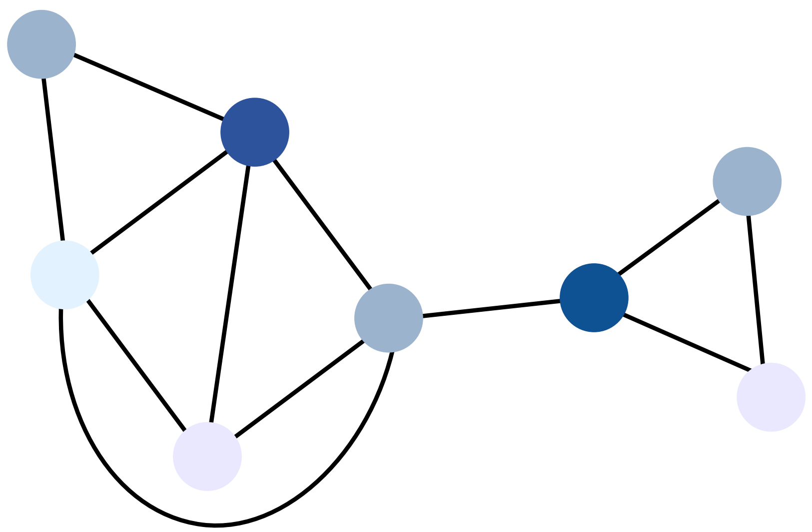
Chemical graph theory



Jacob Kautzky

MacMillan Group Meeting

April 3, 2018

Chemical graph theory

What is graph theory?

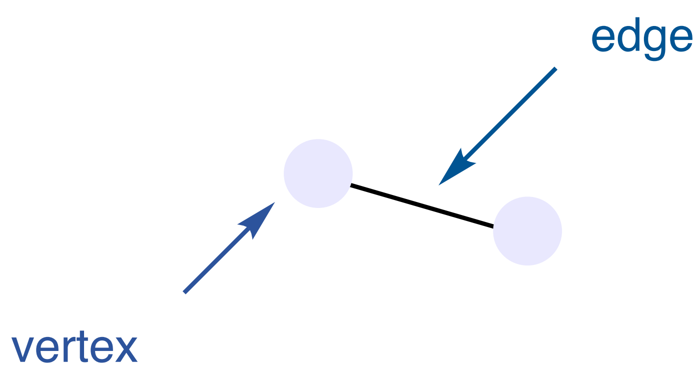
Historical uses of chemical graph theory

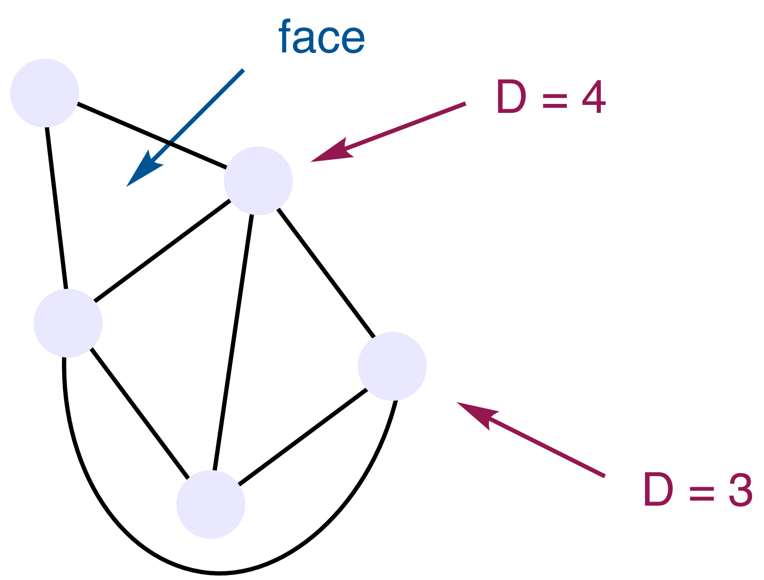
- **Isomer counting**
- **Chemical bonding**
- **Kinetics**

Modern uses of chemical graph theory

What is a graph?

- A graph is defined as a non empty set of vertices and a set of edges





Order of the graph (N) = # of vertices

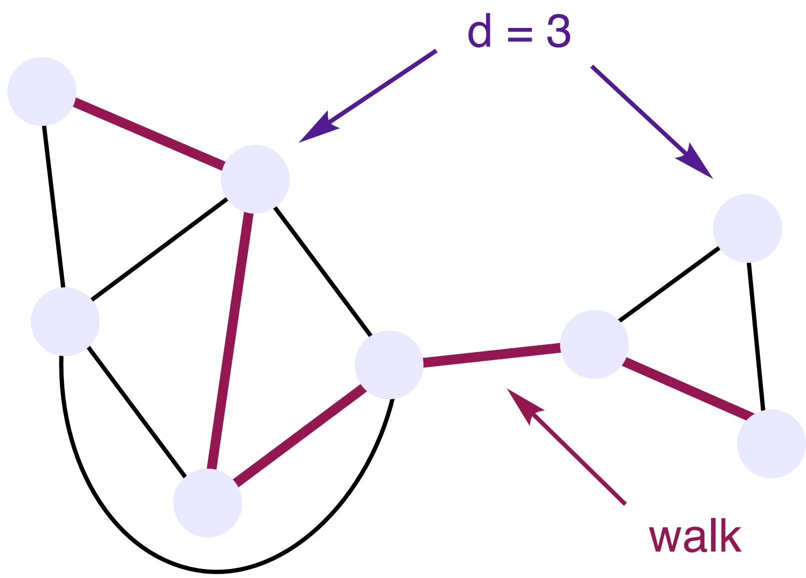
Size of the graph (M) = # of edges

Degree of a vertex (D) = # of edges incident with a vertex

$$\sum_{i=1}^{N} D(i) = 2M \qquad N - M + F = 2$$

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Walks, trails, paths, and cycles

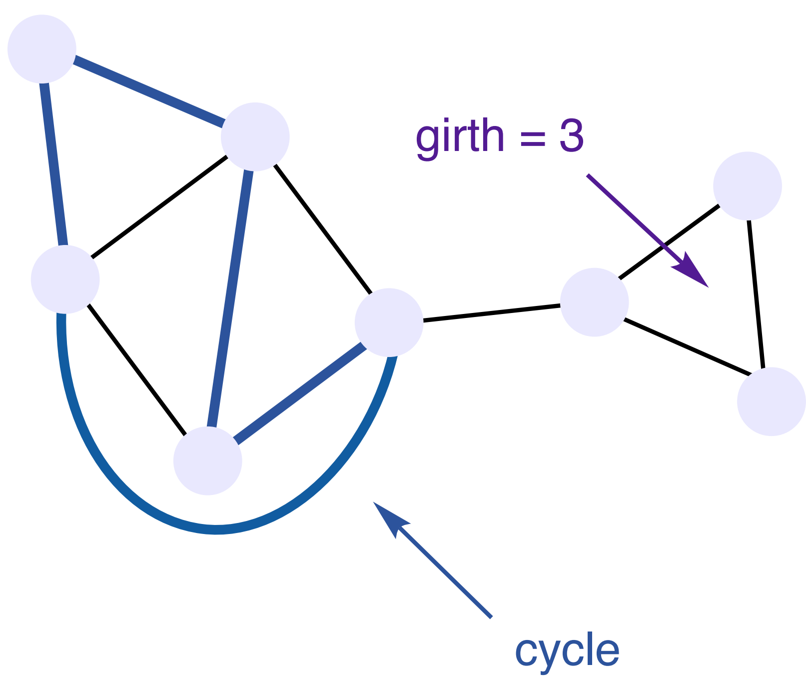


Walk - an alternate sequence of vertices and edges, begining and ending with a vertice

