vascular-Prototype Learning

Although RGPL enables robust GPE learning for capturing modality-aware structural priors, GPE alone has limited impact without direct interaction during upsampling, motivating the need for pixel-wise semantic enhancement. To address this limitation, we introduce vascular prototype embeddings (VPEs) for capturing modality-aware semantic prototypes of vessels and directly integrate them into the upsampling process of the mask decoder.

To accurately represent vessel features, VPEs are computed from ground-truth masks and multi-scale feature maps extracted by a parallel ResNet-style (He et al. 2016) CNN image encoder. Unlike vision transformers (Dosovitskiy et al. 2020) that operate at a uniform resolution, CNNs naturally learn hierarchical representations, making them well-suited for vascular prototype learning. Specifically, given a feature

map $\mathbf{F}_l \in \mathbb{R}^{c_l \times h_l \times w_l}$ at scale l , the ground-truth mask is resized via interpolation to the corresponding resolution, yielding $\mathbf{M}_l \in \{0, 1\}^{h_l \times w_l}$. Masked average pooling is applied for extracting a scale-specific vascular embedding $\mathbf{p}_l \in \mathbb{R}^{c_l}$:

$$\mathbf{p}_l = \frac{\sum_{x,y} \mathbf{F}_l(x,y) \cdot \mathbf{M}_l(x,y)}{\sum_{x,y} \mathbf{M}_l(x,y)}. \quad (5)$$

The multi-scale embeddings are concatenated and fused through an MLP to produce the prototype embedding $\mathbf{p}_q \in \mathbb{R}^{c_p}$ of the image.

Similarly to GPEs, VPEs should also be independent of ground-truth masks during inference while preserving robust modality-aware vessel semantic priors. Therefore, we adopt a similar strategy by introducing another graph encoder $\mathcal{G}_p$ and an MLP $\mathcal{H}_p$. Specifically, $\mathcal{G}_p$ first encodes each graph in $\{G_i\}$ individually to compute graph-level embeddings:

$$\mathbf{p}_i = \text{GAP}(\mathcal{G}_p(G_i)), \quad (6)$$

which are then aggregated and passed through $\mathcal{H}_p$:

$$\mathbf{p}_{\{G_i\}} = \mathcal{H}_p(\text{CONCAT}(\{\mathbf{p}_i \mid i \in N_q\})). \quad (7)$$

During training, the VPE is obtained by averaging $\mathbf{p}_q$ and $\mathbf{p}_{\{G_i\}}$, still enabling both representations to be jointly optimized while encouraging their alignment:

$$\mathbf{p}_{\text{train}} = \frac{1}{2}(\mathbf{p}_q + \mathbf{p}_{\{G_i\}}), \quad (8)$$

whereas $\mathbf{p}_{\{G_i\}}$ is directly used as the VPE during inference.

Vessel-Aware Fine-Grained Decoding

In the original SAM mask decoder, no skip connections are established between the image encoder and the mask decoder. Moreover, the mask decoder of SAM-B consists of only two upsampling stages followed by bilinear interpolation for resolution restoration, which limits the segmentation of fine-grained vascular structures. Therefore, we redesign the mask decoder by introducing skip connections from the CNN encoder, enabling direct integration of multi-scale local features. We further apply four progressive upsampling stages to directly reconstruct the segmentation mask at the original resolution.

Furthermore, we incorporate the learned VPE $\mathbf{p} \in \mathbb{R}^{c_p}$ for injecting modality-aware vessel semantic priors into the decoding process. Specifically, we introduce a vascular prototype attention (VPA) module at the end of each upsampling stage. Given a feature map $\mathbf{F}_l \in \mathbb{R}^{c_l \times h_l \times w_l}$ at scale l , the VPE $\mathbf{p}$ is first projected to the corresponding channel dimension c_l through an MLP, yielding $\mathbf{p}_l \in \mathbb{R}^{c_l}$. A scaled dot-product similarity is then computed at each spatial location, followed by a sigmoid activation σ for generating an attention map:

$$\mathbf{A}_l = \sigma \left(\frac{\mathbf{p}_l^\top \mathbf{F}_l}{\sqrt{c_l}} \right), \quad (9)$$

which is then used to modulate the feature map via a residual gating mechanism:

$$\mathbf{F}_l' = \mathbf{F}_l \cdot (1 + \mathbf{A}_l). \quad (10)$$

This mechanism enables vessel-aware decoding for fine-grained segmentation of vascular structures.

