MODELING FLOW THROUGH REALISTIC, ALGORITHMICALLY GENERATED VASCULAR STRUCTURES IN THE LIVER

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virtual liver network

Fraunhofer MEVIS

The Liver

- central metabolic organ (glucose storage, detoxication, …)

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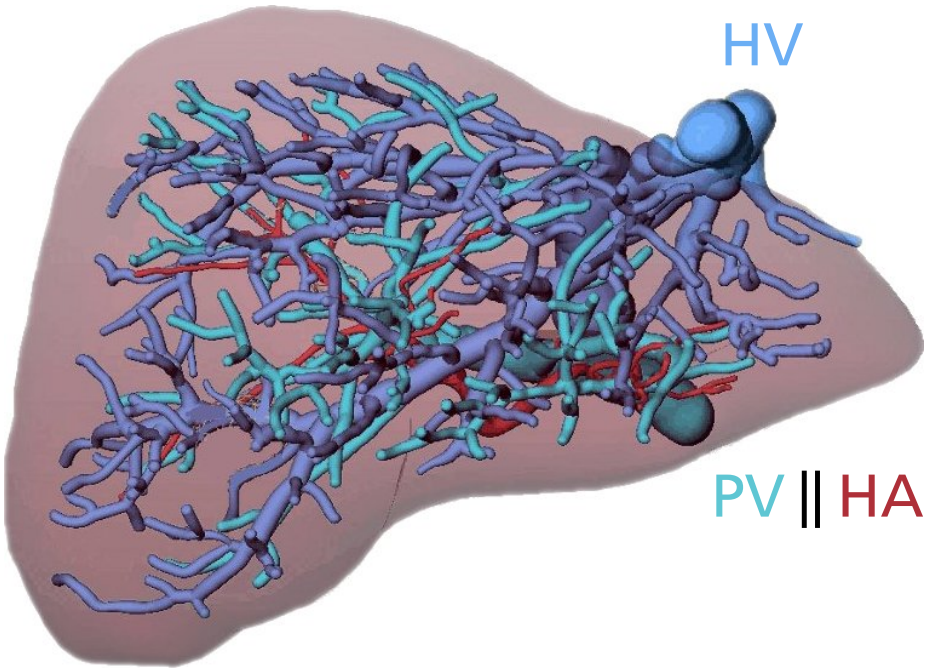
- blood: organism ⟷ liver by three vascular systems
  - hepatic artery (HA) supplies oxygen
  - portal vein (PV) supplies nutrients and toxins,
  - hepatic vein (HV) drains



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- central metabolic organ (glucose storage, detoxication, …)
- blood: organism ⟷ liver by three vascular systems
  - hepatic artery (HA) supplies oxygen
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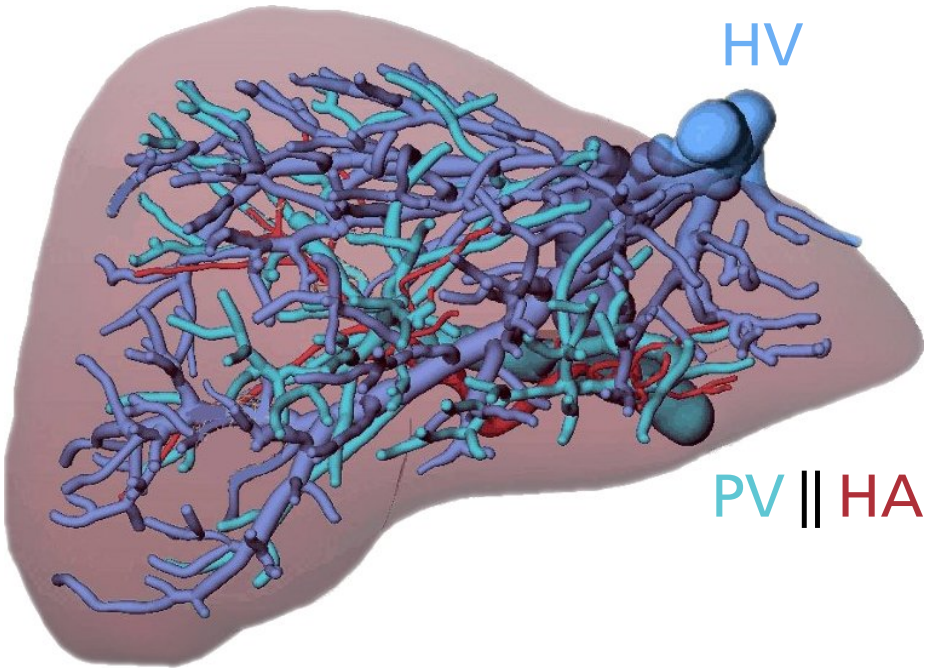
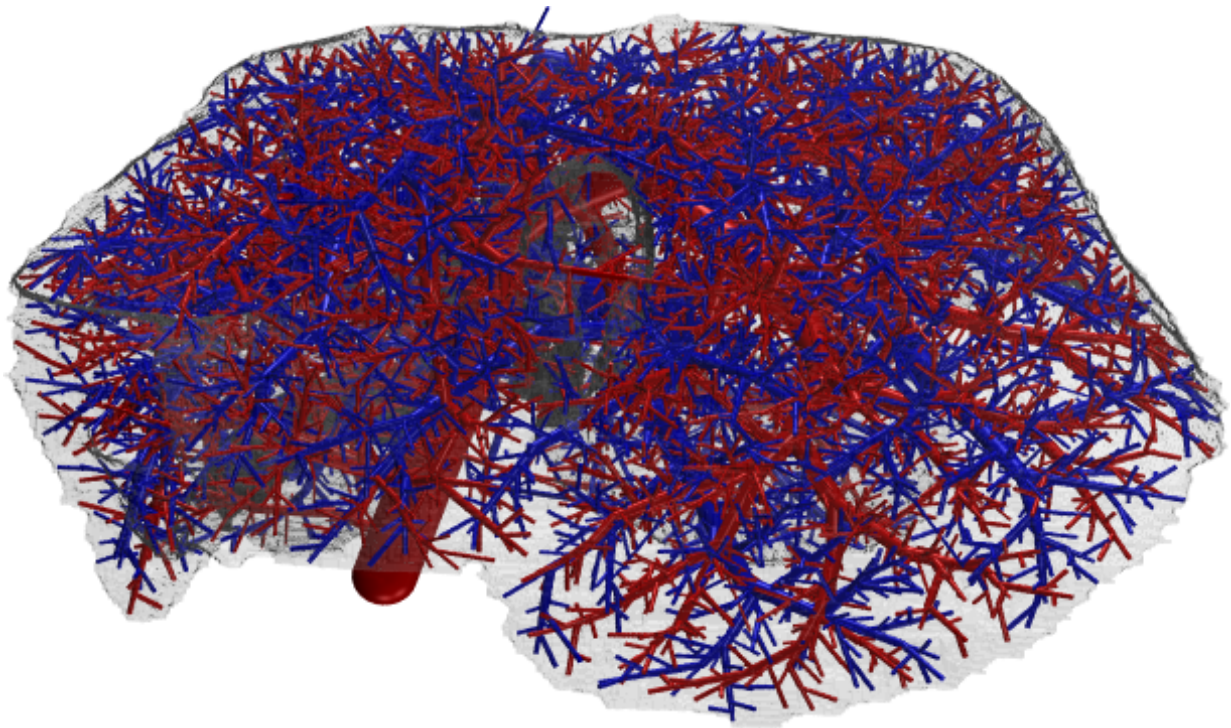
  - hepatic vein (HV) drains
- ~ 1.5 M lobuli (⌀ ≈ 1 mm) as functional units



Goal



- blood flow simulation (distribution of e.g. drug or contrast agent)
- using geometrically realistic model

Outline

1. Introduction
2. Constrained Constructive Optimization
3. Generating Realistic Vascular Systems
4. Application: Flow Simulations

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2. Constrained Constructive Optimization

3. Generating Realistic Vascular Systems

4. Application: Flow Simulations

Cooperation Partners within Virtual Liver Network *(funded by BMBF)*

Niko Komin, Andrea Schenk (MEVIS)
Uta Dahmen, Olaf Dirsch (UK Jena)
Felix Gremse, Fabian Kiessling (UK Aachen)
Markus Krauss, Lars Küpfer (BTS Leverkusen)

1. Introduction

Contents

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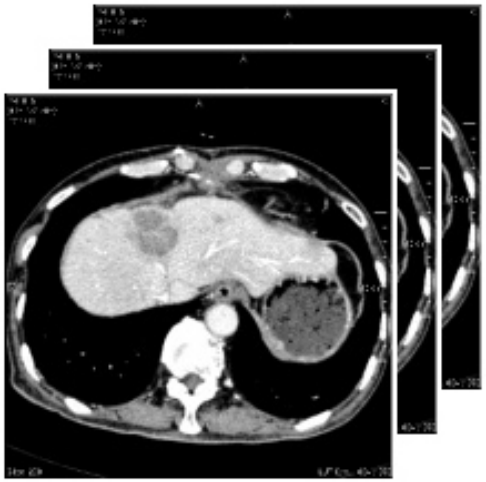
Image Data Acquisition

- in vivo 3D imaging
- corrosion casts and µCT (3D)



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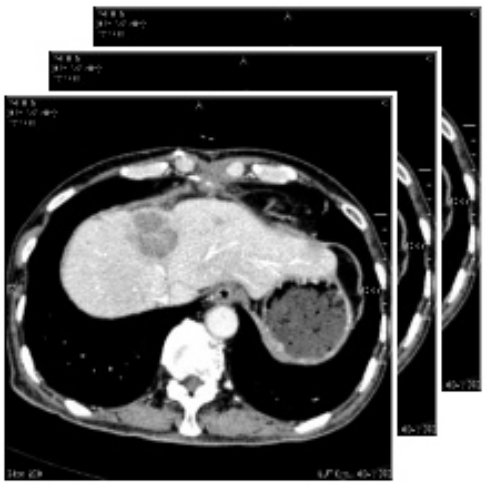

- insufficient resolution for lobular scale

1. Introduction

Generating Vascular Systems

Goal: bridge the resolutional gap

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2. implement algorithm for generating vascular trees

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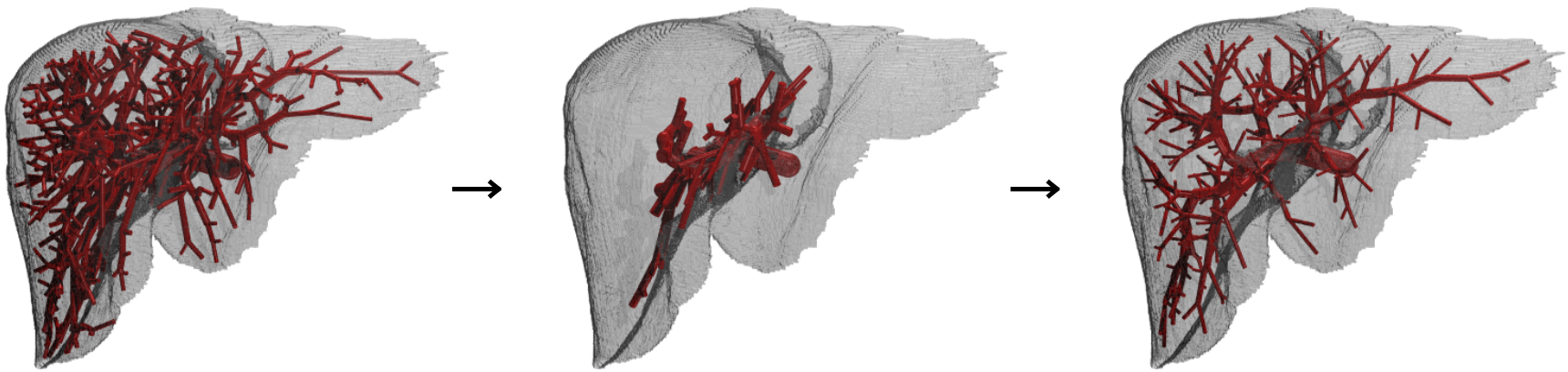
4. starting from coarsened trees, validate semi-fine generated against measured trees (validation/postprocessing)



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2. implement algorithm for generating vascular trees
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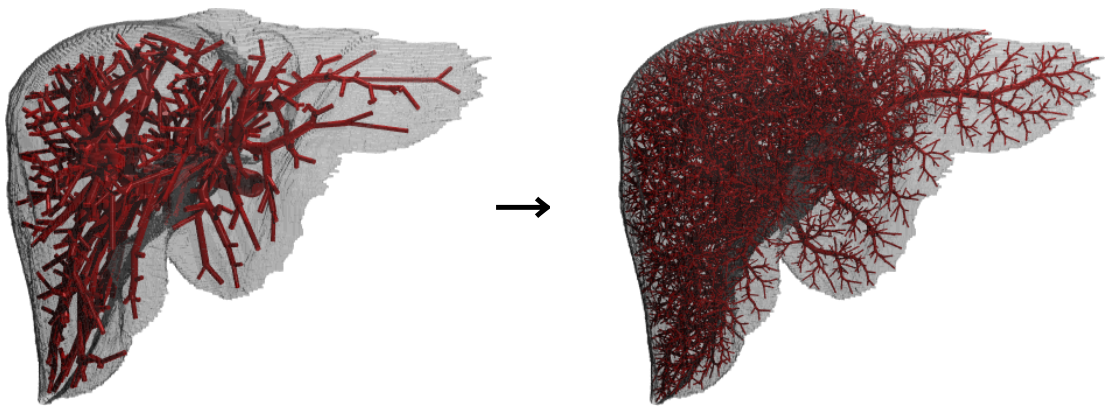
5. starting from measured trees, generate additional resolution (application)



2. Constrained Constructive Optimization

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2. Constrained Constructive Optimization

Idea of the Algorithm

[Schreiner et al. 1993]

- find optimal vascular network for supplying/draining given volume
- assume homogeneous supply
- respect coarse anatomic details and organ shape
- physiologically reasonable assumptions, *no* angiogenesis model

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Input

- initial tree
- desired end points ($\hat{=}$ connection to lobuli or regions)

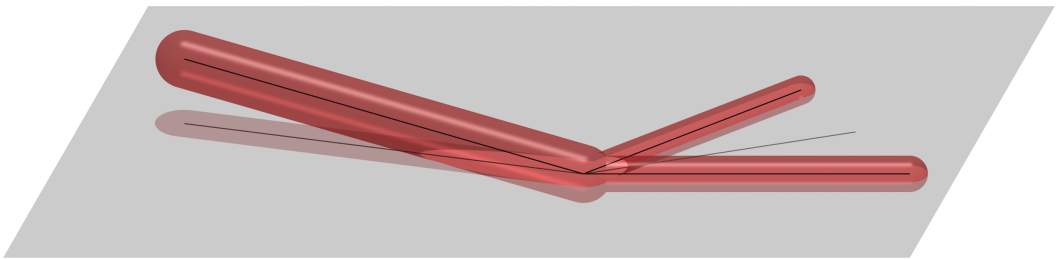
2. Constrained Constructive Optimization

Physical Assumptions

[Schreiner et al. 1993]

Edge radii determined by

- $r_0^\gamma = r_1^\gamma + r_2^\gamma$ with $\gamma = 3$ (Murray's law)