- **Open** - starts and ends at different vertices
- **Closed** - starts and ends at the same vertex

Length (l) - number of occurence of edges in a walk

Trail - a walk where all edges are distinct



Path - a walk where all vertices are distinct

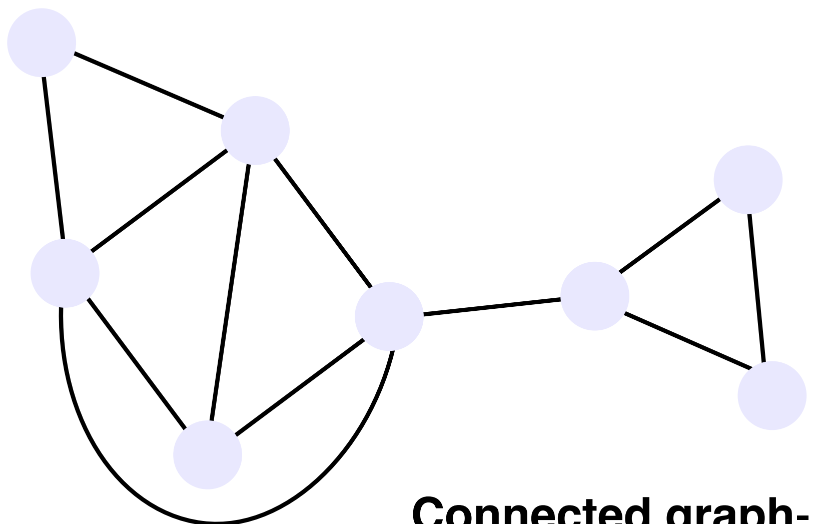
Distance (d) - the length of the shortest path between 2 vertices

Cycle - a path that starts and ends at the same vertex

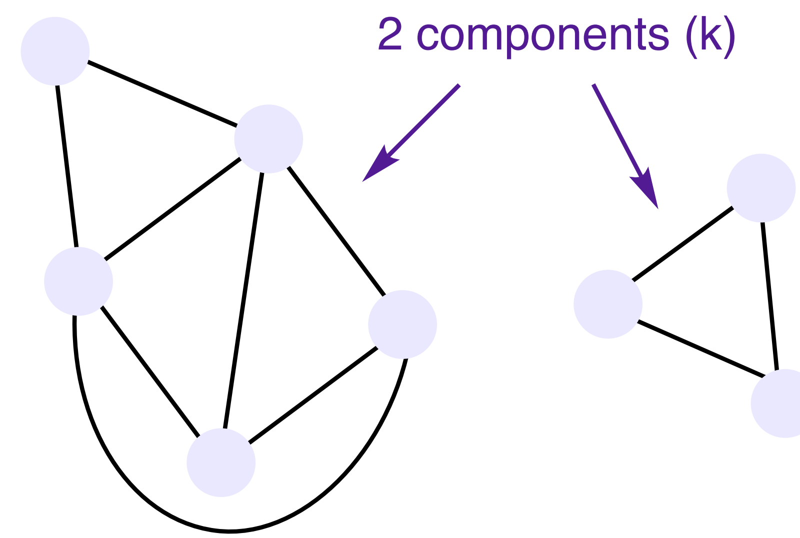
Girth - length of the smalest cycle in a graph

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Connected vs disconnected and simple, general, and multigraphs

