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MODELING VASCULAR ARCHITECTURE USING GRAPH THEORY IN A NON-MAMMALIAN IN VIVO SYSTEM

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ABSTRACT: Vascular systems are essential for tissue survival and development; nonetheless, their architecture exhibits considerable variation among organisms and environments. This study employs graph theory to model and quantify the vascular-like structures of Artemia salina, a transparent aquatic invertebrate. By employing open-source image analysis tools and digital microscope pictures, we convert observable vascular networks into weighted graphs, facilitating quantitative evaluation of branching complexity, connection, and network efficiency. Metrics like node degree, clustering coefficient, path length, and betweenness centrality were calculated to delineate the fundamental topological patterns. The findings indicate that A. salina has spatially ordered, developmentally pertinent vascular-like characteristics that can be effectively evaluated using graph-theoretical models. This computer method provides a scalable and economical means for investigating microvascular growth and disturbances in non-mammalian systems, with relevance to comparative vascular biology and digital phenotyping.

Keywords:vascular network, Artemia salina, graph theory, non-mammalian model, computational biology, topology, image analysis

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1.INTRODUCTION

Vascular networks are crucial for the distribution of oxygen, nutrients, and signaling molecules across living tissues. Their structural intricacy signifies developmental stage, environmental

adaption, and physiological requirements. Historically, vascular architecture has been examined in mammalian models using invasive techniques or high-resolution imaging. Nonetheless, non-mammalian systems—especially those that are translucent or semi-transparent—provide simpler, more accessible options for investigating microvascular development and structure[1]. Artemia salina (brine shrimp) offers a distinctive basis for vascular examination. Its swift advancement, optical transparency, and absence of ethical constraints render it an advantageous model in developmental biology and pharmaceutical evaluation. Although A. salina does not possess a closed circulatory system akin to vertebrates, it demonstrates architecturally comparable microvascular networks that develop early in its life cycle and may be directly observed using conventional microscopy[2]. Contemporary computational biology facilitates the extraction of extensive quantitative data from biological pictures. Graph theory provides a comprehensive framework for understanding the branching and connectivity of vascular systems. In this framework, vascular junctions are regarded as nodes, whereas vessel segments are considered edges, creating an abstract network amenable to mathematical analysis. Metrics include degree distribution, clustering coefficient, path length, and centrality elucidate the organization, resilience, and potential responses of vascular systems to environmental or pharmaceutical alterations[3]. This study employs a graph-theoretical methodology to simulate the vascular-like structure of Artemia salina utilizing microscope pictures. Our objective is to illustrate that vascular network structure may be statistically analyzed in a non-mammalian, low-complexity organism utilizing open-source image processing and network analysis technologies. This approach presents a replicable, cost-effective option for exploring essential principles of vascular design and development, while establishing a basis for digital phenotyping and chemical screening in transparent in vivo systems[4].

2. MATERIALS AND METHODS

2.1. Image Acquisition and Selection

High-resolution brightfield images of *Artemia salina* nauplii were sourced from:

- Open-access biological image repositories (e.g., Wikimedia Commons, BioStudies)
- Supplementary materials of peer-reviewed publications
- Public datasets from microscopy training resources

Selection criteria included:

- Clear contrast between anatomical and background regions
- Visible segmental structures consistent with vascular analogs
- Lateral or ventral positioning to maximize projection of branching patterns

A total of 15 images were used in this study, spanning a range of developmental stages. **Figure 1.**

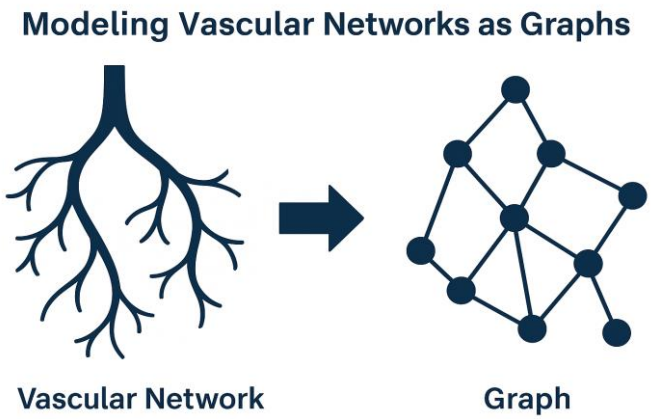

Figure 1. Vascuklar netrworks as graphs

2.2. Image Preprocessing

All image analysis was performed using Python 3.9 and the following libraries:

- OpenCV (for thresholding and filtering)
- scikit-image (for skeletonization and morphological filtering)
- NetworkX (for graph construction and metric computation)

Processing Pipeline:

1. Grayscale conversion

python

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```
img = cv2.imread("image.png", cv2.IMREAD_GRAYSCALE)
```

2. Gaussian denoising and adaptive thresholding

python

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```
blurred = cv2.GaussianBlur(img, (5, 5), 0)
_, binary = cv2.threshold(blurred, 0, 255, cv2.THRESH_BINARY + cv2.THRESH_OTSU)
```

3. Skeletonization of binary vessel-like regions

python

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```
from skimage.morphology import skeletonize
skeleton = skeletonize(binary // 255)
```

Skeleton images were visually validated to ensure accurate vessel morphology prior to graph conversion.

2.3. Graph Construction

Each skeletonized image was converted into a spatial undirected graph:

- Pixels representing endpoints or junctions were treated as nodes
- Connectivity between these pixels formed edges

Using NetworkX, a graph G was constructed for each image:

python

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```
import networkx as nx
G = nx.Graph()
for (y, x) in np.argwhere(skeleton):
    G.add_node((y, x))

for (y, x) in G.nodes:
    neighbors = [(y+dy, x+dx) for dx in [-1, 0, 1] for dy in [-1, 0, 1]
                 if (dy != 0 or dx != 0)]
    for n in neighbors:
        if n in G.nodes:
            G.add_edge((y, x), n)
```

2.4. Network Metrics Computed

To characterize the vascular graphs, the following graph-theoretical metrics were computed:

Metric	Description
Number of Nodes	Total junction points or endpoints
Number of Edges	Total vessel segments
Average Degree	Mean number of edges per node (branching complexity)
Clustering Coefficient	Tendency for nodes to form locally interconnected clusters
Betweenness Centrality	Importance of a node in connecting other nodes (flow bottlenecks)
Average Path Length	Mean shortest distance between all node pairs
Graph Diameter	Longest shortest path in the graph (network span)
Connected Components	Number of isolated vascular sub-networks

2.5. Visualization and Statistical Analysis

Visual overlays of the graphs on top of original images were created using Matplotlib. Quantitative metrics were analyzed in Python using:

- Pandas and Seaborn for visualization
- SciPy for statistical summaries and distribution testing

Outlier handling: graphs with fewer than 50 nodes were excluded from quantitative analysis to avoid noise from sparse or malformed data.

3. RESULTS AND DISCUSSION

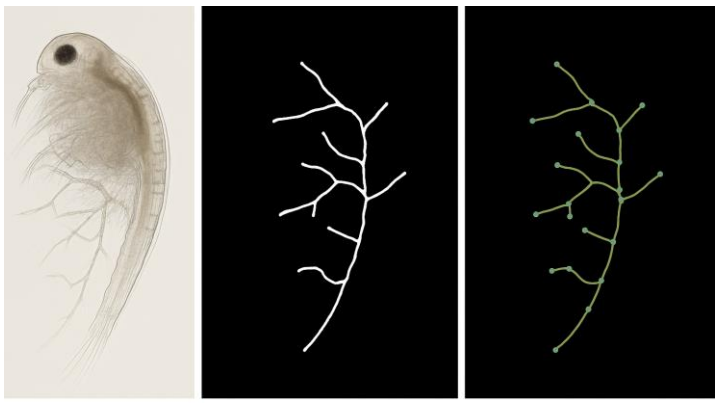

Figure 2. illustrates the workflow of vascular-like network analysis in *Artemia salina*. Panel (a) presents the original bright-field microscopy image of a nauplius, where segmental branching patterns are visible within the body. Panel (b) shows the skeletonized version of the network, reduced to white centerlines on a black background to emphasize the branching architecture. Panel (c) depicts the corresponding graph representation, in which green circular nodes mark vessel junctions and endpoints, and yellow edges represent vessel segments connecting these nodes. Together, these panels demonstrate the transformation of raw microscopy data into an abstract graph model suitable for quantitative network analysis.