Loss Function

The overall loss function consists of three components. Following the original design, the segmentation loss $\mathcal{L}_{seg}$ is defined as the sum of the Dice loss and binary cross-entropy (BCE) loss.

To facilitate the reference-guided representation learning schemes for GPEs and VPEs, we employ an $\mathcal{L}_1$ loss and a contrastive loss during training. The $\mathcal{L}_1$ loss directly minimizes the discrepancy between the estimated embeddings using the sampled graph set and the actual embeddings using the ground-truth masks, and the contrastive loss encourages modality-level semantic consistency by pulling embeddings from the same modality closer and pushing those from different modalities apart. Accordingly, the GPE alignment loss is defined as

$$\mathcal{L}_g = \lambda_{ag} \mathcal{L}_1(\mathbf{g}_q, \mathbf{g}_{\{G_i\}}) + \lambda_{cg} \mathcal{L}_{con}(\mathbf{g}_q, \mathbf{g}_{\{G_i\}}). \quad (11)$$

Similarly, the VPE alignment loss is defined as

$$\mathcal{L}_p = \lambda_{ap} \mathcal{L}_1(\mathbf{p}_q, \mathbf{p}_{\{G_i\}}) + \lambda_{cp} \mathcal{L}_{con}(\mathbf{p}_q, \mathbf{p}_{\{G_i\}}). \quad (12)$$

Correspondingly, the overall loss function is formulated as:

$$\mathcal{L} = \mathcal{L}_{seg} + \mathcal{L}_g + \mathcal{L}_p. \quad (13)$$

Experiments

Datasets

We collected 19 public datasets spanning six imaging modalities to construct a comprehensive benchmark. Dataset details are summarized in Table 1. Except for ORVS (Sarhan et al. 2021), all datasets were merged and split into training and test sets at the 80% to 20% ratio, yielding 3349 and 844 samples, respectively. The ORVS dataset, comprising 49 samples, was held out as a zero-shot test set. All images were converted to 3 channels and resized to 1024×1024 pixels using bicubic interpolation. Pixel values were normalized to the range $[0, 1]$. During training, we applied data augmentation, including random contrast, gamma correction, brightness adjustment, and Gaussian noise.

Implementation Details

Given the limited data volume, rather than fully fine-tuning the SAM image encoder, we used adapter modules (Chen et al. 2022) for each transformer block of the image encoder to efficiently adapt to vascular images. During training, the original encoder weights were frozen, and only the adapter parameters were optimized. To initialize ReG-SAM, we used the pretrained MedSAM-B weights (Ma et al. 2024b).

ReG-SAM was implemented in PyTorch 2.6.0 and trained on an NVIDIA A100 GPU (80 GB memory) for 25 epochs using the AdamW optimizer with an initial learning rate of 1×10^{-4} and a batch size of 2. A reduction-on-plateau scheduler was employed to decay the learning rate. The loss coefficients λ_{ag} , λ_{cg} , λ_{ap} , λ_{cp} are set to 0.05, 0.05, 0.1, 0.1, respectively. Since the segmentation loss remains the primary objective, these coefficients mainly serve as regularization terms. Notably, the vascular prototype embedding, which emphasizes local fine-grained processing, is more closely aligned with the nature of vessel segmentation and was therefore assigned higher weights. The value of k in database sampling was set to 3 through extensive experiments.

Dataset	Modality
FS-CAD (Zeng et al. 2024)	X-Ray
XACV (Wu et al. 2025a)	X-Ray
XCAD (Ma et al. 2021)	X-Ray
Dr-SAM (Zohranyan et al. 2024)	X-Ray
DIAS (Liu et al. 2024)	DSA
DSCA (Zhang et al. 2025)	DSA
FPD (Bano et al. 2020)	PF
OCTA-500 3mm (Li et al. 2024b)	OCTA
OCTA-500 6mm (Li et al. 2024b)	OCTA
ROSE-1 (Ma et al. 2020)	OCTA
ROSSA (Ning et al. 2024)	OCTA
RAVIR (Hatamizadeh et al. 2022; Hatamizadeh 2020)	SLO
ARIA (Farnell et al. 2008)	Fundus
CHASE-AV (Fraz et al. 2012)	Fundus
DRIVE (Staal et al. 2004)	Fundus
FIVES (Jin et al. 2022)	Fundus
LES-AV (Orlando et al. 2018)	Fundus
STARE (Hoover, Kouznetsova, and Goldbaum 2000)	Fundus
ORVS (Sarhan et al. 2021)	Fundus

Table 1: A summary of the datasets. DSA: digital subtraction angiography, PF: placental fetoscopy, OCTA: optical coherence tomography angiography, SLO: scanning laser ophthalmoscopy.