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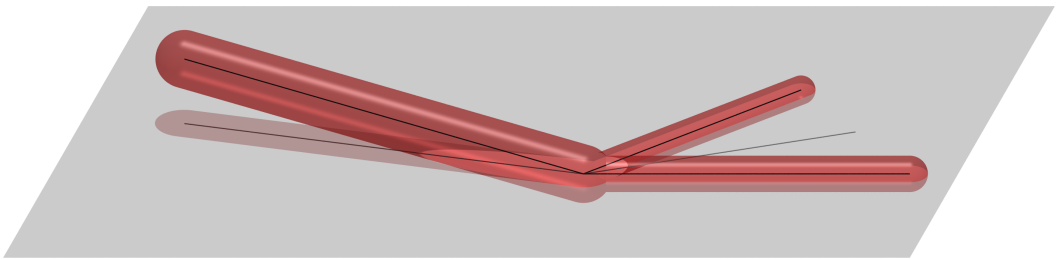
- r_1 and r_2 such that flow resistances of subtrees are balanced



- Poiseuille's law for laminar flow

$$R = \frac{8 \cdot \text{viscosity} \cdot \text{length}}{\pi \cdot \text{radius}^4}$$

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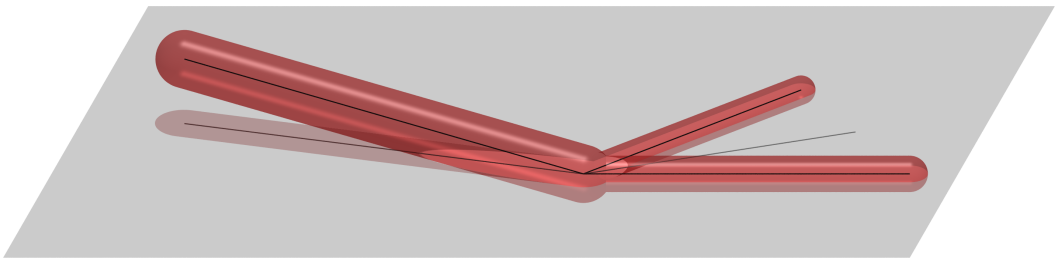

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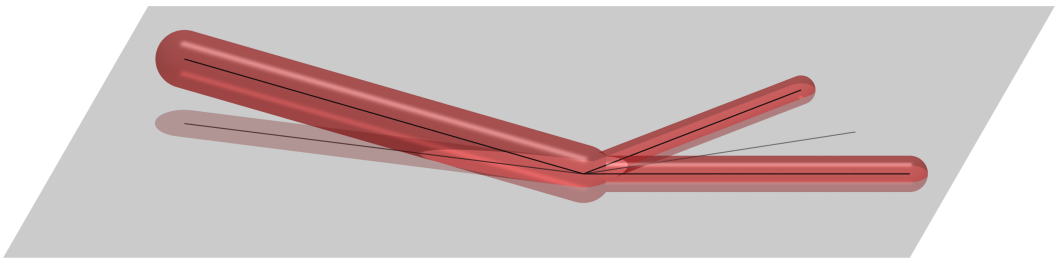

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- decreasing viscosity for radius < 150 µm (Fåhræus-Lindqvist effect)
- serial and parallel connection of edges (Kirchhoff's law)

2. Constrained Constructive Optimization

Physiological Formulation

[Schreiner et al. 1993]

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over

subject to

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over set of vascular trees (topology and geometry)

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over set of vascular trees (topology and geometry)
with constant root radius
supplying given leaf nodes
with given outflow amounts

subject to

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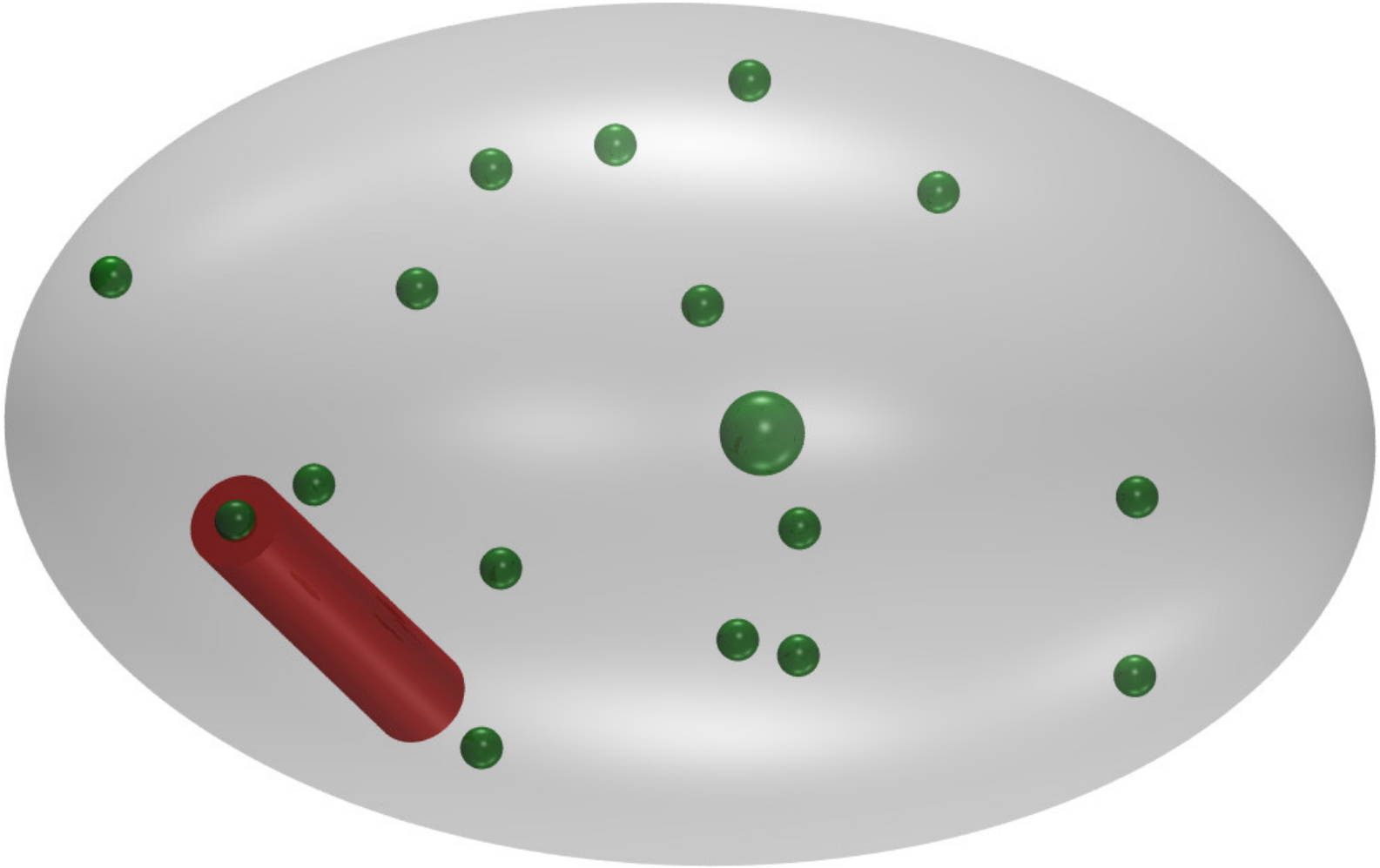
subject to physical constraints for radii

2. Constrained Constructive Optimization

Demo



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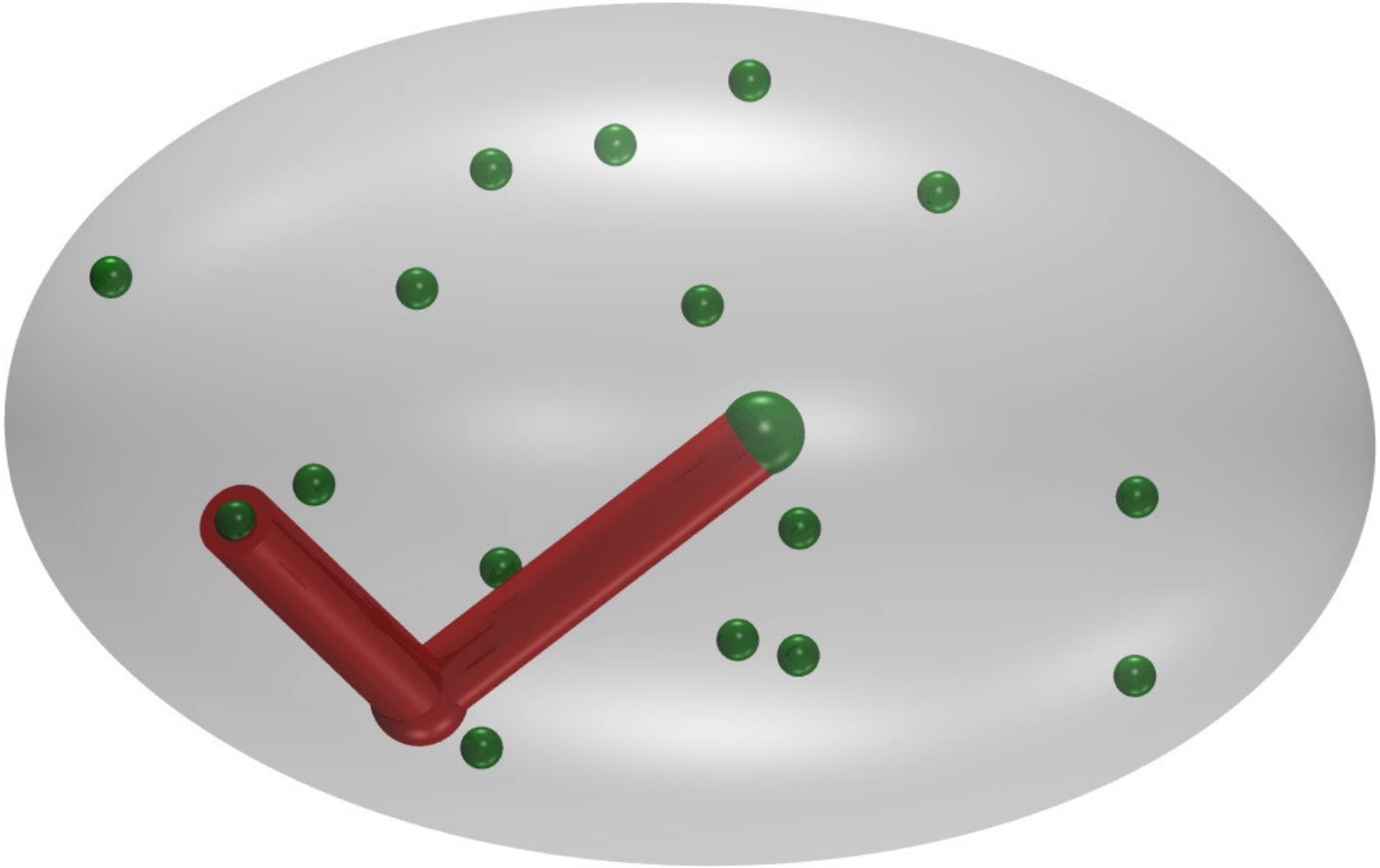

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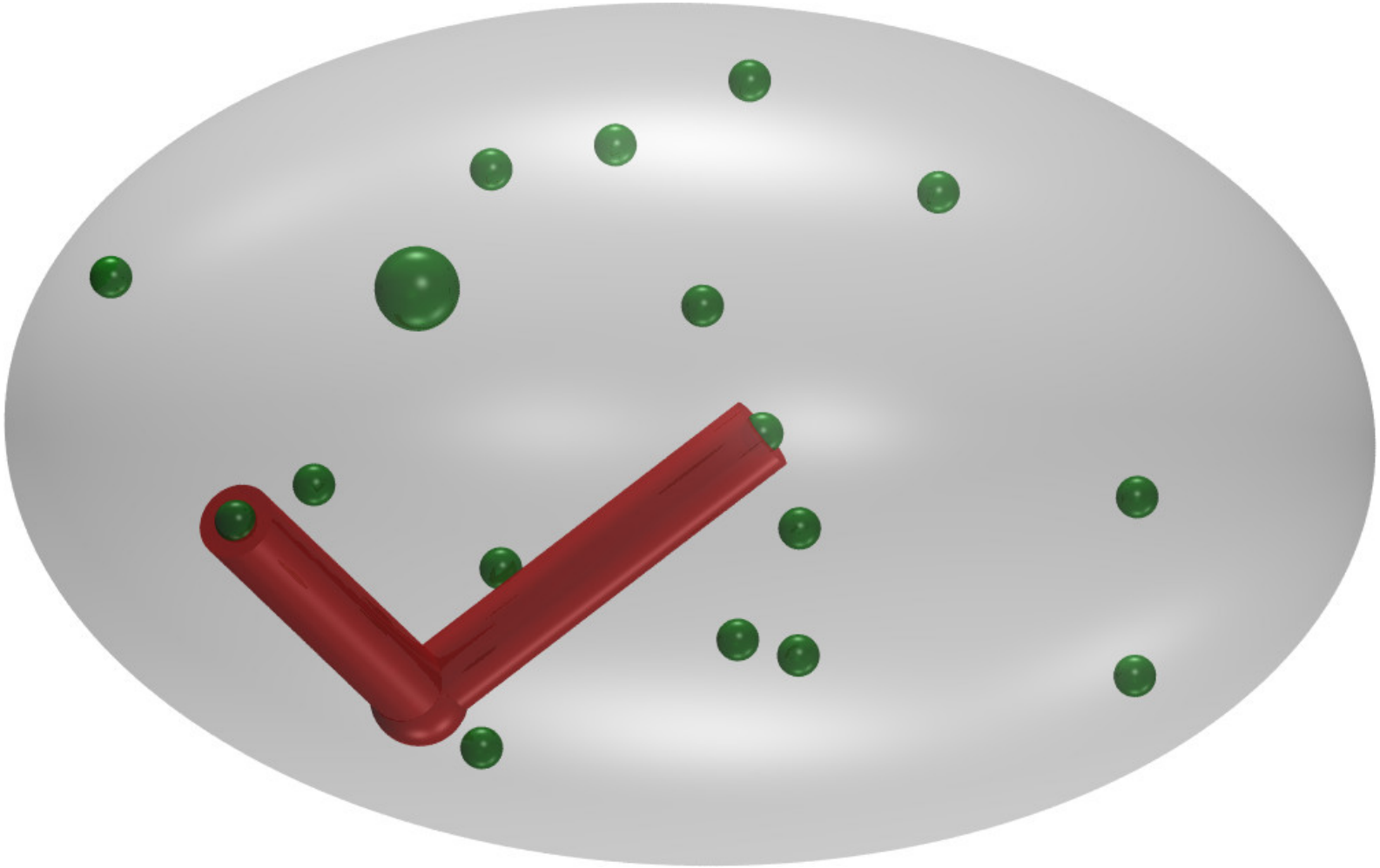