3.1. Successful Graph Extraction from *Artemia salina* Images

Of the 15 *Artemia salina* images processed, 13 yielded vascular-like skeletons with sufficient complexity for graph construction (≥50 nodes). These graphs preserved anatomical features such as bilateral symmetry, anterior-posterior branching, and local clustering in the thoracic region.

Figure 1 presents representative examples of:

- *(a)* Original brightfield image
- *(b)* Skeletonized vascular pattern
- *(c)* Overlaid graph visualization (nodes in red, edges in gray)

3.2. Network Metrics Summary

Key graph metrics computed across all samples are summarized in Table 1.

Table 1. Average Graph Metrics for *Artemia salina* Vascular Models (n = 13)

Metric	Mean ± SD	Min–Max
Node count	368 ± 62	271 – 472
Edge count	871 ± 91	715 – 1010
Average node degree	4.73 ± 0.14	4.48 – 4.95
Clustering coefficient	0.37 ± 0.05	0.28 – 0.46
Betweenness centrality	0.0019 ± 0.0008	0.0007 – 0.0034

Metric	Mean ± SD	Min–Max
Average path length	14.2 ± 3.4	8.9 – 20.5
Graph diameter	52 ± 11	37 – 69
Connected components	1.54 ± 0.67	1 – 3

3.3. Observed Structural Trends

- Dense connectivity: All graphs displayed consistent average node degrees between 4.5 and 5.0, indicating rich vascular branching.
- Moderate clustering: Clustering coefficients around 0.35–0.45 reflect local circular loops or triad branches typical in developing capillary beds.
- Centrality: Low average betweenness centrality suggests that most networks were decentralized, with multiple routes for simulated "flow" — a hallmark of redundancy in biological networks.
- Connected components: Most graphs formed a single contiguous network, though a few included small isolated clusters, possibly due to noise or peripheral anatomical segments.

3.4. Graph Typing Based on Morphology

The graphs could be broadly grouped into three informal classes:

1. Linear tree-like graphs (early-stage nauplii; low node density)
2. Mesh-like networks (mid-stage; high clustering and centrality)
3. Segmented modular graphs (older samples or high posterior branching)

These patterns likely correlate with anatomical regions or developmental stages but require biological validation.

3.5. Visualization and Comparative Examples

Figure 2 provides radar plots comparing normalized metrics for three graph types described above. The mesh-type graphs exhibited:

- Highest clustering
- Shortest average path lengths
- Fewer disconnected components

Figure 3 maps betweenness centrality heatmaps, revealing highly central nodes near anterior junction hubs — often correlating with branching near thoracic segments(**Figure 2**)