Compared Methods

We selected five representative benchmark methods for comparison. SAM-Med2D (Cheng et al. 2023) and MedSAM (Ma et al. 2024a) are widely used foundation models in medical image segmentation. SAM-HQ (Ke et al. 2023), designed for high-fidelity natural image segmentation, was adopted here as a strong baseline. ASPS (Li et al. 2024a), a strong polyp segmentor, is included due to its potential in vessel segmentation. OVS-Net (Song et al. 2025) is the current state-of-the-art general 2D vessel segmentor. Regarding prompting, SAM-Med2D and SAM-HQ support both bounding-box and point prompts, so we evaluated two variants for each. The prompting for MedSAM and OVS-Net follows their original designs, emphasizing bounding-box and point prompts, respectively, while ASPS is prompt-free. For a fair evaluation, all the methods were retrained on the benchmark dataset. Notably, given the large domain gap between natural and vascular images, we initialized SAM-HQ with MedSAM weights. For quantitative evaluation, we adopted the Dice coefficient (Dice) and intersection-over-union (IoU) as metrics to evaluate the segmented vascular morphology.

Quantitative Results

Quantitative results reported in Table 2, grouped by modality, demonstrate that ReG-SAM achieves the best overall segmentation performance on both regular and zero-shot test sets. Although it does not rank first in each modality, it consistently excels on the three most challenging modalities, including Fundus, DSA, and OCTA, where complex

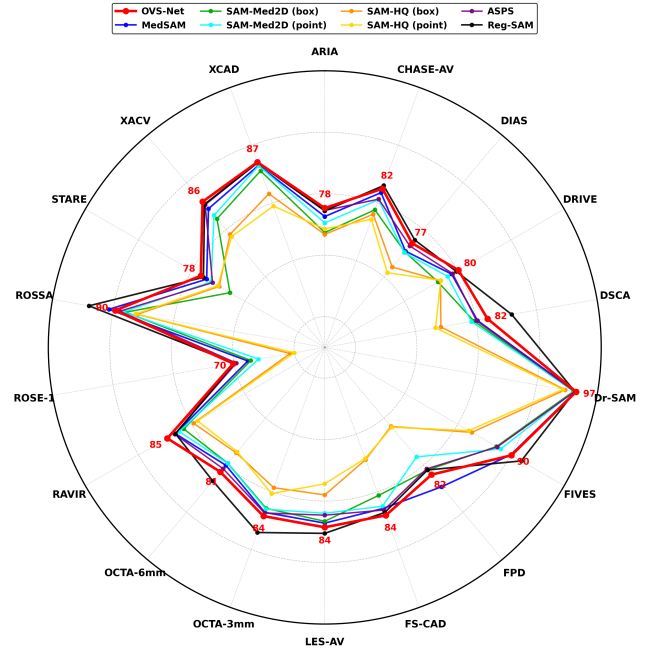


Figure 2: Radar chart comparing dataset-wise Dice scores of different methods.

vascular morphologies with numerous thin and branching vessels make accurate segmentation particularly difficult. On the zero-shot set, ReG-SAM also outperforms OVS-Net, demonstrating strong generalization ability. Notably, these improvements are achieved without requiring any prompt inputs, further highlighting the practicality of ReG-SAM. Figure 2 provides a dataset-level comparison, showing that ReG-SAM delivers more balanced performance by achieving the best results on most datasets while exhibiting only limited performance degradation on a few, consistent with the modality-wise analysis.

Qualitative Results

Figure 3 presents qualitative results to provide a more comprehensive evaluation of ReG-SAM. We highlight several challenging vascular modalities characterized by complex, highly branched vessel structures. As shown in the regions marked by green boxes, baseline methods tend to under-segment fine vessels, whereas ReG-SAM preserves these fine structures more effectively. Although ReG-SAM still misses some vessel details, it consistently demonstrates a stronger capability to capture intricate vascular morphology, resulting in more accurate segmentation. These qualitative results further validate the effectiveness of ReG-SAM for fine-grained vessel segmentation.