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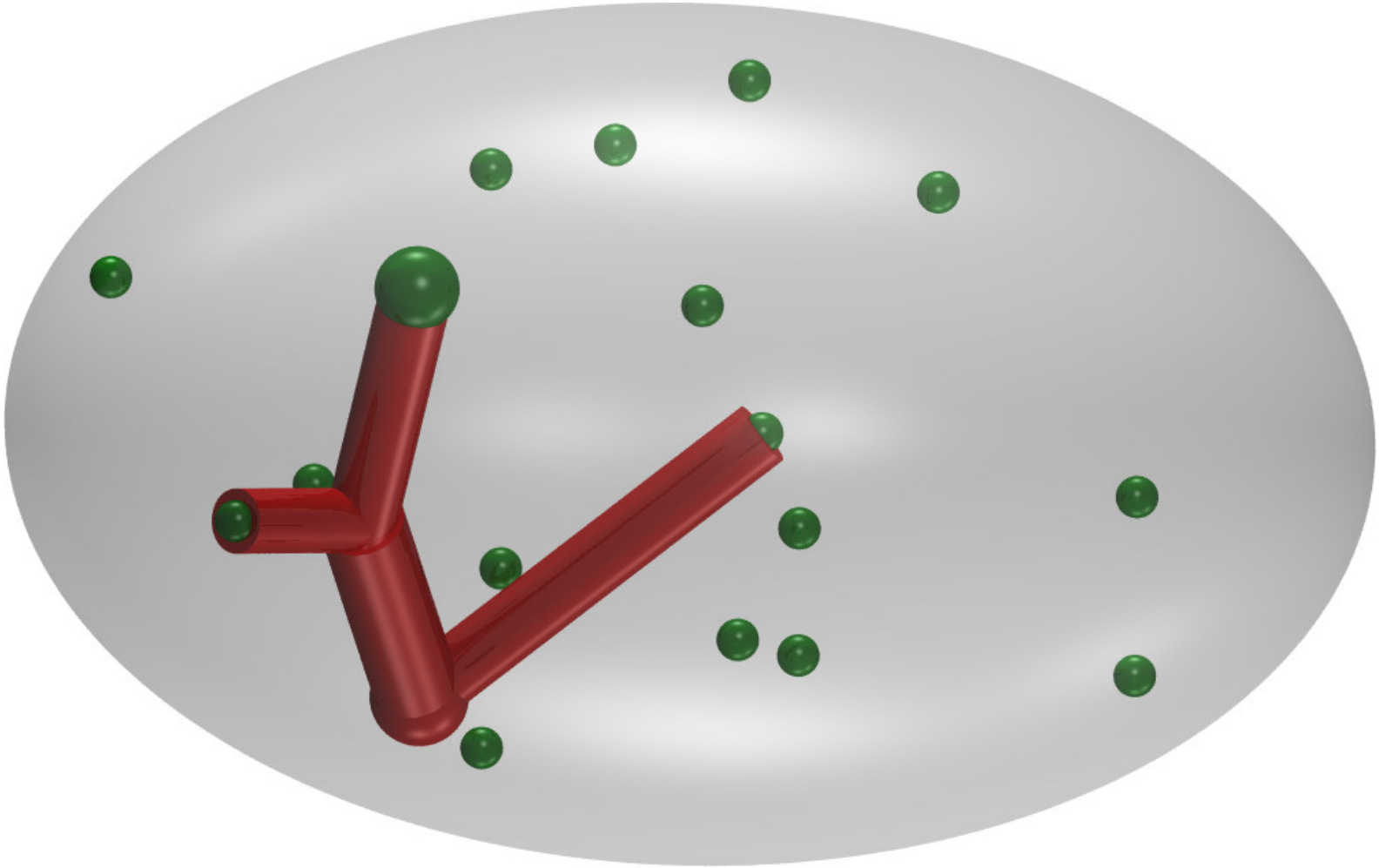

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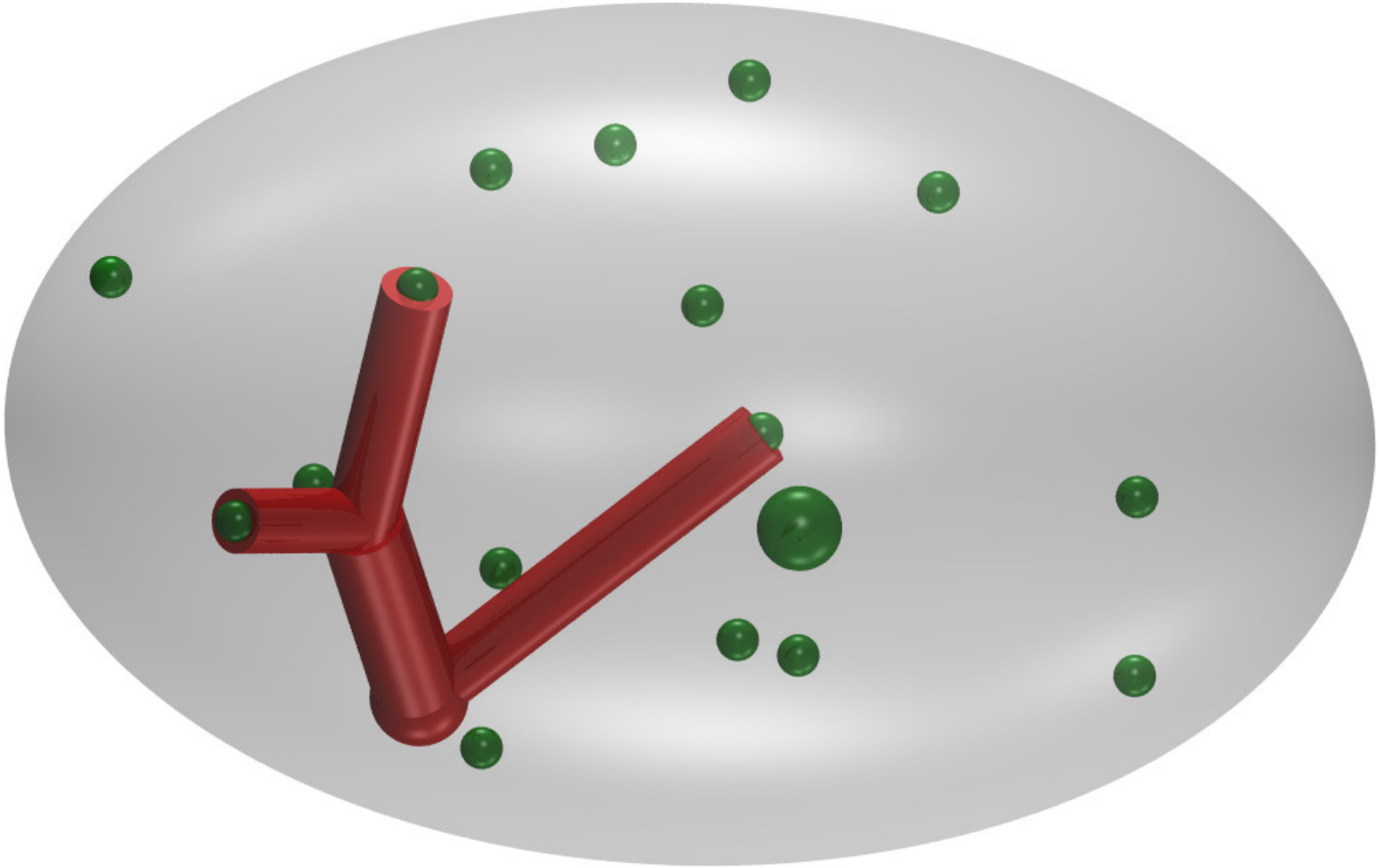

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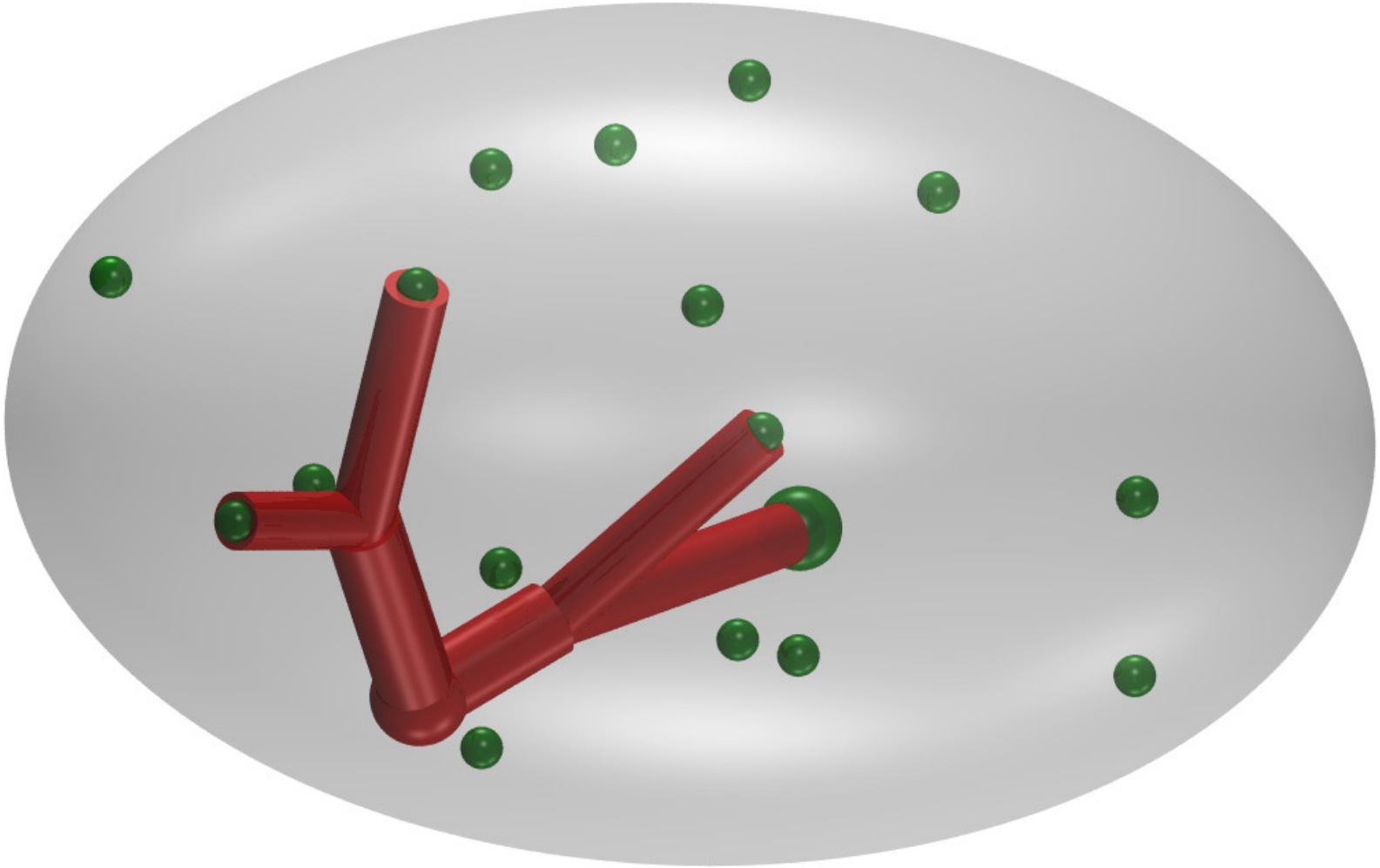

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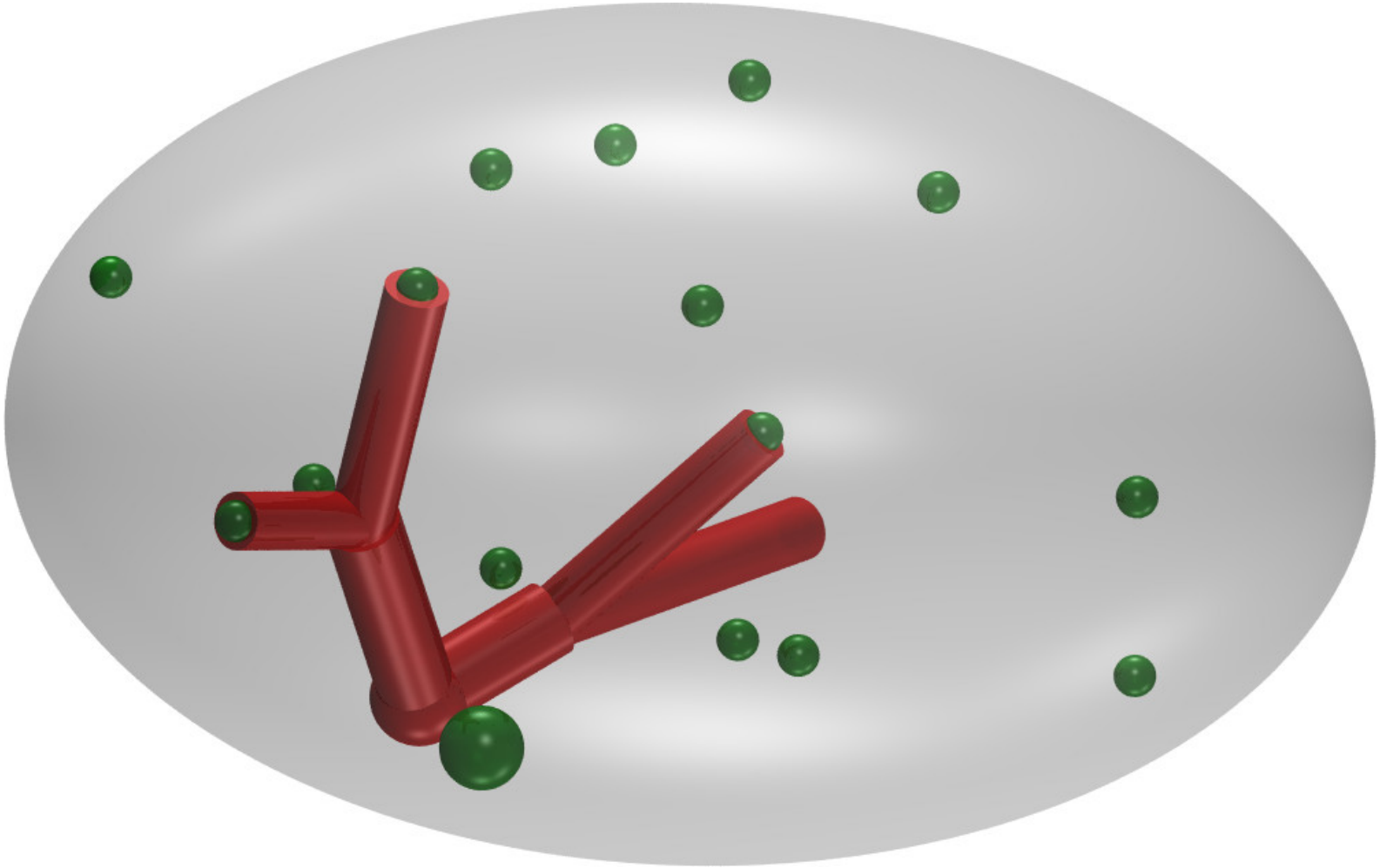