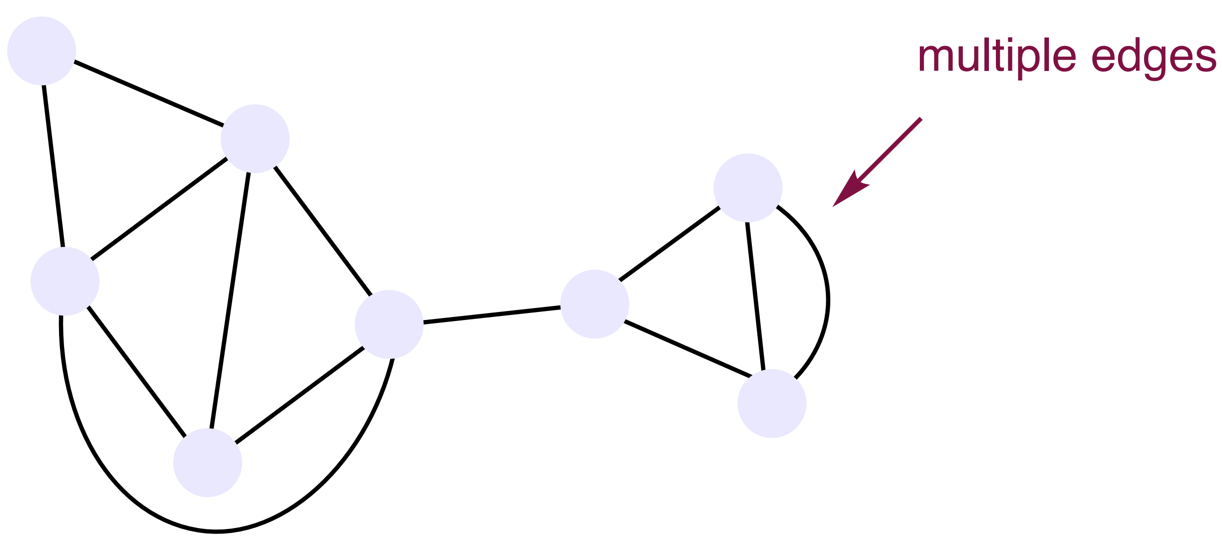


Connected graph- ∃ a path between any 2 vertices

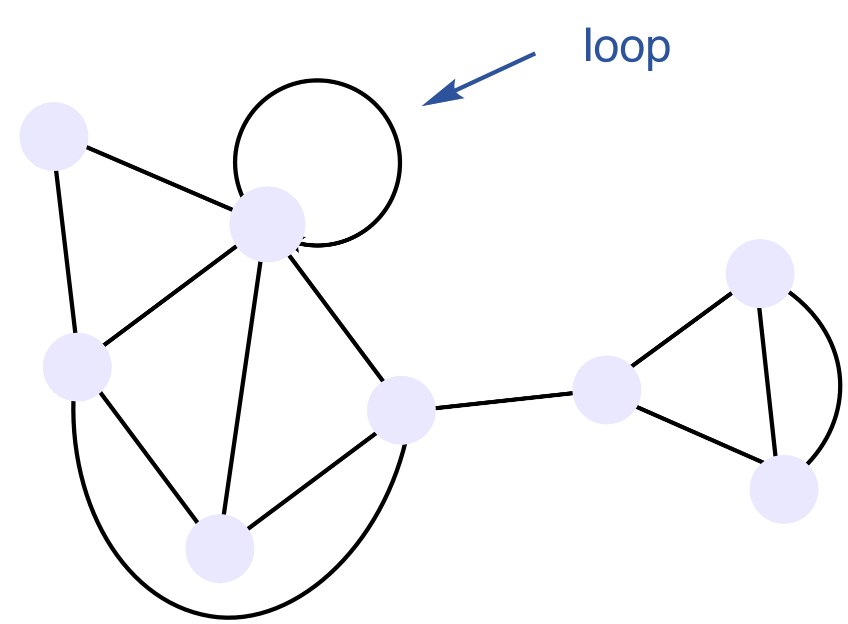


Disconnected graph

Simple graph - a graph without loops or multiple edges between two vertices



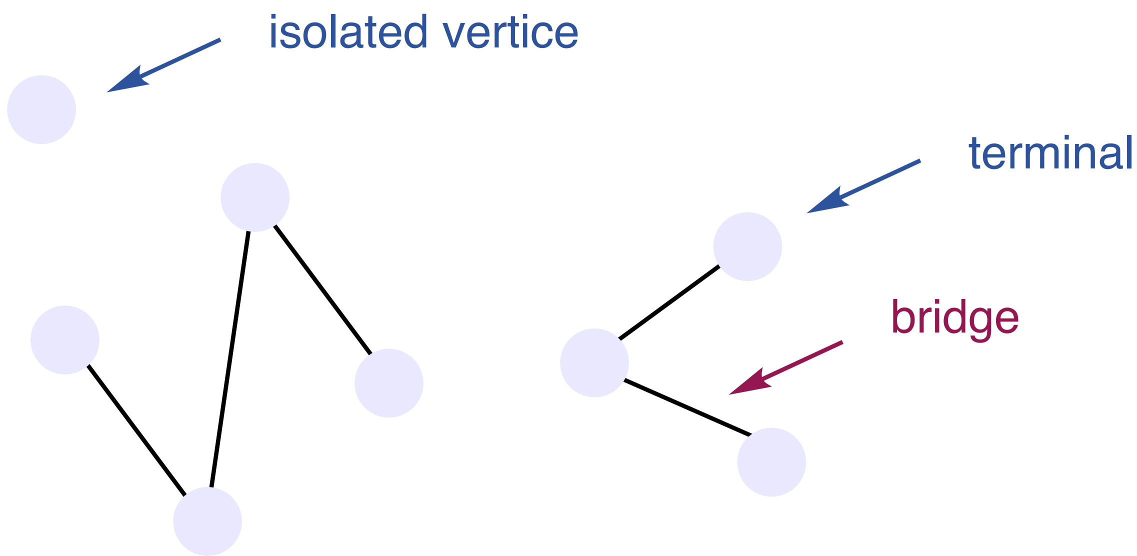
Multigraph - a graph that allows multiple edges between 2 vertices



General graph - a graph that allows multiple edges and loops

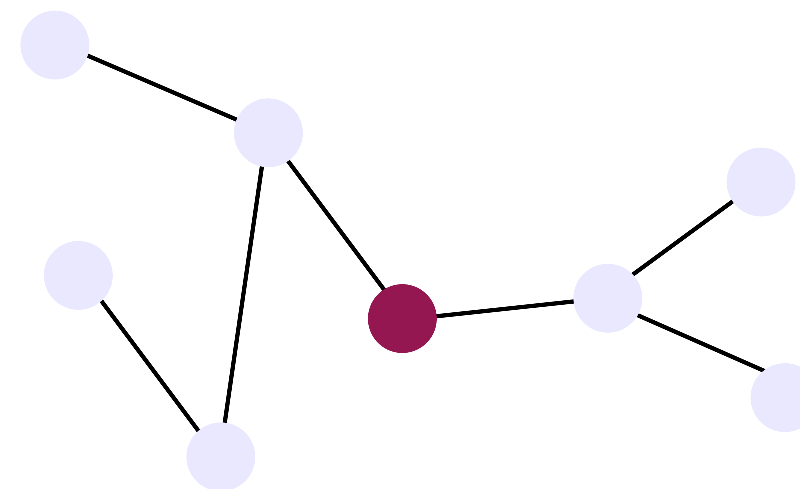
Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Forests and trees