Ablation Studies

Ablation studies are conducted to evaluate the key components of ReG-SAM, with results summarized in Table 3. The first three rows examine the architecture by reducing the decoder upsampling stages from four to the original two in

Method	Fundus		DSA		X-Ray		PF	
	Dice↑	IoU↑	Dice↑	IoU↑	Dice↑	IoU↑	Dice↑	IoU↑
ASPS (auto)	85.17±7.72	74.83±9.87	79.34±4.75	66.00±6.45	91.51±5.90	84.89±9.78	80.79±11.35	69.12±14.22
MedSAM (box)	87.04±8.54	77.89±11.34	79.22±4.85	65.86±6.57	91.28±6.28	84.56±10.33	84.59±8.14	74.08±11.29
OVS-Net (point)	<i>87.44±8.19</i>	<i>78.46±10.87</i>	<i>80.89±4.57</i>	<i>68.15±6.33</i>	91.86±5.75	85.46±9.59	<i>82.02±10.66</i>	<i>70.75±13.70</i>
SAM-HQ (box)	80.80±8.58	68.51±10.29	73.74±5.29	58.69±6.60	87.82±8.75	79.32±13.33	71.77±18.08	58.61±19.06
SAM-HQ (point)	80.41±8.08	67.89±9.65	72.78±5.54	57.51±6.79	87.18±9.07	78.38±13.75	71.95±18.80	58.97±19.34
SAM-Med2D (box)	84.38±8.80	73.84±11.36	78.74±5.03	65.21±6.69	90.31±7.19	83.09±11.52	81.04±10.33	69.28±13.38
SAM-Med2D (point)	85.35±8.45	75.24±10.97	78.37±5.33	64.74±6.98	90.79±6.72	83.80±10.89	78.24±11.84	65.70±14.86
ReG-SAM (auto)	88.78±8.93	80.79±12.30	84.19±5.08	73.02±7.37	<i>91.56±5.84</i>	<i>84.96±9.70</i>	81.03±10.95	69.36±13.76

Method	OCTA		SLO		Average		Zero Shot	
	Dice↑	IoU↑	Dice↑	IoU↑	Dice↑	IoU↑	Dice↑	IoU↑
ASPS (auto)	85.97±5.15	75.72±7.45	83.20±1.88	71.28±2.78	85.90±7.80	76.02±10.95	64.00±5.97	47.34±6.40
MedSAM (box)	86.89±6.19	77.31±9.08	83.06±1.85	71.07±2.74	87.06±7.62	77.83±11.08	64.77±5.41	48.13±5.88
OVS-Net (point)	86.66±5.18	76.81±7.56	84.59±1.85	73.34±2.79	87.04±7.63	77.78±10.89	<i>65.27±5.67</i>	<i>48.71±6.16</i>
SAM-HQ (box)	82.62±6.04	70.80±8.09	79.67±3.63	66.36±4.96	81.41±10.54	69.81±13.24	62.08±5.73	45.26±5.94
SAM-HQ (point)	82.86±6.21	71.17±8.26	78.91±3.94	65.34±5.31	81.21±10.66	69.53±13.22	61.03±5.87	44.17±5.99
SAM-Med2D (box)	84.96±5.36	74.21±7.54	81.51±2.80	68.88±3.97	85.07±8.07	74.81±11.37	64.24±5.30	47.54±5.69
SAM-Med2D (point)	85.15±5.63	74.53±7.89	82.38±2.17	70.10±3.14	85.14±8.49	74.99±11.83	63.86±5.73	47.17±6.03
ReG-SAM (auto)	90.18±6.40	82.69±9.86	83.07±1.68	71.08±2.50	88.63±8.24	80.45±11.91	66.20±5.67	49.74±6.25

Table 2: Modality-wise, average, and zero-shot segmentation performance. The best results are highlighted in **bold** and the second-best in *italic*.