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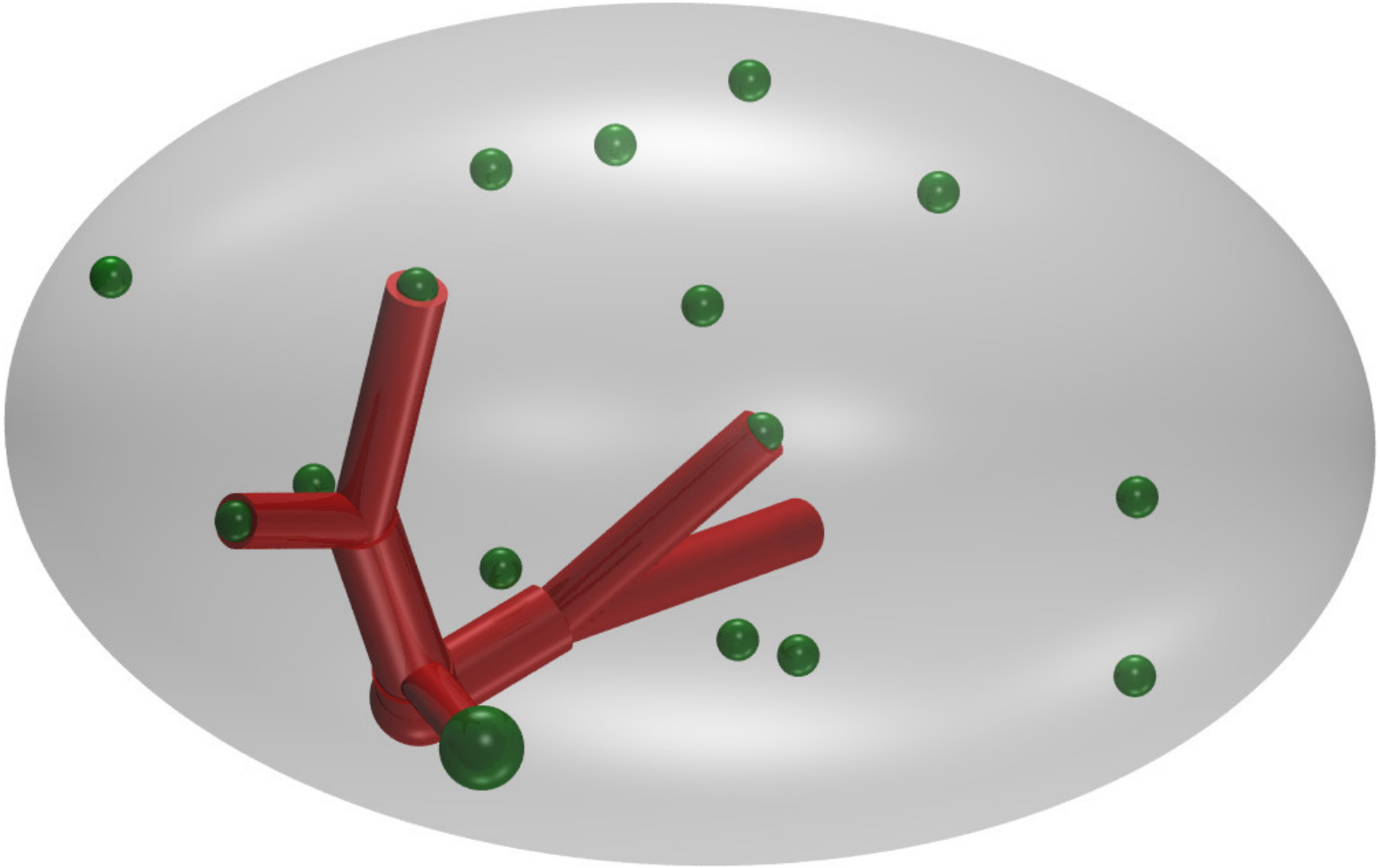

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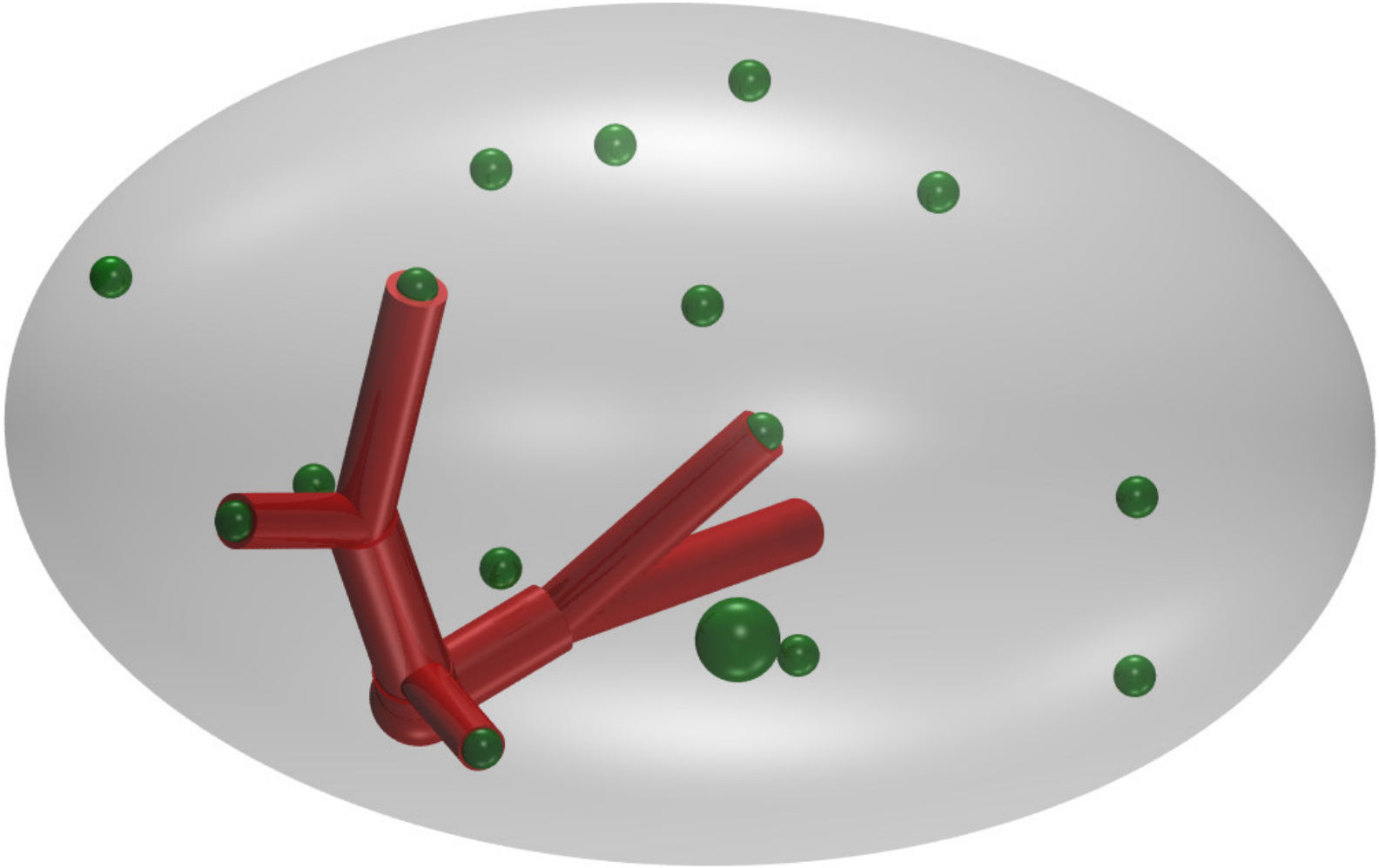

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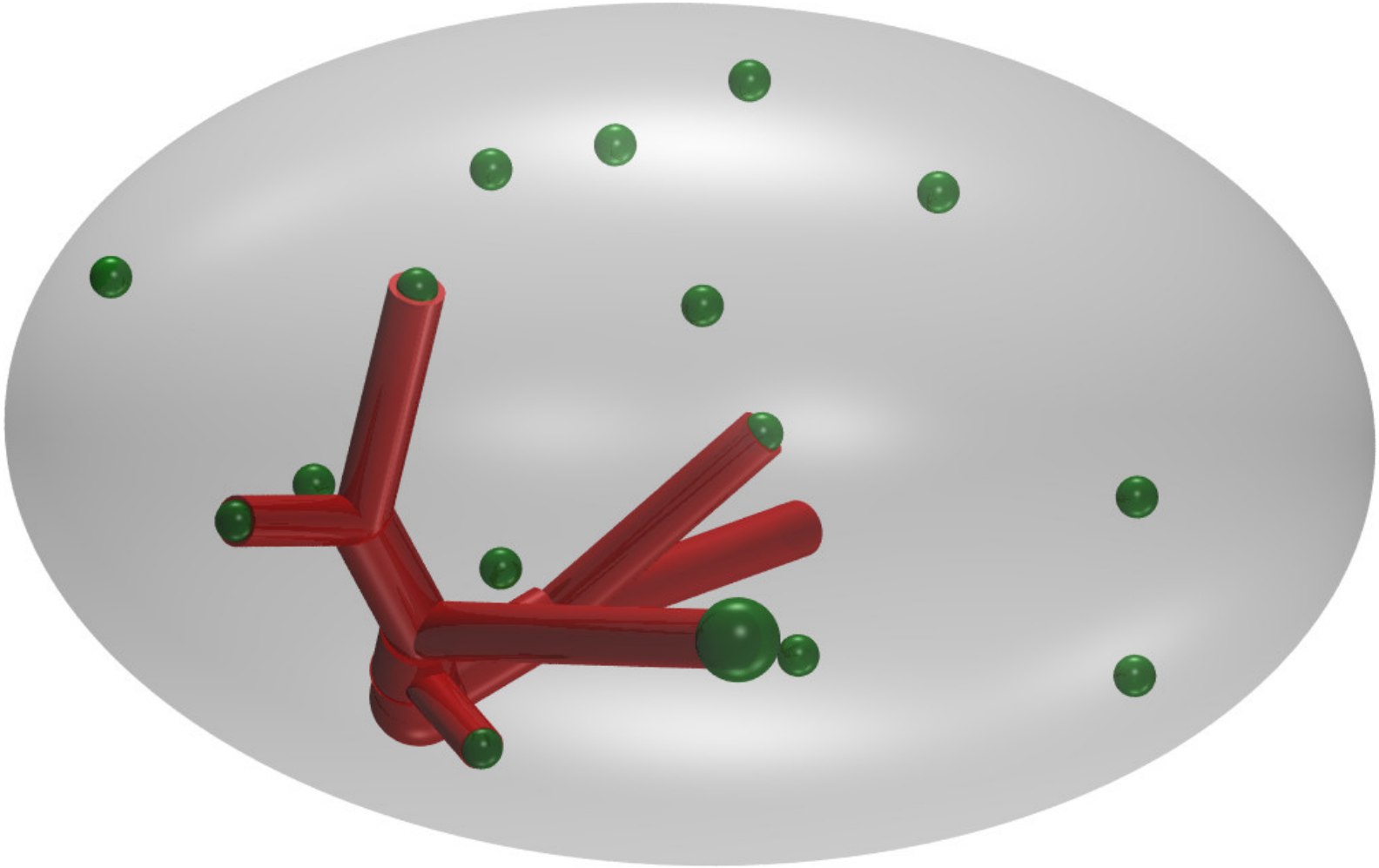

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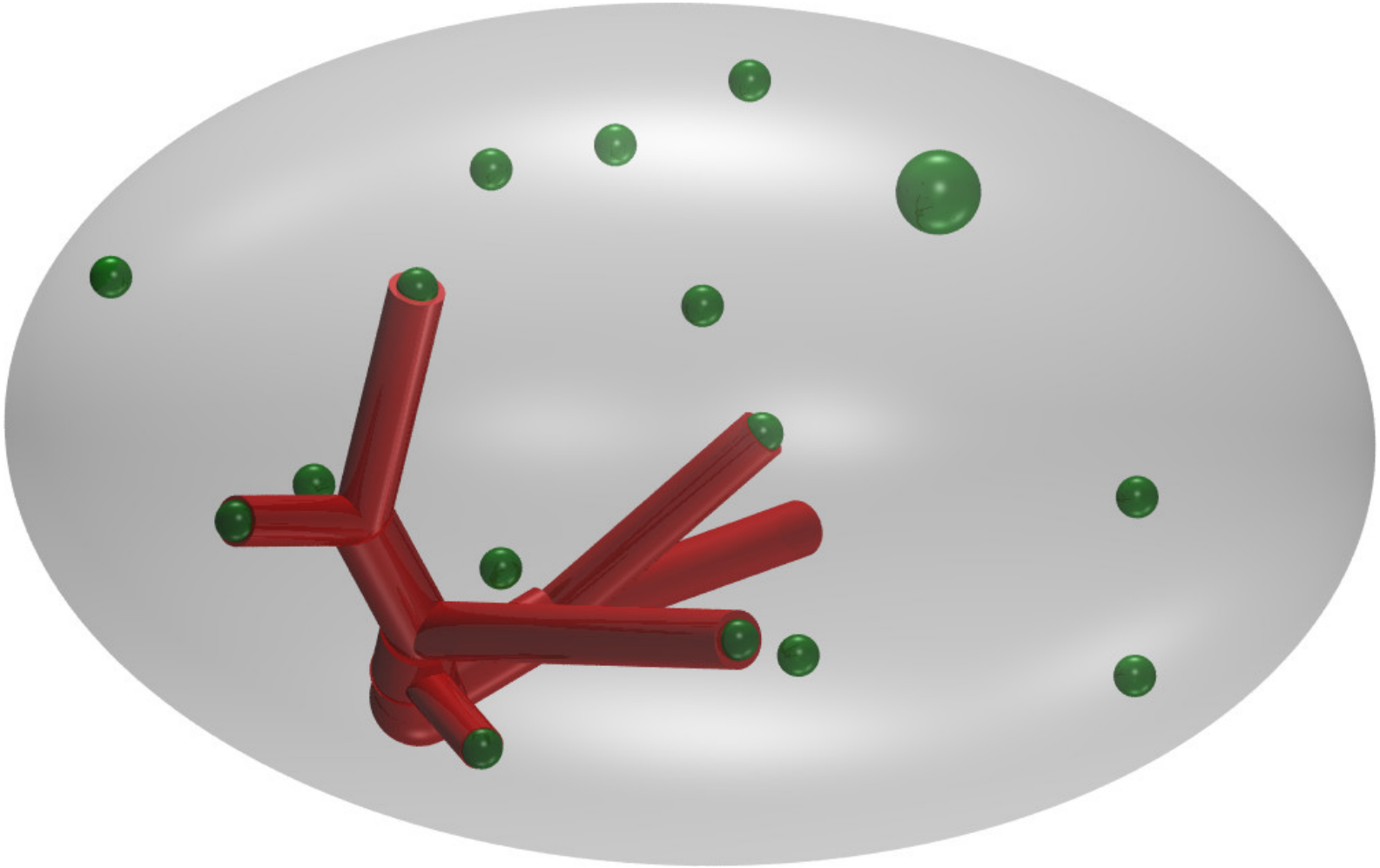