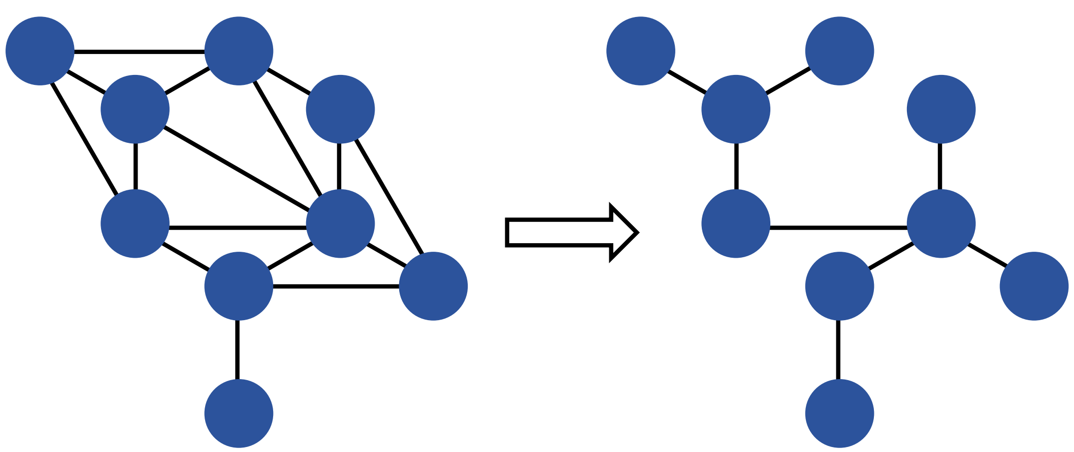
Forest - an acyclic graph

Bridge - an edge that when removed disconnects a graph

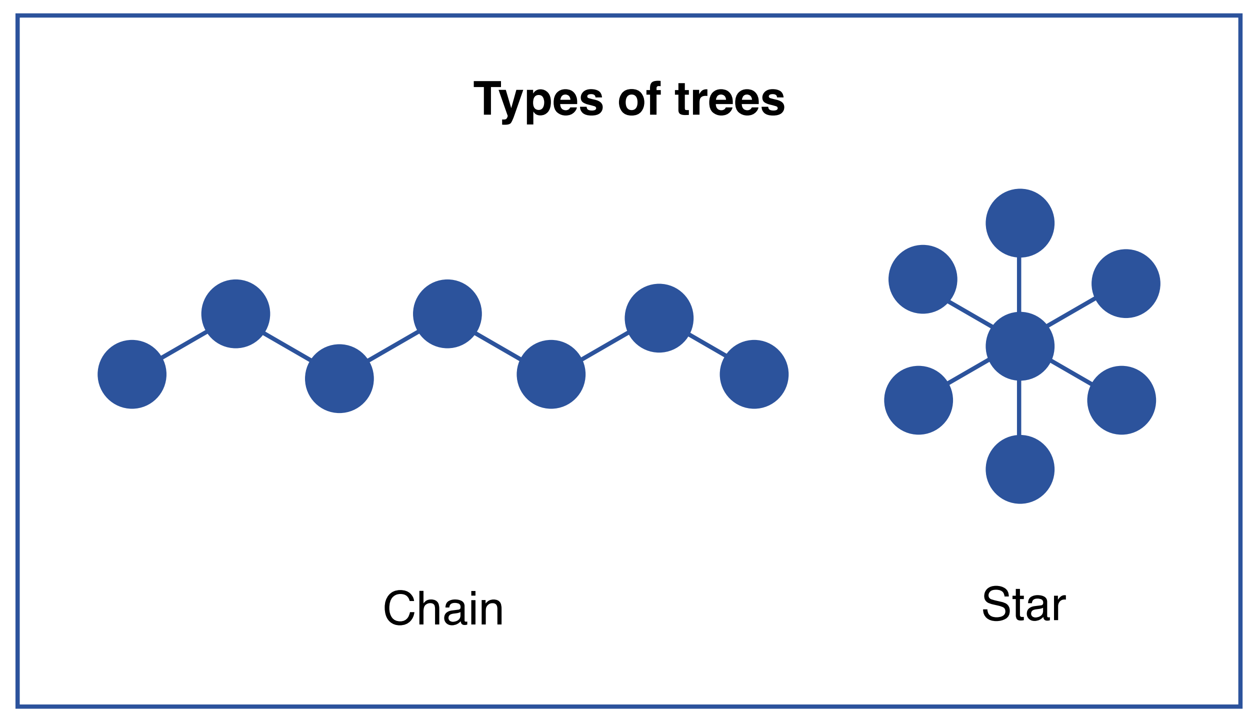


Tree - a connected acyclic graph

Rooted tree - a tree with a vertice distinguished in some fashion



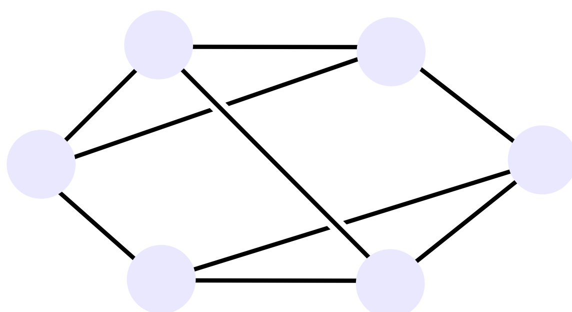
Spanning tree - a graph subgraph that includes all vertices of a graph with the minimal number of edges to remain connected



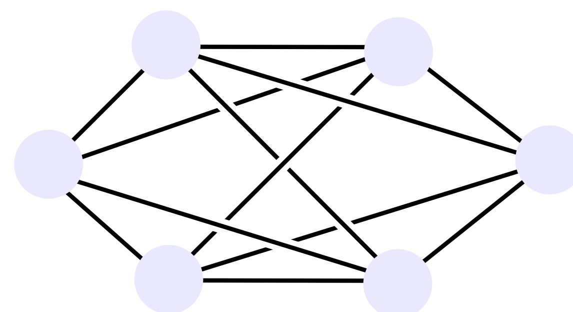
Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Types of graphs — regular graphs

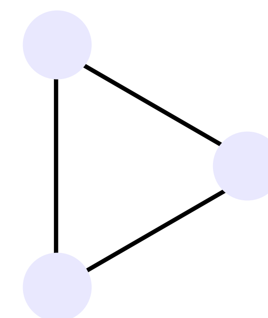
A regular graph is a graph where every vertex has the same valency



regular graph of degree 3



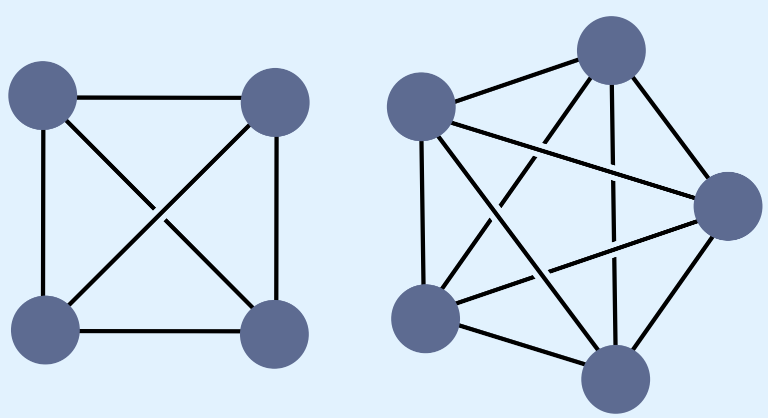
regular graph of degree 4



regular graph of degree 2

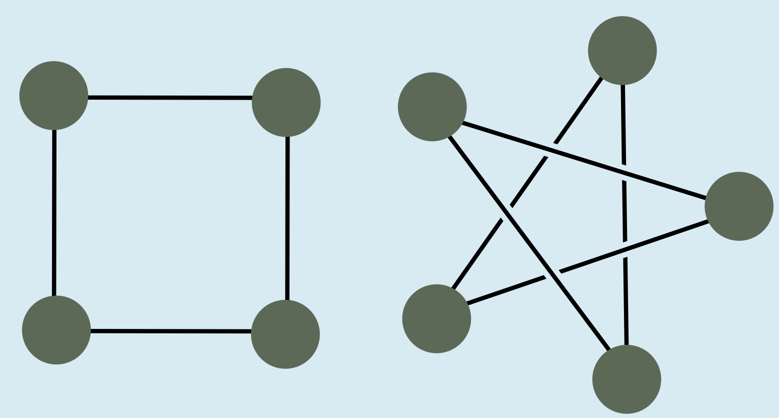
$M = 0.5*N*D$

complete graph



- A graph where each vertice has $D = N - 1$
- Denoted by K_N
- $M = \binom{N}{2}$

cycle



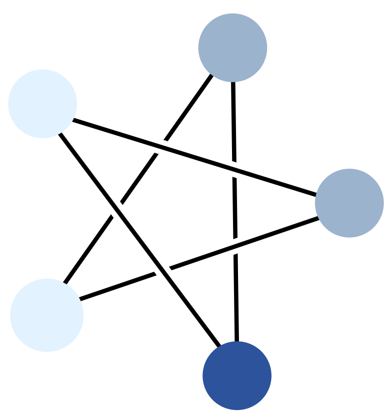
- A graph where each vertice has $D = 2$
- Denoted by C_N
- A cycle is termed even/odd if N is even/odd