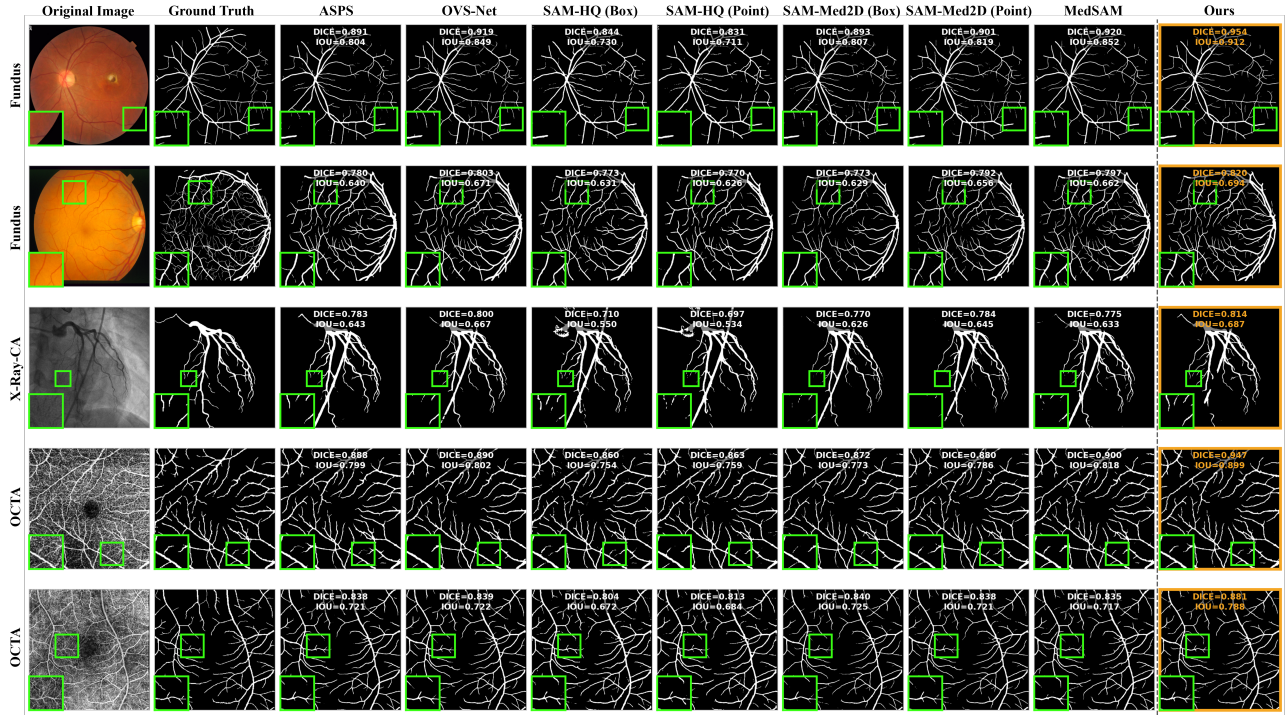


Figure 3: Qualitative comparison of different methods. Challenging regions are highlighted by green boxes and enlarged in the bottom left corner. Evaluation metrics for each case are shown at the top, with the highest values highlighted in yellow.

Configurations	Regular	
	Dice $\uparrow$	IoU $\uparrow$
w/o 4 Upsampling	88.08 $\pm$ 8.46	79.61 $\pm$ 12.23
w/o GPEs	88.34 $\pm$ 8.32	80.00 $\pm$ 11.99
w/o VPEs & VPA	85.10 $\pm$ 10.36	75.32 $\pm$ 14.05
w/o $\mathcal{L}_g$	88.52 $\pm$ 8.24	80.28 $\pm$ 11.98
w/o $\mathcal{L}_p$	86.92 $\pm$ 8.09	77.67 $\pm$ 11.46
ReG-SAM	88.63$\pm$8.24	80.45$\pm$11.91

Configurations	Zero Shot	
	Dice $\uparrow$	IoU $\uparrow$
w/o 4 Upsampling	64.91 $\pm$ 5.67	48.30 $\pm$ 6.14
w/o GPEs	64.27 $\pm$ 5.64	47.60 $\pm$ 6.03
w/o VPEs & VPA	62.97 $\pm$ 5.58	46.19 $\pm$ 5.88
w/o $\mathcal{L}_g$	65.46 $\pm$ 5.78	48.93 $\pm$ 6.32
w/o $\mathcal{L}_p$	61.57 $\pm$ 5.51	44.71 $\pm$ 5.72
ReG-SAM	66.20$\pm$5.67	49.74$\pm$6.25

Table 3: Experimental results of the ablation studies on architectures and loss functions. The best results are highlighted in **bold**.