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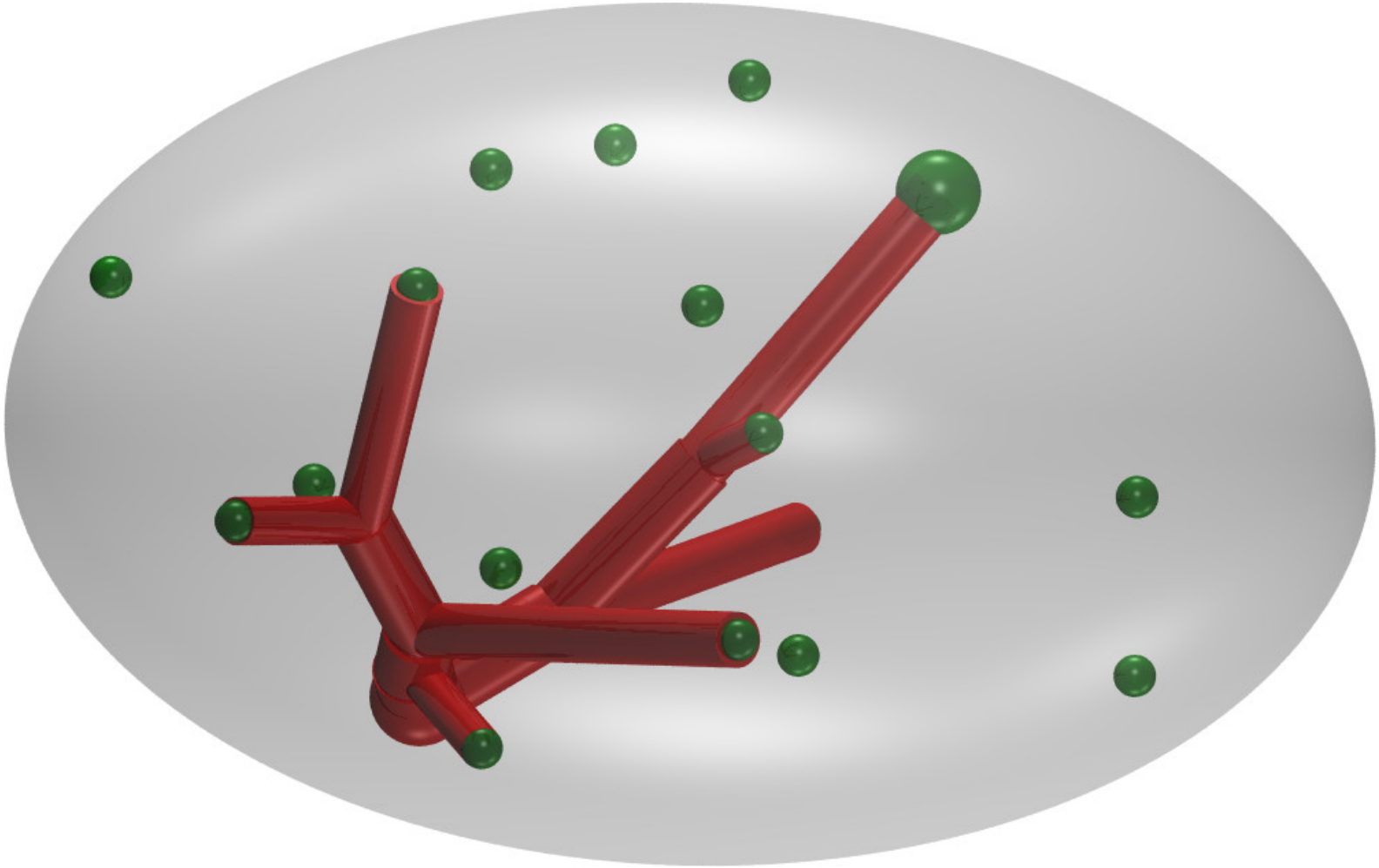

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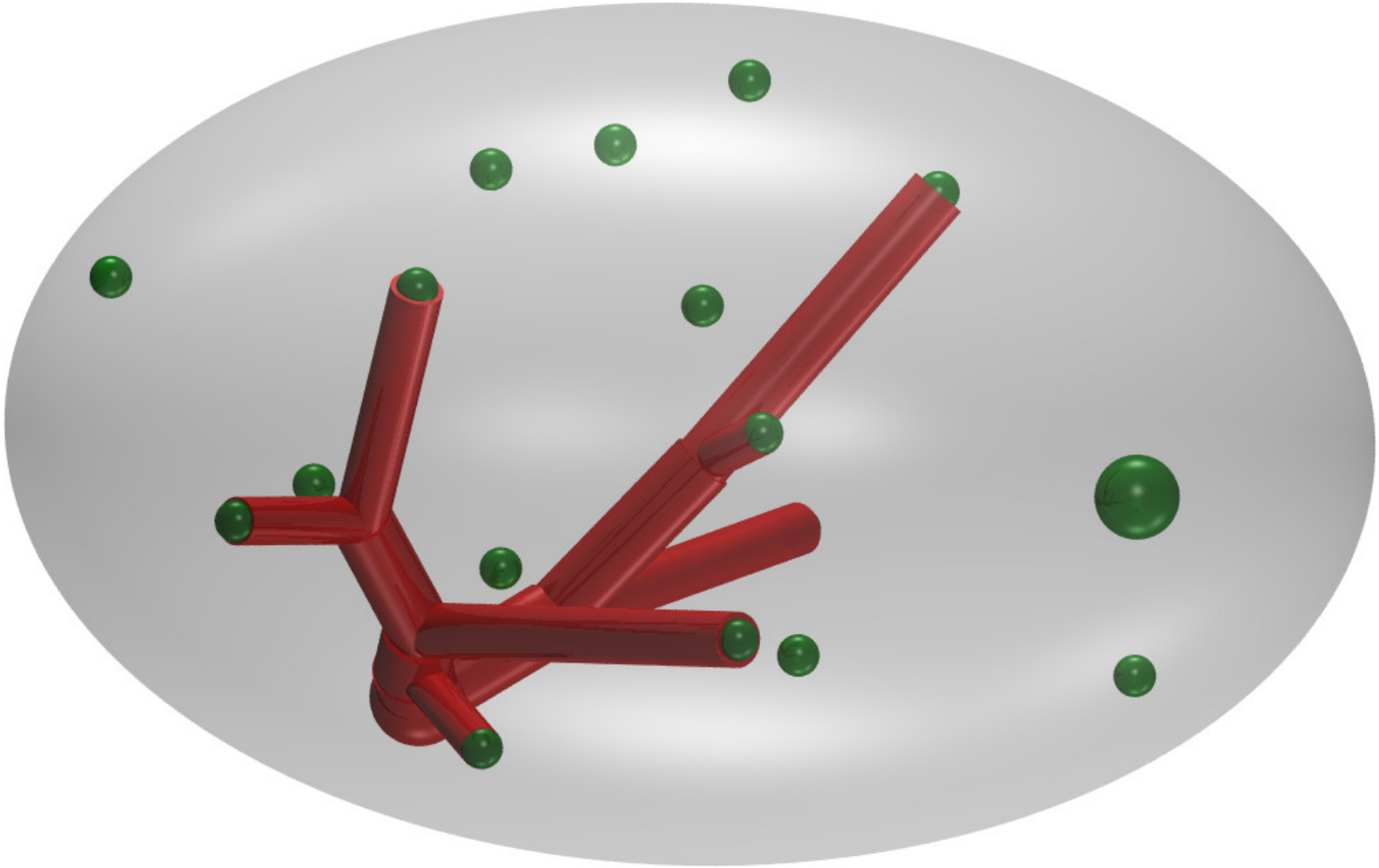

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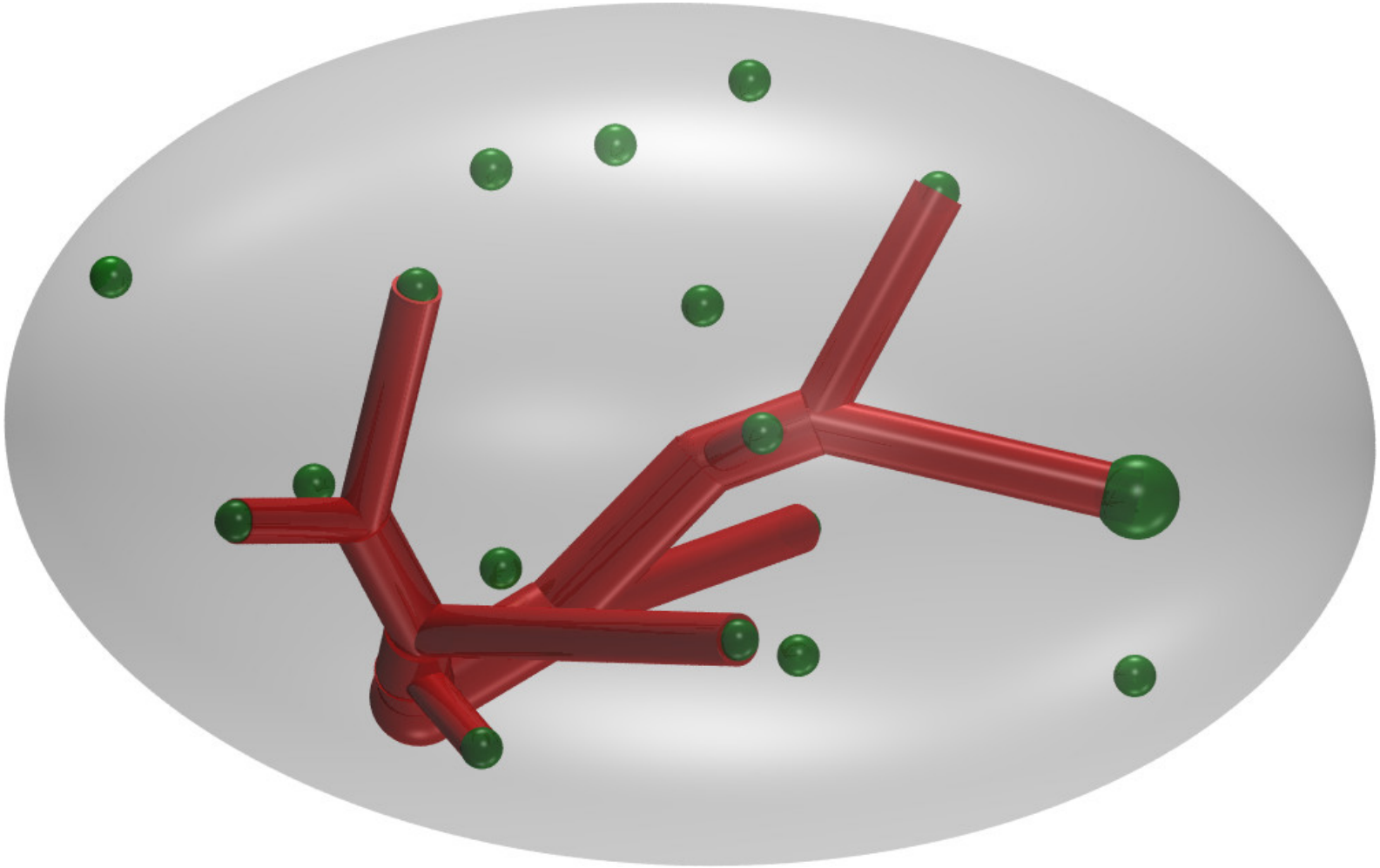

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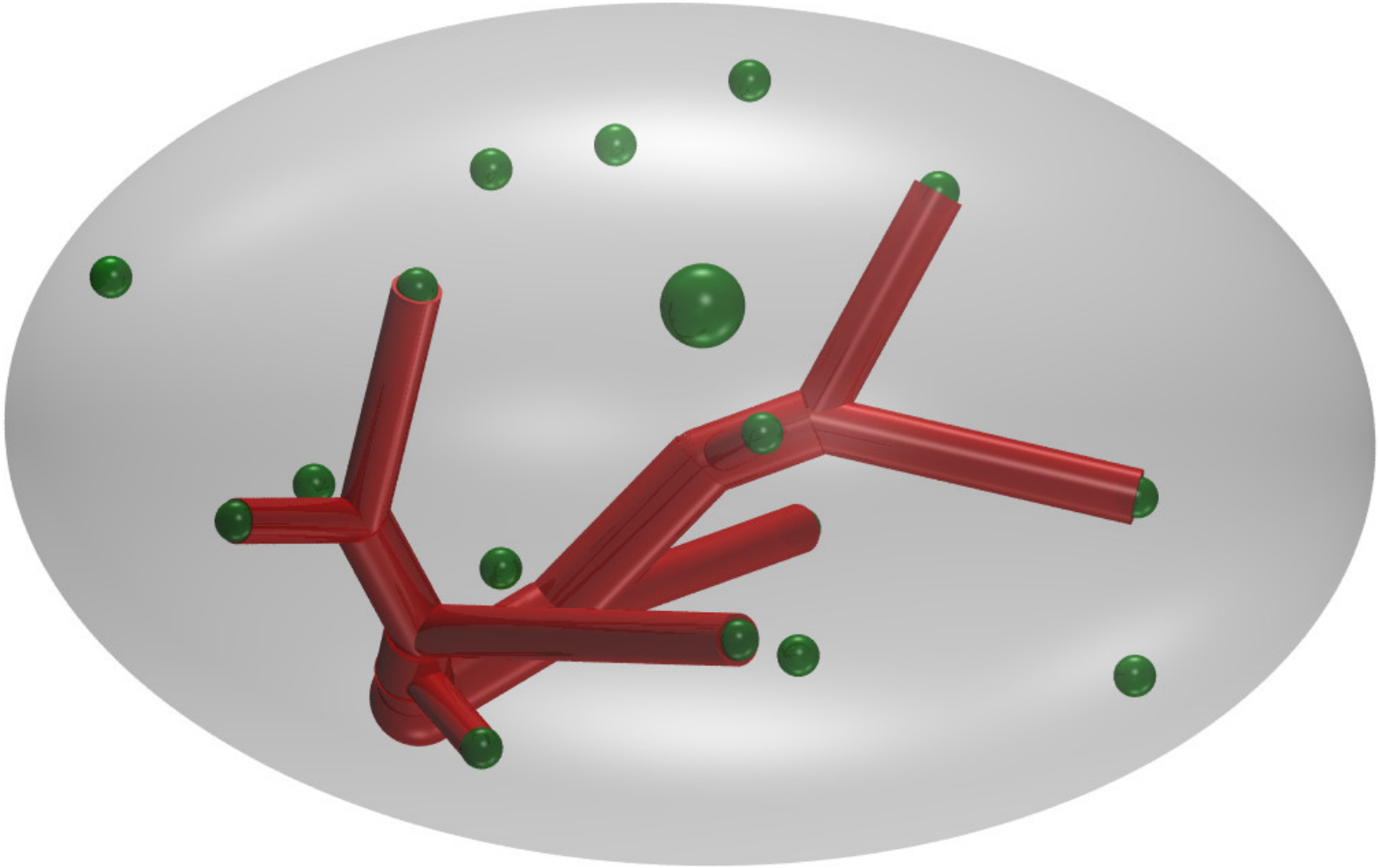

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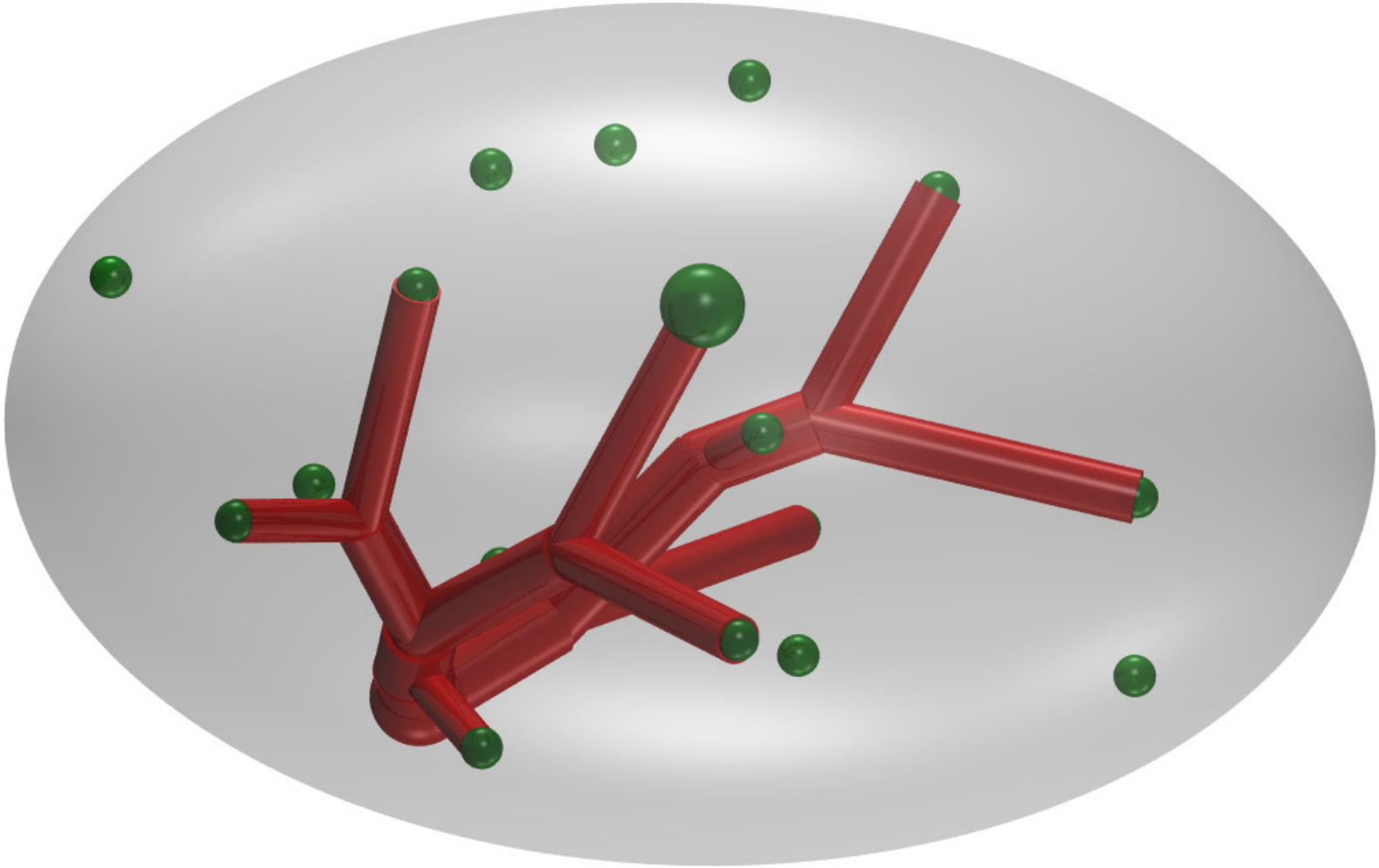