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

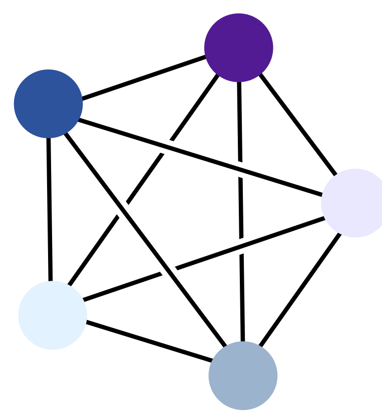
Vertex coloring

Assigning colors to vertices so that no two adjacent vertices have the same color

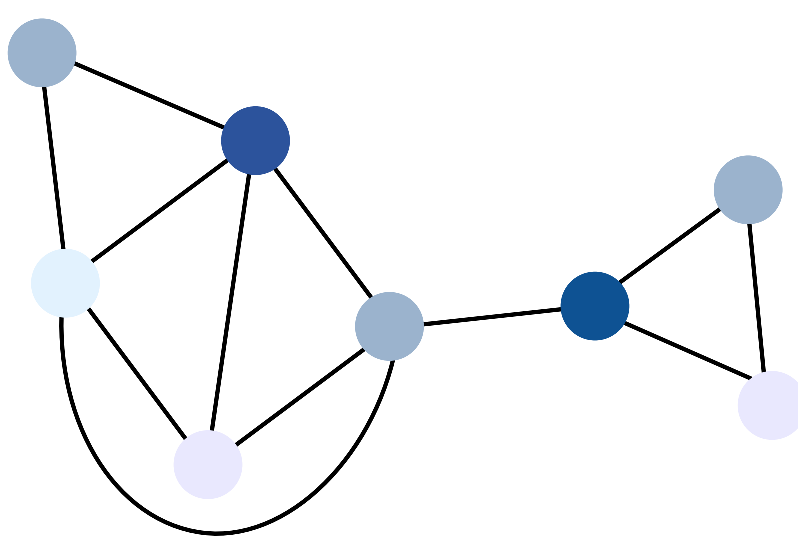
Chromatic number (k) - the minimal number of colors required to color a graph



k = 3

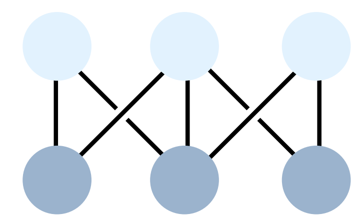


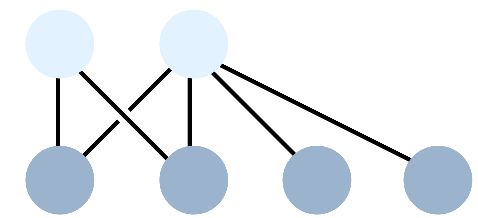
k = 5



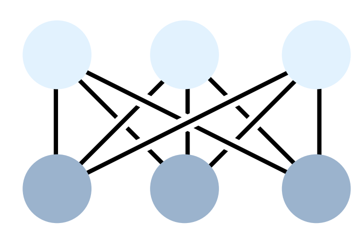
k = 4

Bipartite graph - a graph where the vertice set can be split into V_1 and V_2 where every edge connects a vertice in V_1 to one in V_2

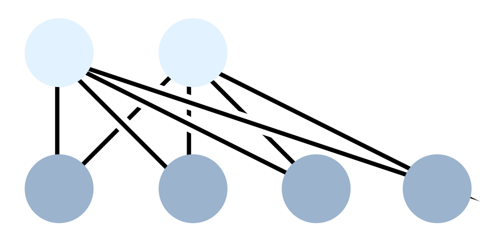




- A graph is a bipartite graph if and only if every cycle is of even number
- All bipartite graphs are 2 colorable



$K_{3,3}$



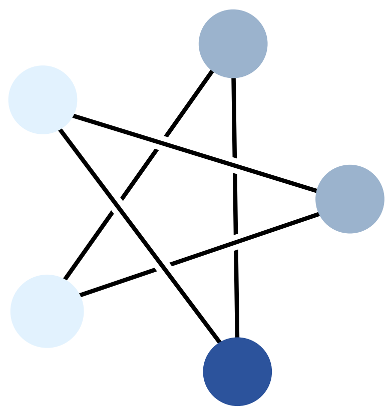
$K_{4,2}$

Complete bipartite graph $K_{s,u}$- every vertex in V_1 is joined to every vertex in V_2

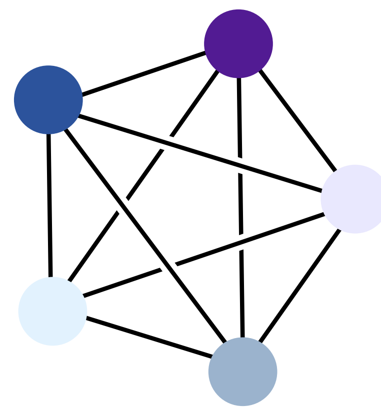
Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Planar graphs

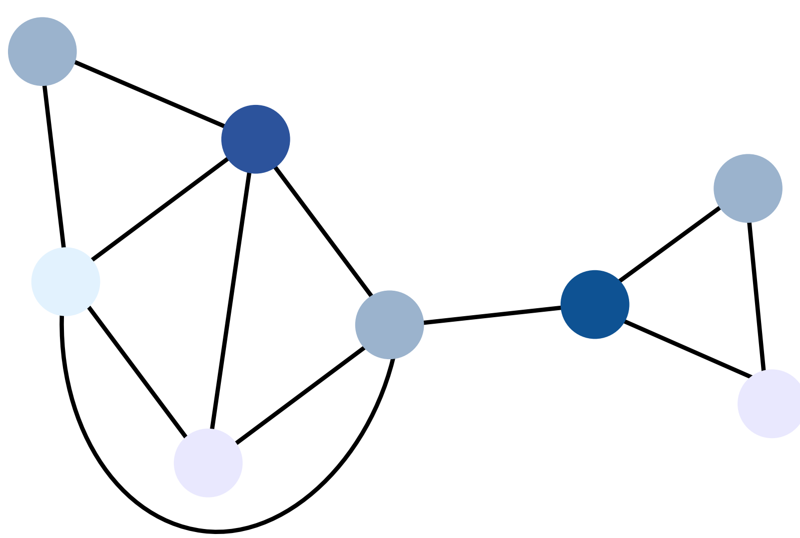
A graph is planar if it can be drawn such that no edges intersect