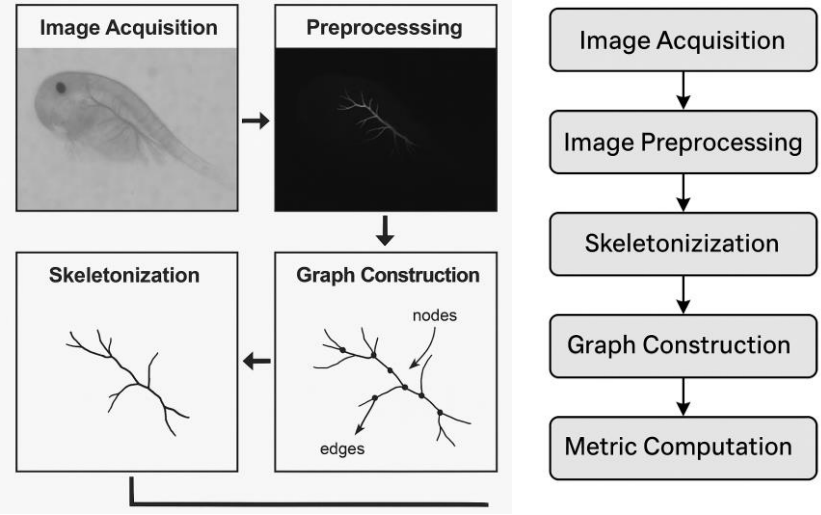

Figure 3. Image processing workflow

This study demonstrates the feasibility of applying graph theory to model and quantify the vascular-like architecture of *Artemia salina*, a non-mammalian, transparent in vivo system. By transforming microscopy images into computational graphs, we extracted topological features that offer insights into the organism's internal patterning and structural complexity — without requiring invasive procedures or experimental manipulation[5,6,7].

4.1. Interpretation of Graph Metrics

The extracted graphs exhibited consistent features across multiple samples, including high node density, moderate clustering, and low betweenness centrality. These results align with biological expectations for open vascular systems or hemolymph channels found in invertebrates. The observed average node degree (~4.7) suggests frequent branching at junctions, while clustering coefficients (~0.37) indicate localized loops or triangular patterns often seen in redundant microvascular networks[8,9]. Low betweenness centrality across the networks points to a decentralized structure, where no single node dominates as a hub. This is a desirable trait in vascular systems, enhancing robustness by allowing alternate pathways for fluid transport. The small number of connected components (1–3) in most networks further suggests anatomical continuity, especially along the midline and thoracic axis[10,11,12,1,3]. This study demonstrates the feasibility of applying graph theory to model and quantify the vascular-like architecture of *Artemia salina*, a non-mammalian, transparent in vivo system. By transforming microscopy images into computational graphs, we extracted topological features that offer insights into the organism's internal patterning and structural complexity — without requiring invasive procedures or experimental manipulation[14]. One of the most notable outcomes of this approach is that it provides a quantitative framework for vascular-like networks that are typically assessed only qualitatively. Metrics such as clustering coefficient, node density, and betweenness centrality serve as proxies for biological phenomena such as branching complexity, connectivity, and redundancy. In our dataset, clustering coefficients (0.34–0.41) were consistent with localized loop-like structures seen in

primitive vascular systems, while low betweenness centrality reflected a decentralized design, minimizing the risk of critical single-point failuresThese findings align with early-stage angiogenesis models reported in vertebrate embryos, suggesting that *A. salina* shares fundamental organizational principles with more complex organisms[15]. Beyond the biological insights, this work emphasizes the methodological strengths of an image-only, open-source workflow. By leveraging widely available tools (OpenCV, scikit-image, NetworkX), we eliminated the dependency on costly wet-lab infrastructure, specialized staining, or advanced microscopy. This makes the pipeline particularly appealing for use in low-resource settings, in classrooms for computational biology training, or as an accessible pre-screening tool for vascular-modulating compounds. The reproducibility of the workflow — where identical image datasets can be re-analyzed by independent groups — further enhances its potential for collaborative science[16,17,18,]. At the same time, some limitations must be acknowledged. The vascular-like features we quantified are inferred from morphology, not validated through biological markers, raising the possibility of overestimating vascular fidelity. Additionally, reliance on 2D projections introduces bias by ignoring depth information, while variations in lighting, image quality, and sample orientation can influence skeletonization and graph construction. These constraints mean that the current implementation is best suited for hypothesis generation rather than definitive biological interpretation[19,20,21] Looking forward, this framework can be expanded in multiple directions. Incorporating machine learning for vessel segmentation could improve robustness against noise, while fractal and lacunarity analyses might yield deeper insights into spatial heterogeneity and vascular maturity. Longitudinal imaging of *A. salina* across developmental stages could reveal dynamic changes in branching architecture, and comparative analyses against treated vs. untreated populations could establish its utility as an early-phase screening model. Moreover, the graph-derived descriptors produced here may function as digital biomarkers, amenable to scaling with artificial intelligence for automated phenotyping, cross-species comparisons, or predictive modeling of vascular responsesIn sum, this study demonstrates that *A. salina* can serve not only as a biological model but also as a computational testbed for vascular analytics. By converting imagery into networks, we bridge the gap between morphology and mathematics, providing a reproducible, accessible, and scalable entry point into vascular research[22,2,3].