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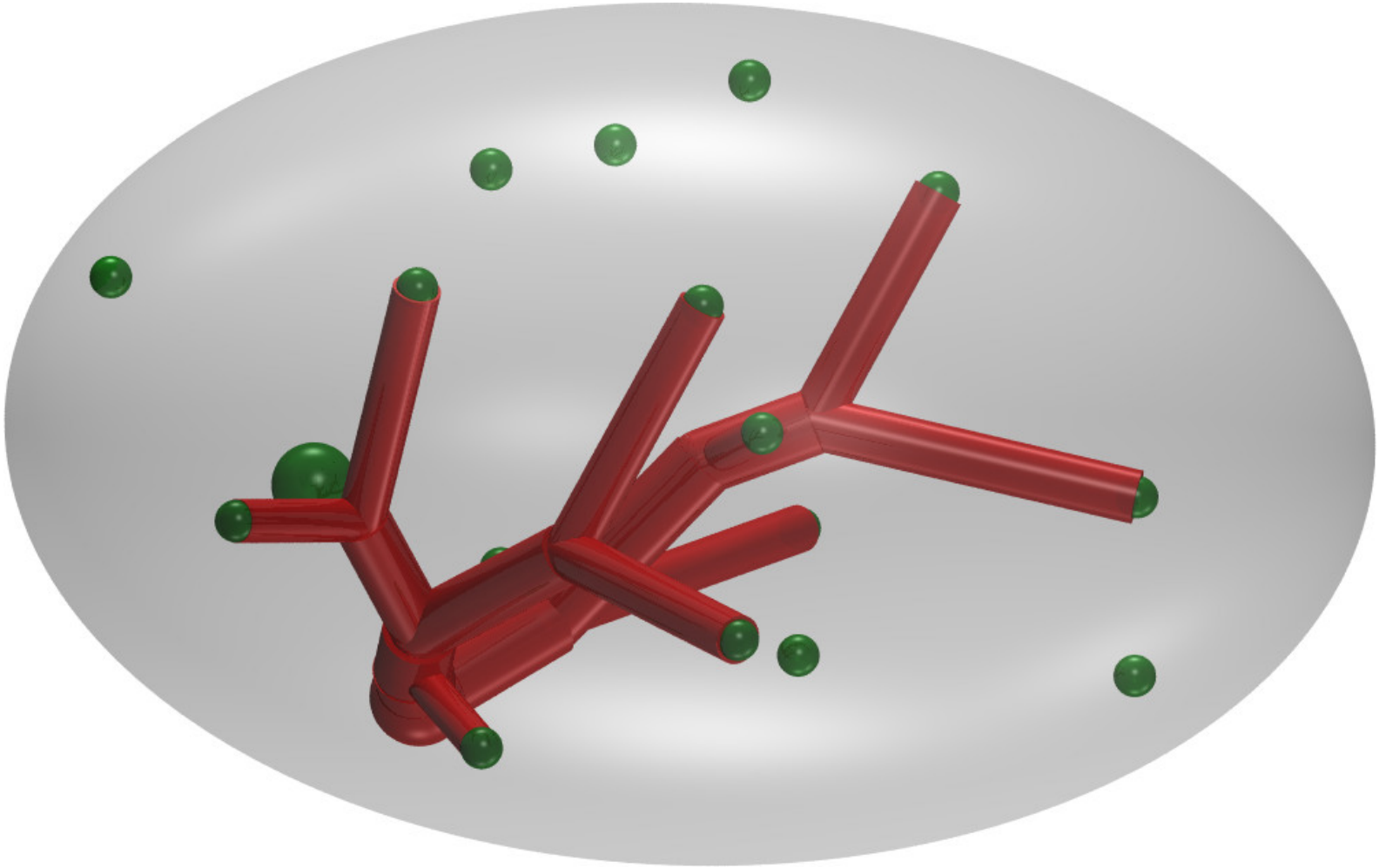
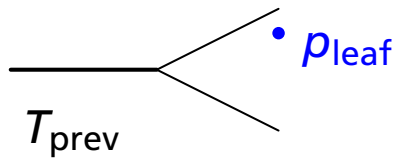


2. Constrained Constructive Optimization

Mathematical Formulation

[Schreiner et al. 1993]



Objective function for adding one leaf node

$$F(e, p_{\text{split}}) := \text{Vol}\left(T_{\text{prev}} \oplus (p_{\text{leaf}}; e, p_{\text{split}})\right)$$

- extended vascular tree with valid radii (as above)
- obtained from tree T_{prev}
- connecting new leaf node p_{leaf}

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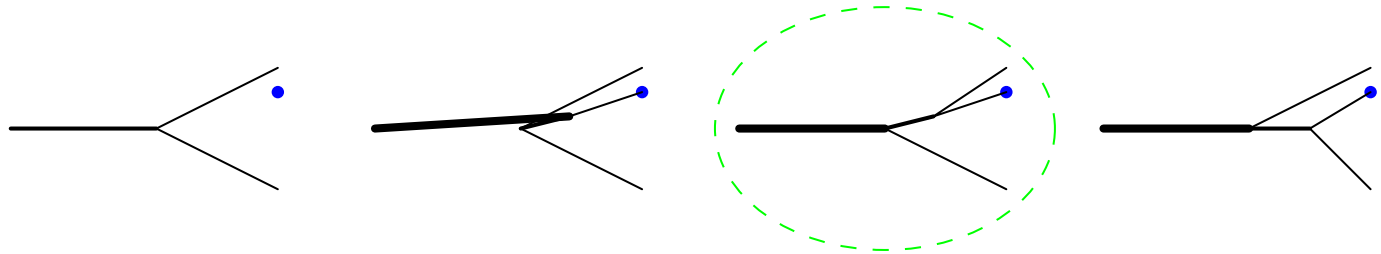

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- by splitting edge $e \in \mathbb{N}_{\#\text{ edges in } T_{\text{prev}}}$
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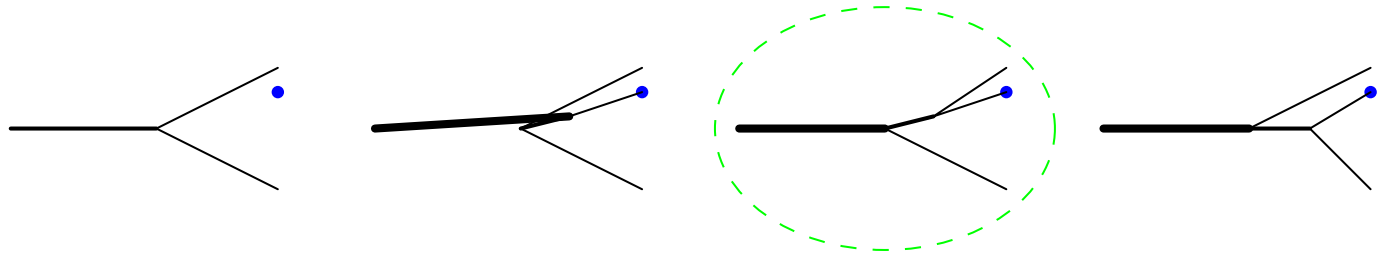

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- penalty term if p_{split} outside organ Λ

2. Constrained Constructive Optimization

Implementation

$$\tilde{F}_e(p_{\text{split}}) := \text{Vol}\left(T_{\text{prev}} \oplus (p_{\text{leaf}}; e, p_{\text{split}})\right) + C\,\text{dist}^2(p_{\text{split}}, \Lambda)$$

minimized by gradient descent with Armijo step size control.

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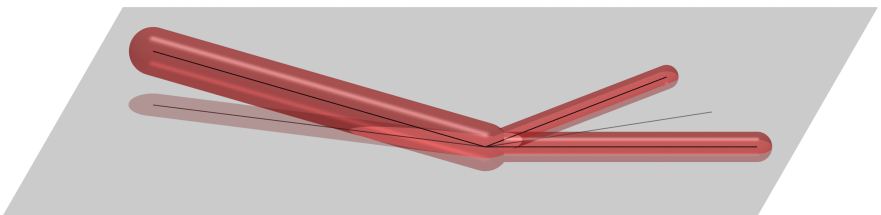
Computationally expensive

- bifurcation moved ⇒ need to recompute 3 lengths and many radii



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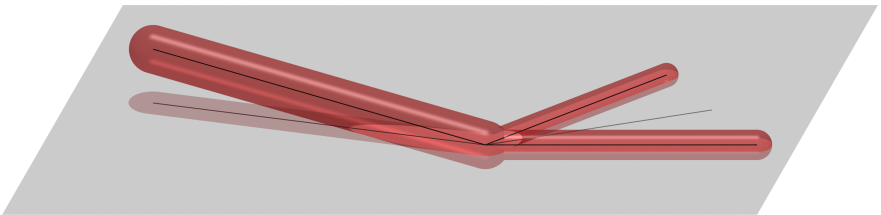

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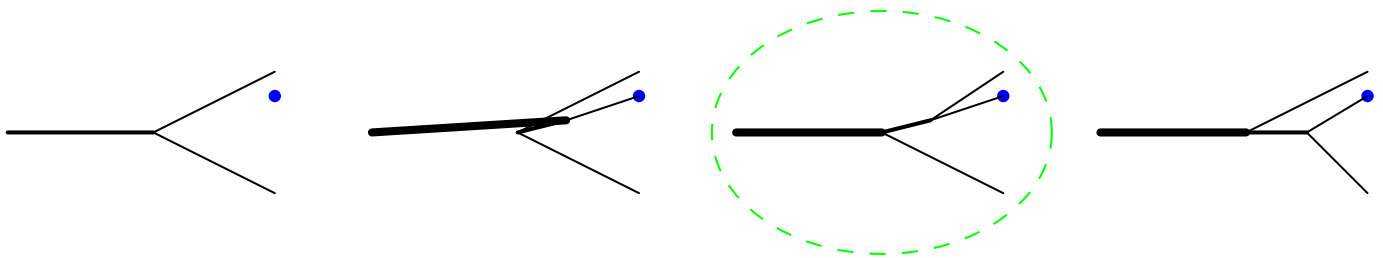
Computationally expensive

- bifurcation moved ⇒ need to recompute 3 lengths and many radii
- no analytic derivative wrt. position of bifurcation
- not clear where (topologically) to introduce new bifurcation (e)



2. Constrained Constructive Optimization

Implementation

[S. and Preusser 2012]

Multi“scale” procedure

- 40 candidate edges with closest midpoints
- ‘rough’ stopping criterion to select 20 candidates
- ‘fine’ stopping criterion to find best topology
- simple parallelization (OpenMP) possible

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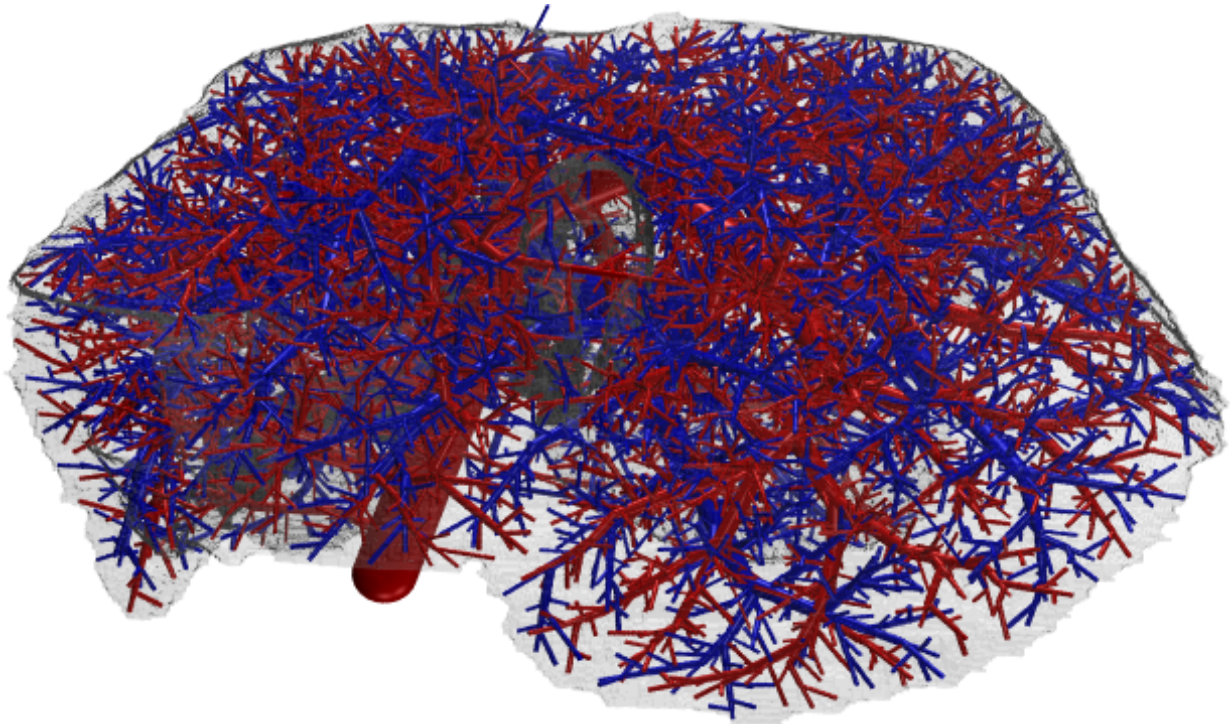
Still $O(N^2 \log N)$ workload for N leaf nodes.