Planar

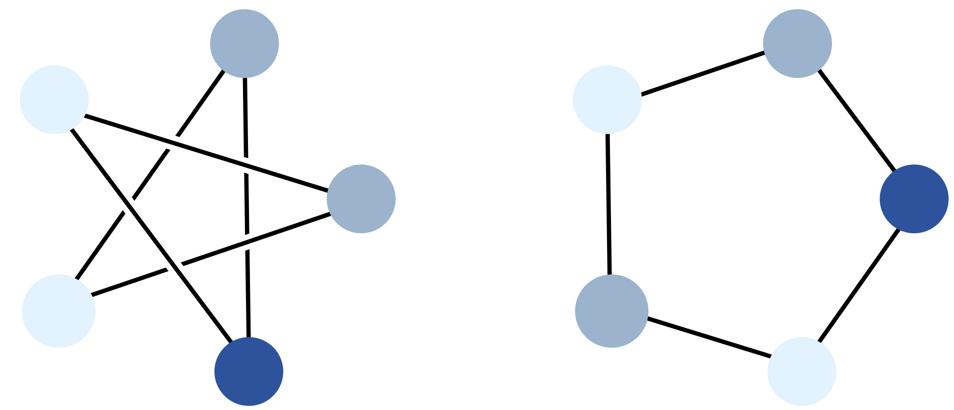


Not planar

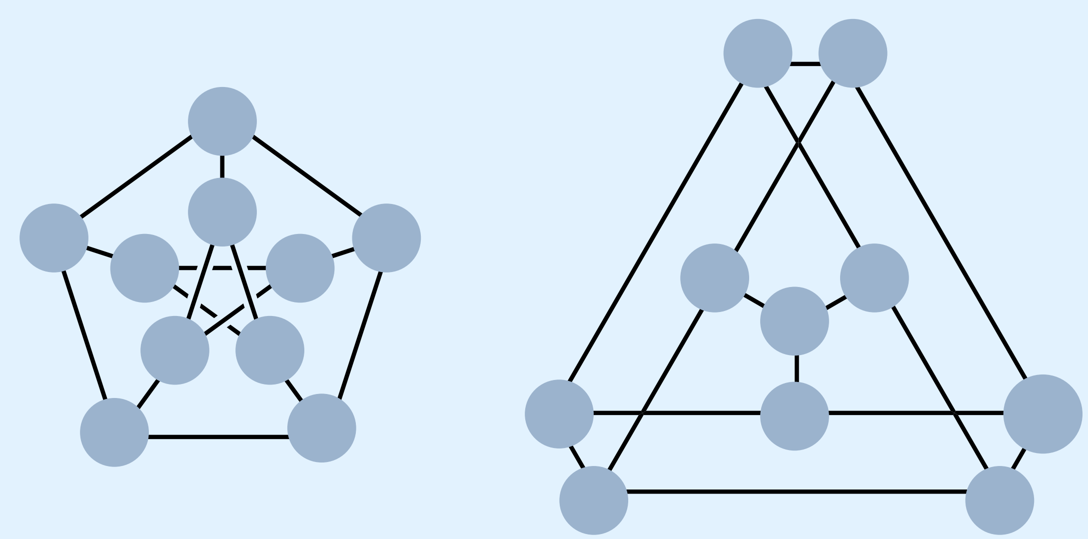


Planar

Two graphs are isomorphic if there exists a 1:1 mapping from one onto the other (i.e. they are identical, but drawn differently)



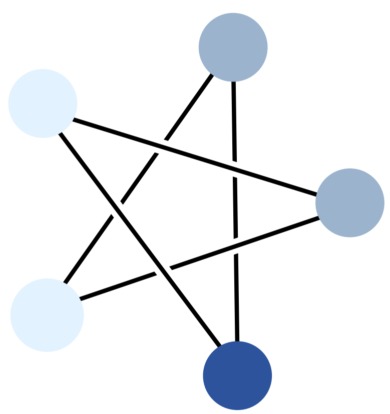
Identifying isomorphic graphs without sampling all N! mappings is challenging and remains a problem in graph theory



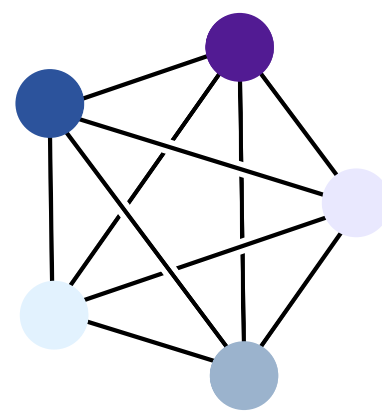
Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Planar graphs

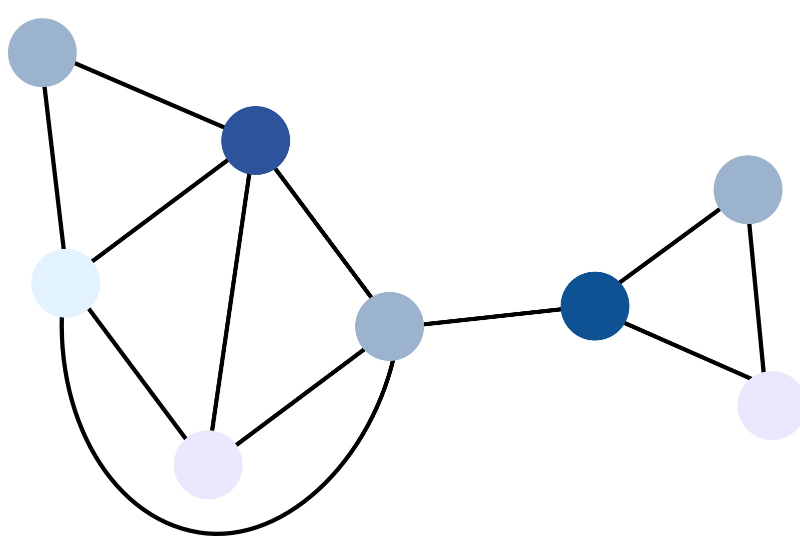
A graph is planar if it can be drawn such that no edges intersect