SAM, or by removing either GPEs or VPEs. Notably, since VPEs are designed to work jointly with the VPA module during upsampling, both VPE and VPA are removed in this ablation. Reducing the number of upsampling stages consistently degrades performance, demonstrating the importance of gradual, learnable upsampling for recovering complex vascular structures. Removing either GPEs or VPEs also degrades performance, with a larger drop observed after removing VPEs, highlighting the importance of vessel-aware fine-grained decoding. Employed in a pixel-wise manner, VPEs and VPA provide rich local semantic guidance for vessel segmentation, whereas GPEs capture global structural priors that provide coarse but informative morphological context.

The next two rows evaluate the representation loss terms, $\mathcal{L}_g$ and $\mathcal{L}_p$, for GPEs and VPEs, respectively. As shown in Table 3, removing either loss degrades performance, indicating that both losses effectively regularize the learned representations by encouraging modality-aware embedding alignment during training. Consequently, more discriminative structural and semantic representations can be obtained during inference, leading to improved segmentation accuracy.

Comparison on Sampling Strategies

Since our goal is to learn robust, modality-aware vascular priors, we adopted random sampling instead of similarity-based top- k sampling to select reference graphs from the vascular database. For top- k sampling, image embeddings were extracted using DINOv2 (Oquab et al. 2023), and the k most similar images were retrieved based on cosine similarity to construct the graph set. Results of comparing both strategies with k ranging from 1 to 5 are shown in Figure 4.

Overall, random sampling outperforms top- k sampling under the current dataset setting. Random sampling with $k = 3$ achieves the best performance in both cases. Smaller k val-

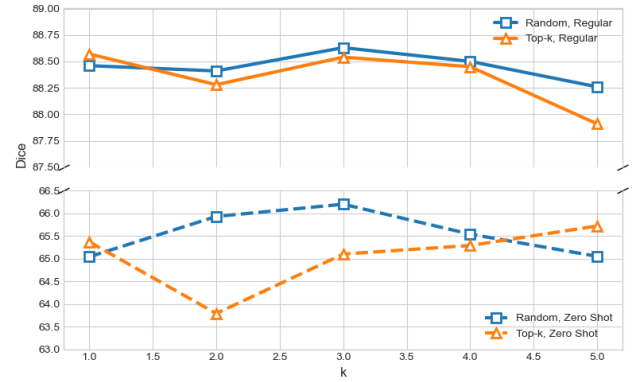


Figure 4: Performance comparison on the regular and zero-shot test sets using random and top- k sampling strategies.

ues provide insufficient information for effective alignment, while larger values increase fitting difficulty and introduce more noise, leading to performance degradation. In addition, random sampling is more stable across different k values, likely because it exposes the model to more diverse graph combinations. In contrast, top- k sampling relies on a limited set of neighbors, resulting in poorer generalization to unseen graph sets, especially under limited data conditions.

Discussion and Conclusion

In this paper, we propose ReG-SAM, a reference graph-guided foundation model for 2D vessel segmentation built upon SAM. Motivated by recent advances in general vessel segmentation, we introduce two embedding representations, GPEs and VPEs, to enhance SAM framework for vessel segmentation. To eliminate their reliance on ground-truth masks during inference while promoting learning robust modality-aware representations, we construct a vascular database and introduce two reference graph-guided representation learning schemes to estimate GPEs and VPEs from randomly sampled graph set. Comprehensive evaluations on 19 public vascular datasets demonstrate that ReG-SAM consistently outperforms existing methods, achieving more accurate overall segmentation and stronger zero-shot generalization.

However, the performance of ReG-SAM is still limited by several factors. First, vessel annotation is highly challenging and labor-intensive, resulting in substantially fewer available samples compared to tasks such as organ segmentation. Even after collecting multiple public datasets, the total data volume remains below 5000 samples, limiting the full potential of foundation models. This is particularly relevant to our framework, as its reference-based mechanism could benefit from a larger and more diverse database, potentially enabling more effective reference selection and alternative sampling strategies. Furthermore, highly accurate predictions may be mistaken for over-segmentation due to low-quality ground-truth annotations, leading to underestimated performance. We therefore expect that larger, higher-quality, and more diverse vessel datasets will further improve ReG-SAM and widen its performance gap over existing methods.

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