2. Constrained Constructive Optimization

Results

two vascular systems ⇐ disjoint set of leaf nodes, independent CCO



3. Generating Realistic Vascular Systems

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3. Generating Realistic Vascular Systems

Overview

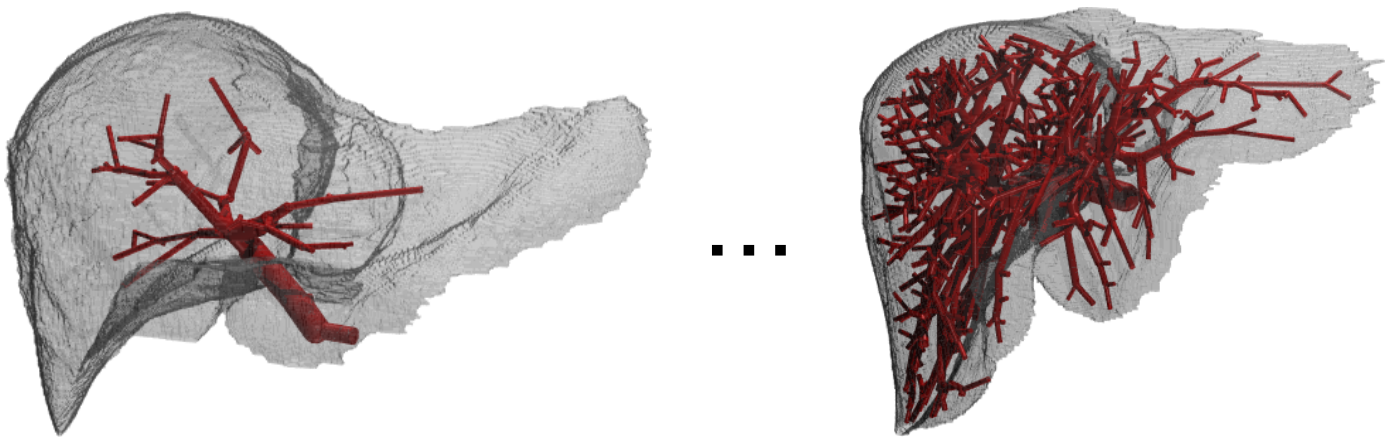
[S. and Preusser 2012]

Goal

- analyze geometric features in real vascular systems
- check whether algorithm produces similar ones
- improve algorithm

Input

- ~ 160 human in vivo scans

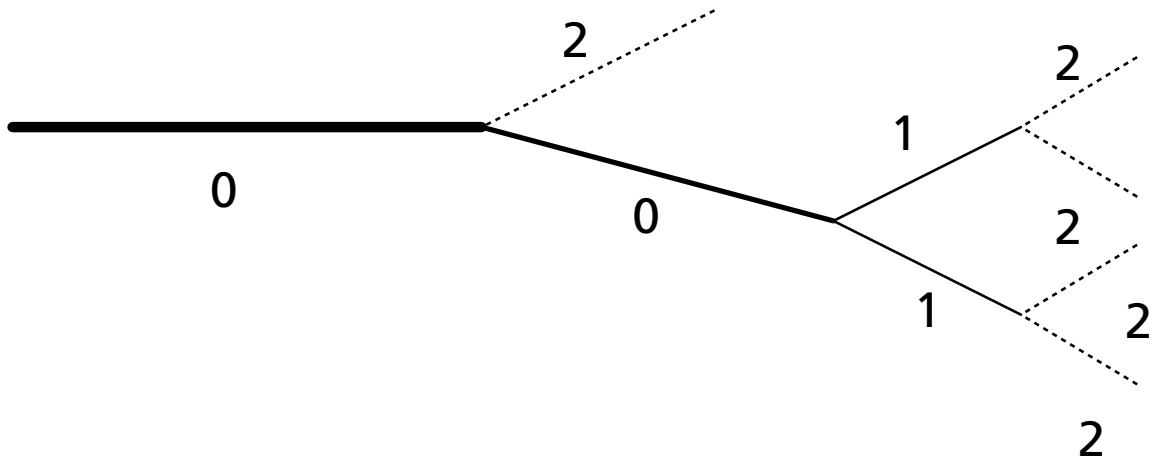


3. Generating Realistic Vascular Systems

Topological and Geometric Analysis

cf. [Strahler 1957]

Rather than bifurcation orders, consider Strahler-type scheme



3. Generating Realistic Vascular Systems

Topological and Geometric Analysis

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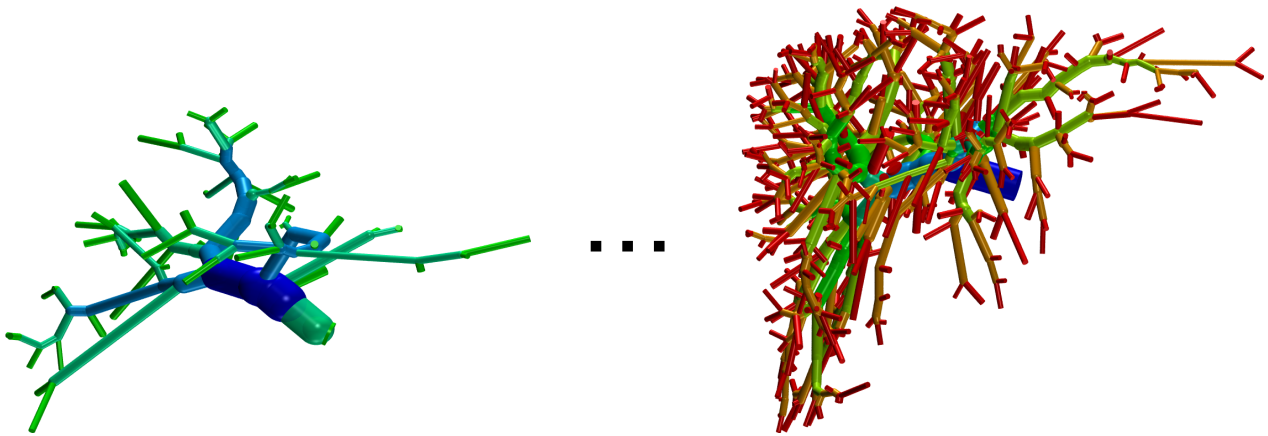
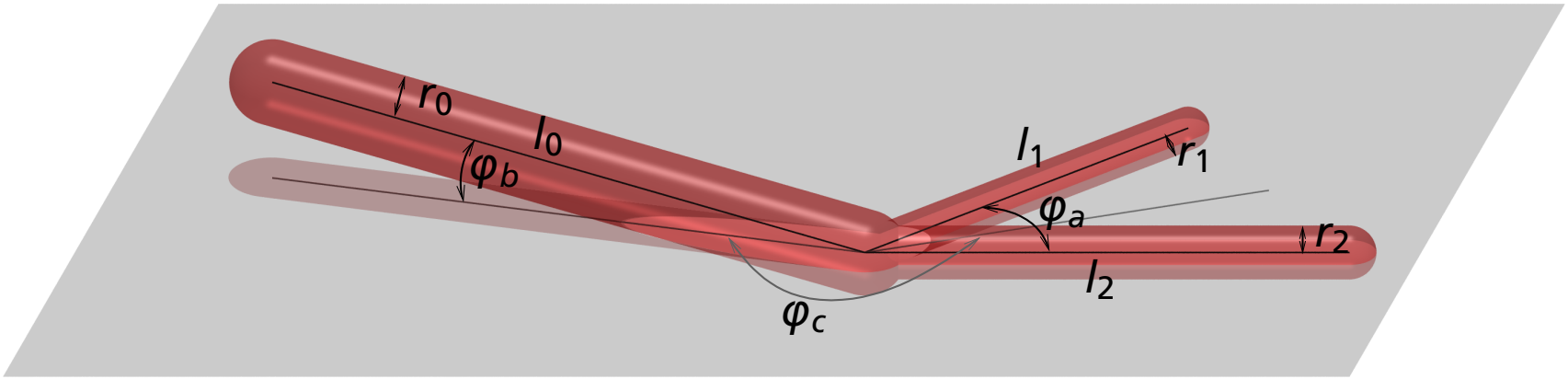


3. Generating Realistic Vascular Systems

Topological and Geometric Analysis

[S. and Preusser 2012]

Geometric features at a single bifurcation



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Topological and Geometric Analysis

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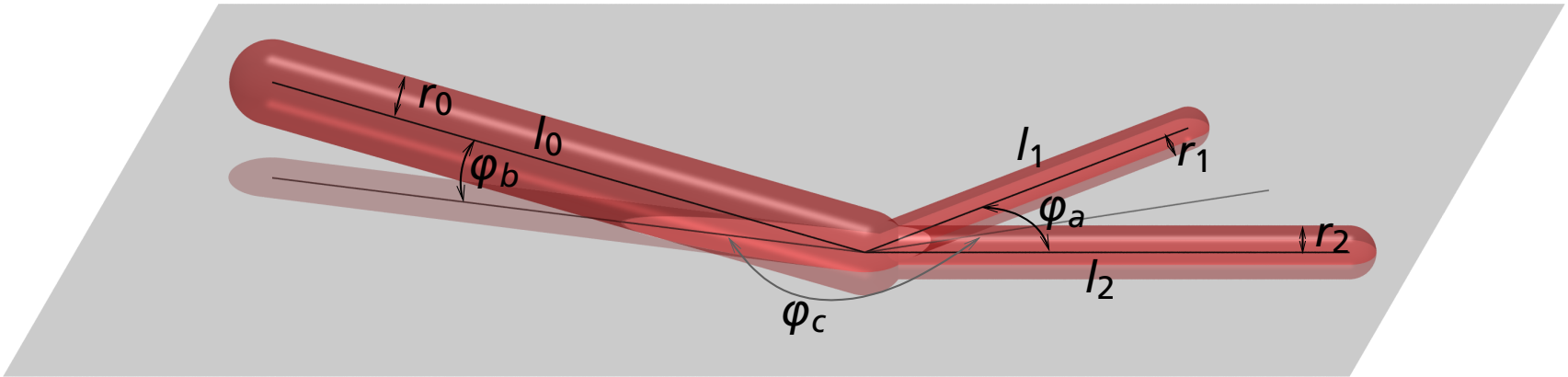
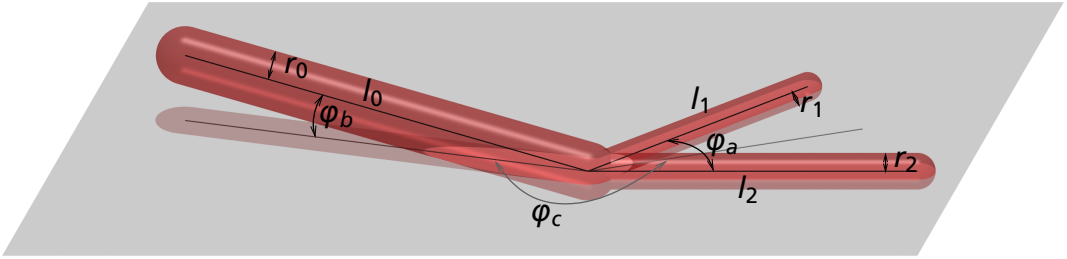


- evaluate histograms for all datasets per level and feature
- perform pairwise Kolmogorov-Smirnov test ($p = 0.05$) for similarity
- compute percentages and weighted average over Strahler* orders

3. Generating Realistic Vascular Systems

CCO Postprocessing

[S. and Preusser 2012]



Postprocessing

- angles between daughters φ_a too small
  → shift in direction of bisector

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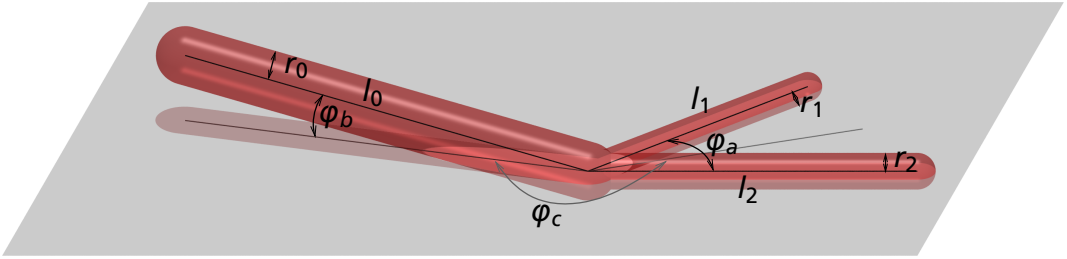

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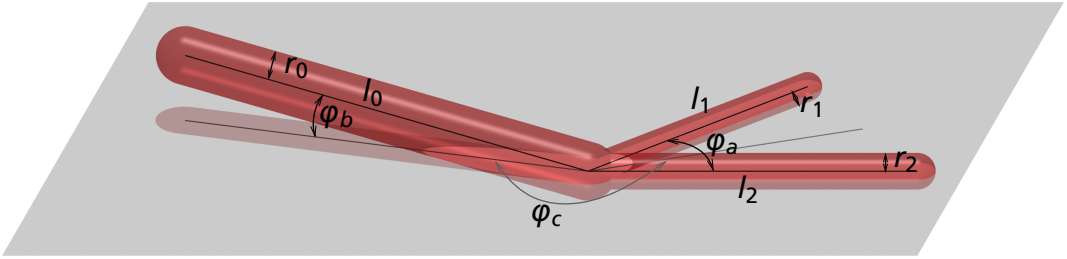

Postprocessing

- angles between daughters φ_a too small
  → shift in direction of bisector
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Observation

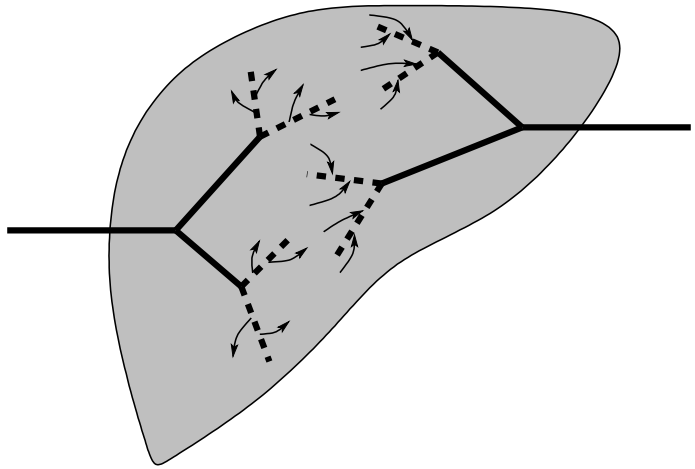
- real vascular trees differ slightly from CCO output
- postprocess rather than build into optimization-based construction