Planar

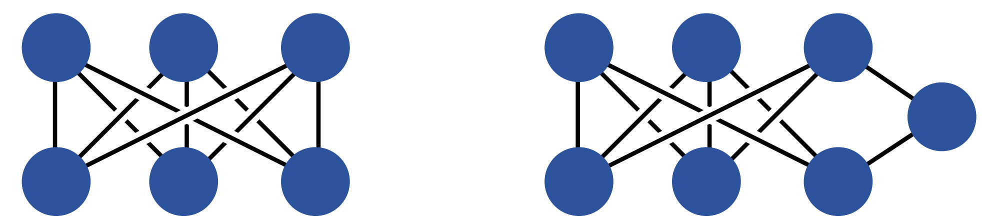


Not planar



Planar

A graph is planar if it does not contain a subgraph homeomorphic to K_5 or $K_{3,3}$

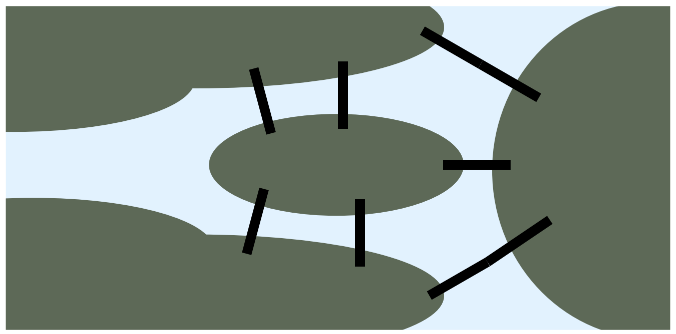


Two graphs are homoemorphic if they can be obtained from the same graph by inserting new vertices of valency 2 into its edges

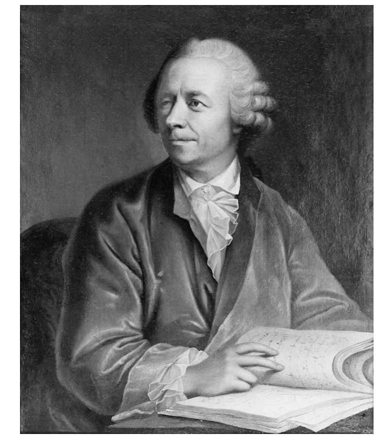
All planar graphs are 4 - colorable

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

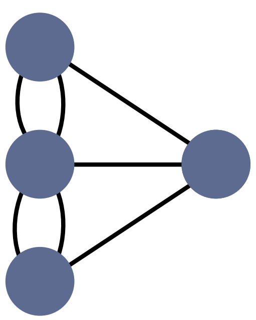
Euler Circuit – the Königsberg bridge problem

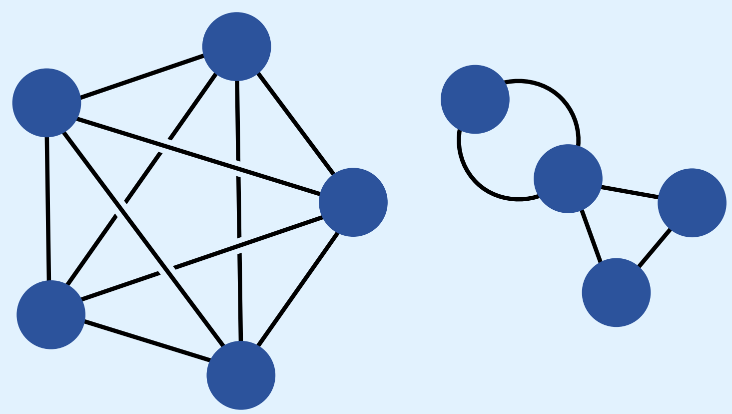


Is it possible to cross every bridge exactly once and start and end at the same spot?

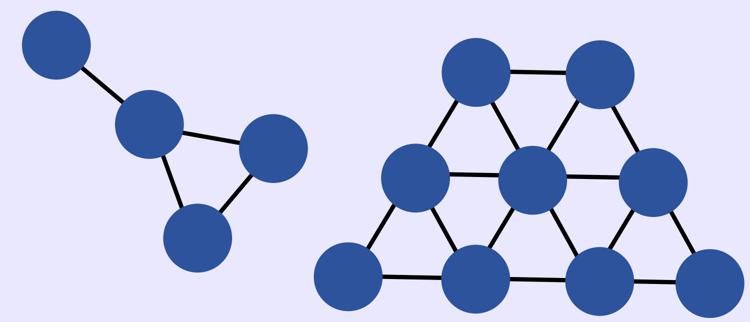


Graphical Model





Examples of Euler Circuits



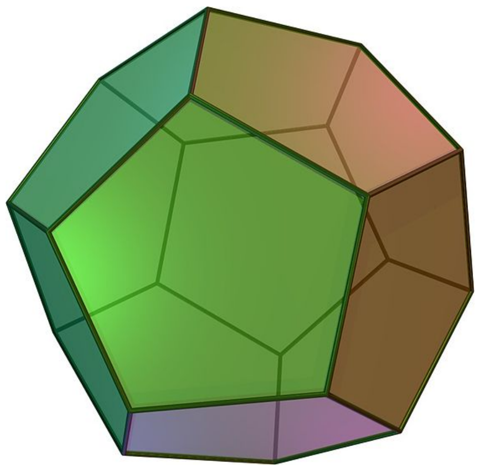
Examples of Euler Paths

- An Euler circuit is a path that starts and ends at the same vertices and traverses every edge exactly once
  - Only occurs if every vertice is of even degree

- An Euler path is a path that traverses every edge exactly once, but doesn't start and end at the same vertice
  - Only occurs if every vertice besides two are of even degree

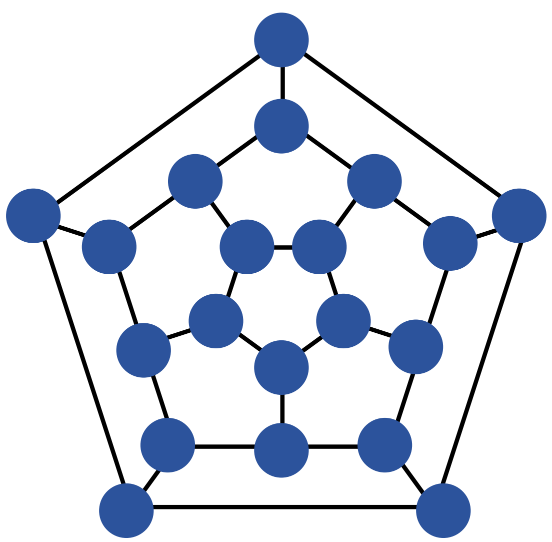
Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

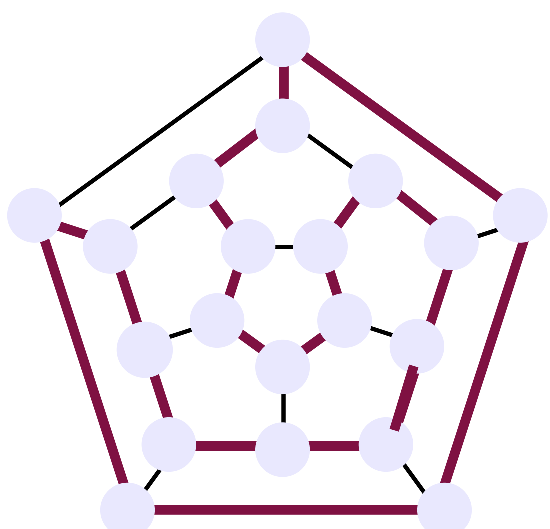
Hamiltonian circuit – the icosian game

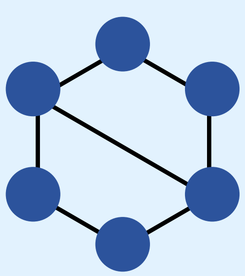


Is it possible to start at one vertice of a dodecahedron, travel to every other vertex on the polyhedra, and then return to the initial vertex without visiting any vertex besides the starting one twice?