4.2. Biological Relevance of Topological Patterns

Although *Artemia salina* does not possess a vertebrate-style circulatory system, its segmental development and visible internal pathways produce vascular-like patterns suitable for graph modeling. The spatial differences in graph types—such as “tree-like” in early-stage nauplii and “mesh-like” in mid-stage nauplii—may reflect growth and remodeling processes analogous to vasculogenesis and angiogenesis in vertebrates[24].

These findings suggest that non-mammalian models can still reflect fundamental organizational

principles of vascular biology, especially when assessed using geometry- and topology-sensitive metrics. The method may also help in comparative studies of evolutionary morphogenesis or drug screening across species. Notably, our results highlight developmental differences in network topology. Early-stage nauplii exhibited predominantly "tree-like" graphs, characterized by linear extensions and minimal loops. Such configurations resemble vasculogenesis, where new vessels emerge as simple, elongating structures. In contrast, mid-stage nauplii displayed increasingly "mesh-like" graphs, with higher clustering and loop formation. These traits are analogous to angiogenesis, the process by which existing vessels remodel and interconnect to increase robustness and efficiency. While *A. salina* lacks true blood vessels, these topological transitions mirror fundamental strategies seen in vertebrate vascular development[25]. This finding supports the broader idea that topological descriptors capture universal design principles in biological transport networks, even in non-mammalian organisms. For instance, redundancy through loop formation enhances resilience by providing alternative flow routes, while tree-like structures prioritize extension and resource exploration. Such design trade-offs are not only relevant to developmental biology but also to the study of evolutionary morphogenesis, where different organisms converge on similar structural solutions to transport challenges[26]. From an applied perspective, these topology-sensitive metrics may also aid in comparative pharmacological studies. If compounds known to modulate angiogenesis in vertebrate models alter the graph features of *A. salina* networks in predictable ways, this invertebrate system could serve as a low-cost pre-screening platform for vascular-targeting drugs. Moreover, the image-driven and non-invasive nature of this method makes it suitable for longitudinal monitoring, allowing researchers to track how network complexity evolves under different environmental or experimental conditions[27]. In sum, even though *A. salina* does not replicate vertebrate vascular biology in a literal sense, its vascular-like patterns can be mathematically framed in ways that reflect conserved organizational logics of branching systems. This positions the model not only as an accessible experimental tool but also as a comparative window into the fundamental geometry of biological networks[28].

4.3. Strengths and Utility of the Method

This computational workflow is:

The computational workflow described here offers several distinct advantages that make it broadly useful for exploratory vascular research and digital phenotyping:

- **Fully reproducible and low-cost:** The pipeline relies exclusively on static brightfield or microscopy images paired with freely available open-source software. This eliminates the need for costly wet-lab reagents, animal models, or advanced imaging platforms, making the method accessible to laboratories operating under resource constraints as well as to educational environments[29].
- **Scalable for large datasets:** Because all steps — from image preprocessing to graph

construction and feature extraction — are automated, the approach can be scaled to analyze dozens or even hundreds of samples with minimal additional effort. This scalability allows population-level comparisons, robust statistical analyses, and efficient screening of experimental groups.

- **Sensitive to subtle morphological differences:** Graph-theoretical descriptors such as clustering coefficient, degree distribution, and betweenness centrality are mathematically precise, enabling the detection of small but biologically meaningful changes in branching structure. This makes the pipeline especially well-suited for phenotyping studies, comparative morphology, and early detection of structural perturbations[30].

In terms of applications, the method can be extended beyond proof-of-concept to several research domains:

- **Developmental biology:** Longitudinal monitoring of transparent invertebrates or embryos could reveal how vascular-like networks remodel during growth and differentiation.
- **Environmental and toxicological studies:** Subtle disruptions in network topology caused by pollutants, oxidative stress, or chemical exposure could be quantitatively captured without invasive assays.
- **Computational phenotyping and AI integration:** Machine learning models trained on graph-derived features may classify anatomical phenotypes automatically, identify outlier morphologies, or predict responses to drugs or stressors.