4. Application: Flow Simulations

Contents

4. Application: Flow Simulations

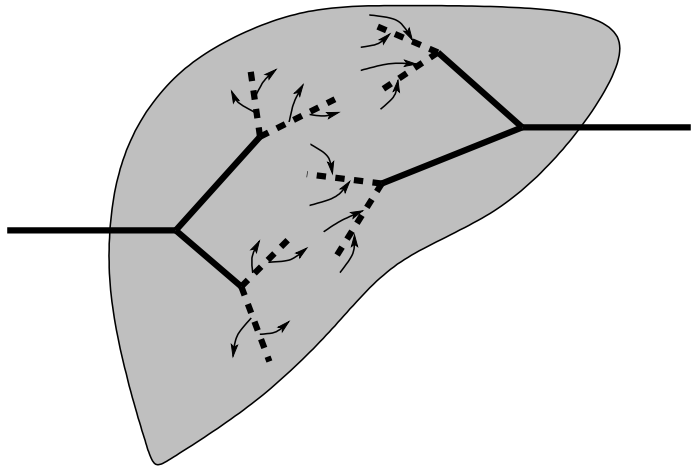
Transport in Vascular Systems



- consider concentration in blood

4. Application: Flow Simulations

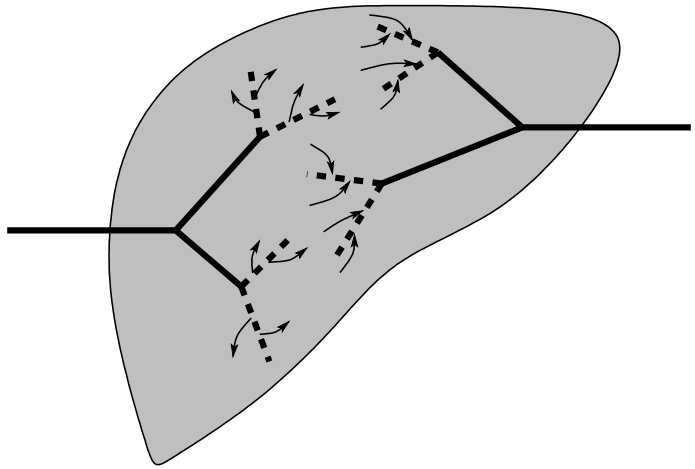
Transport in Vascular Systems



- consider concentration in blood
- transport only through vascular structures

4. Application: Flow Simulations

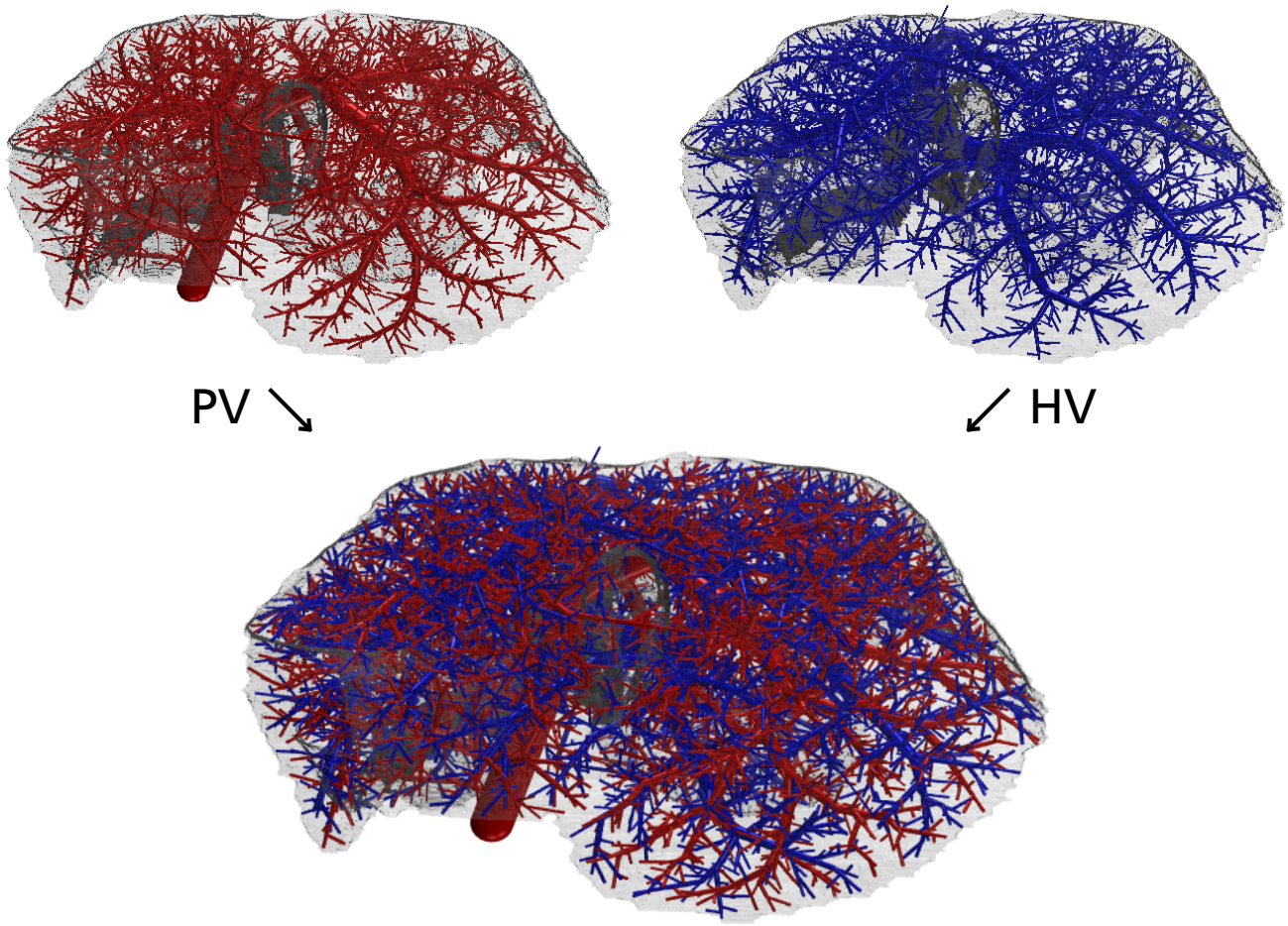
Transport in Vascular Systems



- consider concentration in blood
- transport only through vascular structures
- constant flow velocity per edge (essentially 1D)
- discretized using Eulerian-Lagrangian Locally Adjoint Method (ELLAM) [Celia et al. 1990]

4. Application: Flow Simulations

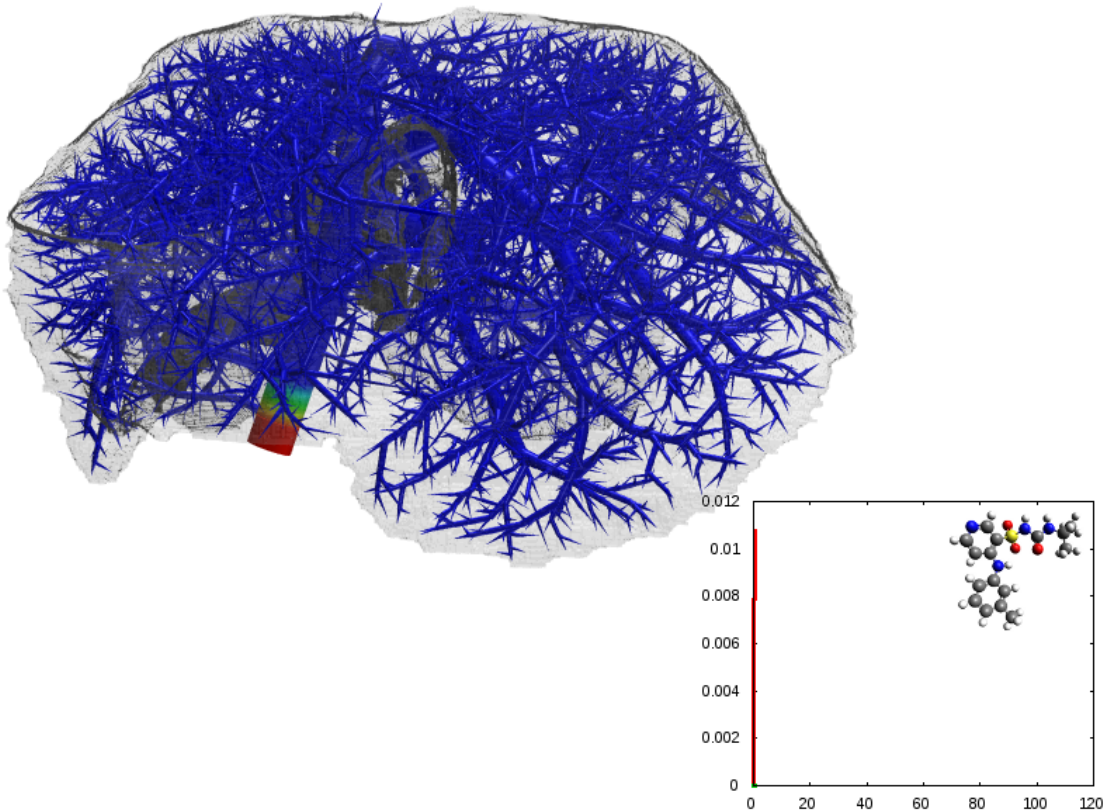
First Results: Dynamic Flow



mouse CCO model (5000 leaves each)

4. Application: Flow Simulations

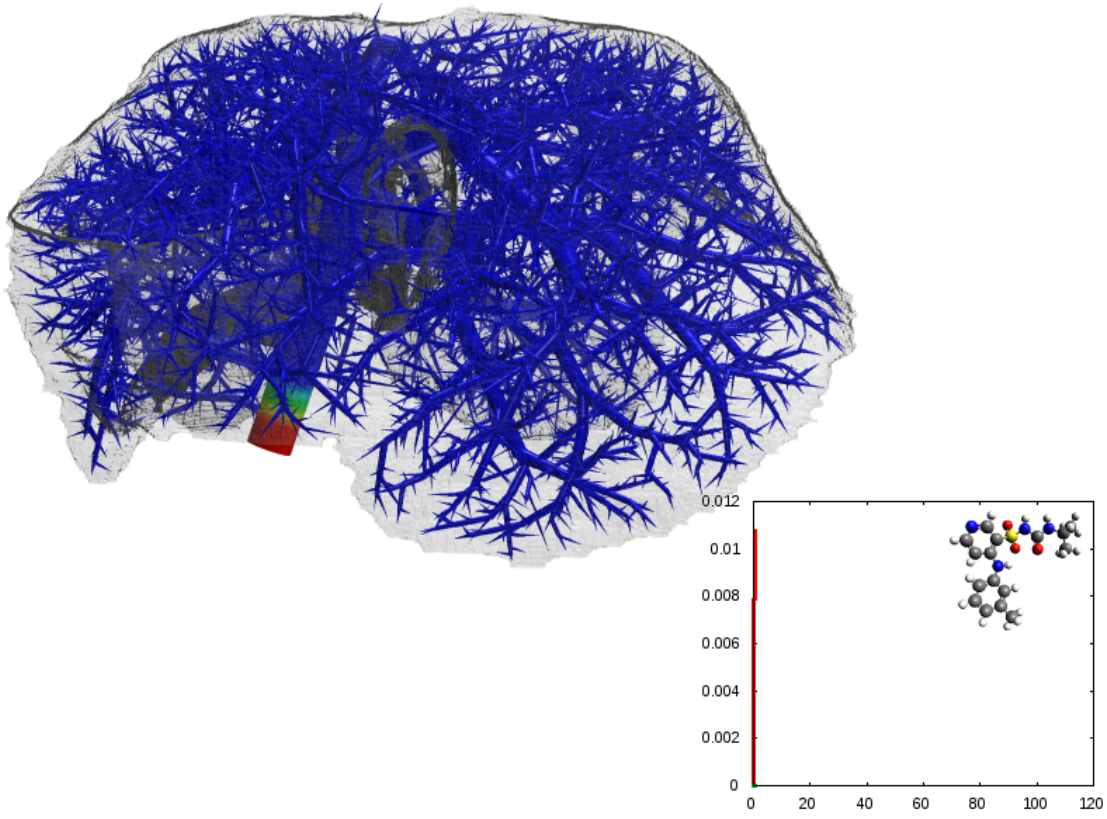
First Results: Dynamic Flow



- concentration profile color-coded

4. Application: Flow Simulations

First Results: Dynamic Flow



- concentration profile color-coded → video

4. Application: Flow Simulations

Outlook

Extend by

- porous medium model for extravascular space
- ⇒ 3D transport

4. Application: Flow Simulations

Outlook

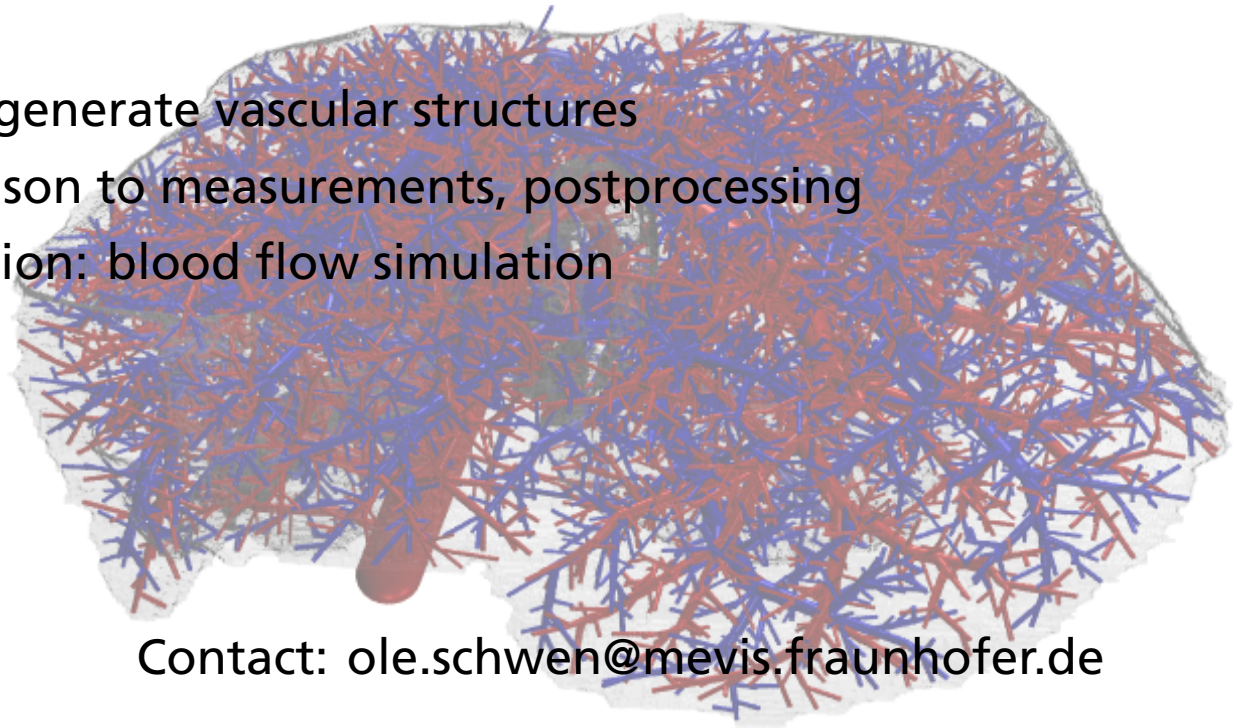
Extend by

- porous medium model for extravascular space
- ⇒ 3D transport

- multiple substances
- reaction term to model metabolization
- pharmacokinetics simulation

Summary

- CCO to generate vascular structures
- comparison to measurements, postprocessing
- application: blood flow simulation



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References

- Fåhræus et al.: *The Viscosity of the Blood in Narrow Capillary Tubes*, Am J Physiol **96** (1931)
- Strahler: *Quantitative analysis of watershed geomorphology*, Trans Am Geophys U **8** (1957)
- Celia et al.: *An Eulerian-Lagrangian localized adjoint method for the advection-diffusion equation*, Adv Water Res **13** (1990)
- Schreiner et al.: *Computer-Optimization of Vascular Trees*, IEEE Trans Biomed Eng **40** (1993)
- Selle et al.: *Analysis of vasculature for liver surgical planning*, IEEE Trans Med Imag **21** (2002)
- Op Den Buijs et al.: *Branching Morphology of the Rat Hepatic Portal Vein Tree: A Micro-CT Study*, Ann Biomed Eng **34** (2006)
- Holzhütter et al.: *The Virtual Liver: A Multidisciplinary, Multi-level Challenge forSystems Biology*, Wiley Interdiscip Rev Syst Biol Med **4** (2012)
- Schwen, Preusser: *Analysis and Algorithmic Generation of Hepatic Vascular Systems*, Int J Hepatol, to appear