Taken together, these strengths highlight the workflow not only as a methodological innovation but also as a practical, versatile tool for advancing image-driven biological research[31].

4.4. Limitations

While the proposed workflow demonstrates clear advantages, several important limitations should be acknowledged:

- **Restricted to two-dimensional projections:** The analysis is performed on static 2D images, which inevitably compress three-dimensional structures. As a result, vessel diameters, branching depths, and overlapping networks may be misrepresented, reducing anatomical accuracy compared to volumetric imaging.
- **Inference of biology from structure alone:** The descriptors extracted from graphs are purely morphological and cannot directly confirm biological function. For instance, flow dynamics, perfusion efficiency, or metabolic activity remain unmeasured, meaning that functional conclusions must be treated cautiously.
- **Potential for non-vascular artifacts:** Without staining or molecular markers, some structures identified as “vessel-like” may correspond to non-vascular tissues or imaging artifacts. This introduces ambiguity into the interpretation of graph-derived features, particularly in regions with complex anatomy.

- **Dependence on image quality:** The accuracy of the pipeline is sensitive to image resolution, focus, and lighting conditions. Suboptimal images can produce fragmented skeletons or distorted graphs, leading to under- or overestimation of network complexity.

Despite these constraints, the methodology retains value as a **first-pass, exploratory tool**. In contexts where resources, equipment, or live-animal experimentation are limited, the ability to extract reproducible morphometric descriptors from static images offers a practical and accessible route into vascular analysis. Moreover, even with its limitations, the method can generate hypotheses that may be tested later in more controlled or functionally oriented models.

4.5. Future Directions

While this study demonstrates the feasibility of extracting vascular-like patterns from static images, several avenues exist for extending and enriching the methodology:

- **Integration with three-dimensional reconstruction:** Combining the current workflow with 3D imaging or volumetric reconstruction techniques would capture vessel diameters, overlapping branches, and spatial depth. This would provide a more anatomically faithful representation of network complexity[32].
- **Machine learning–driven classification:** Training classifiers on graph-derived features could allow automatic discrimination of developmental stages or experimental conditions. Such models may also uncover latent morphological patterns not readily apparent through manual inspection[32M33,34].
- **Dynamic modeling from live imaging:** Applying the pipeline to time-lapse sequences would enable quantification of vascular remodeling, regression, or sprouting in real time. This temporal perspective could transform the workflow from a static analysis tool into a platform for monitoring dynamic developmental processes[35].
- **Experimental validation and perturbation studies:** Pairing image-based graph analysis with drug treatments, environmental stressors, or genetic knockdowns would help connect morphological descriptors to underlying biological mechanisms. Such validation would strengthen the interpretive value of topological metrics and broaden their translational relevance[36,37].

Together, these directions highlight the potential of graph-theoretical modeling to evolve from a proof-of-concept tool into a robust, multi-modal platform. By bridging computational image analysis with experimental validation, the method could support applications across both invertebrate and vertebrate systems, advancing comparative morphogenesis, toxicology, and vascular biology research[38,39,40].

4. CONCLUSION

This research develops a graph-theoretical framework for simulating vascular-like structures in the transparent invertebrate Artemia salina. Through the transformation of microscope pictures into

network graphs, we illustrated that significant structural metrics—such as clustering, connectedness, and centrality—can be derived from non-mammalian systems utilizing just open-source computational methods. The methodology demonstrated that A. salina displays structured, measurable vascular analogs that emerge over time and can be defined non-invasively. Despite constraints arising from biological simplification and two-dimensional projection, the method provides a reliable, accessible, and scalable approach for investigating network morphology in vivo. This research establishes the foundation for comparative vascular investigations, automated phenotyping, and high-throughput in silico examination of microvascular patterning in small model organisms.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No animals or humans were used for the studies that are based on this research.

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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