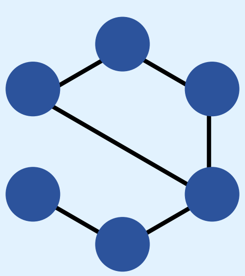
Graphical Model



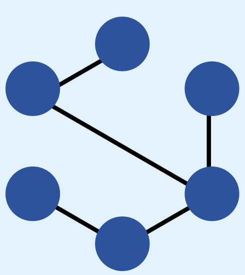




contains a Hamiltonian circuit



contains a Hamiltonian cycle



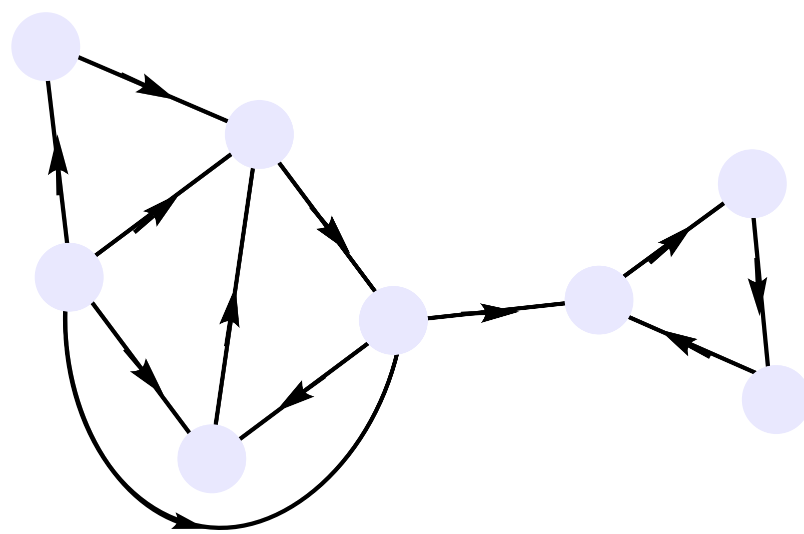
contains neither

Hamiltonian Circuit

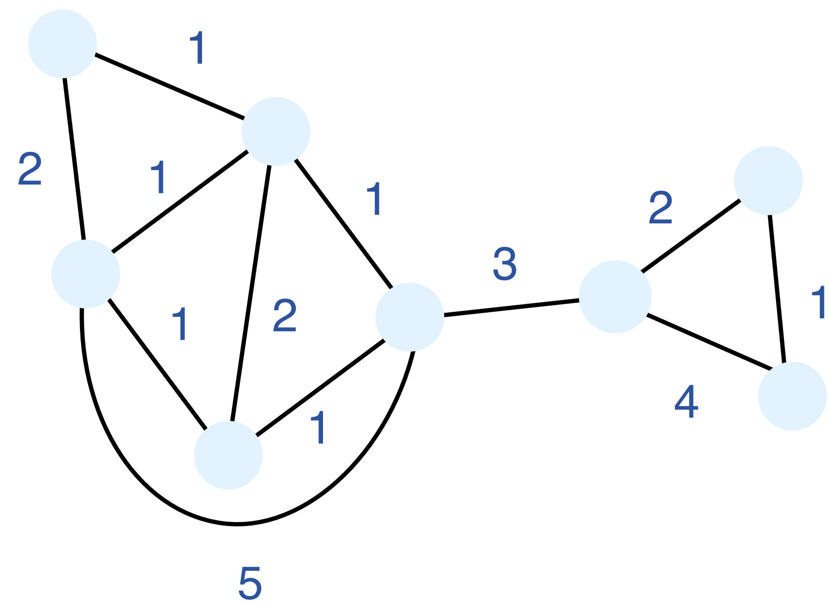
- A circuit that visits every vertex exactly once
- A mathematical formula for if a circuit exists has yet to be developed
- If the D(i) ≥ N/2 for every vertex i, then a circuit exists

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

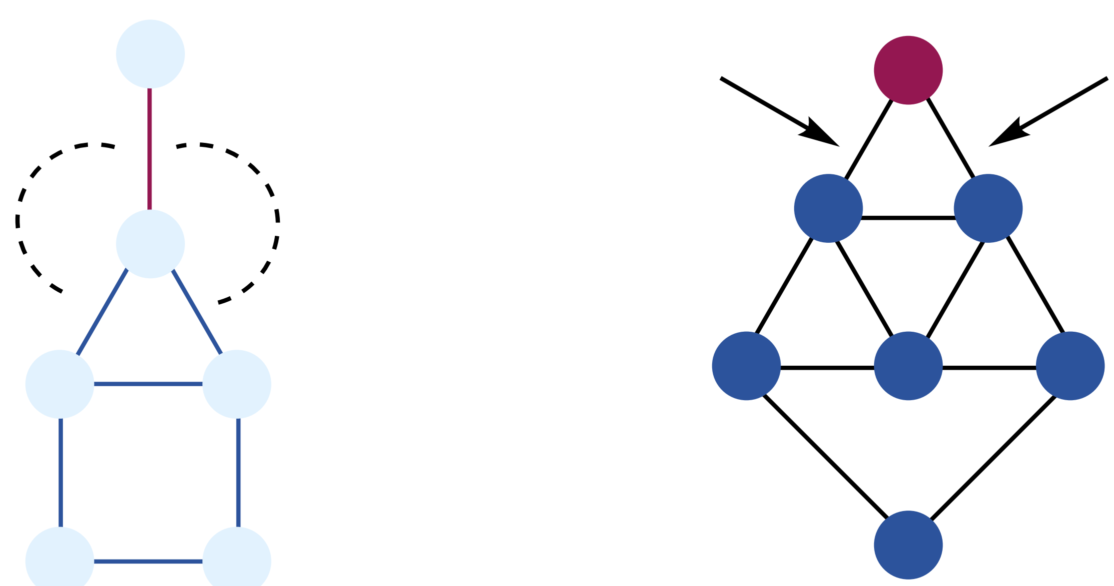
Digraphs, line graphs, and weighted graphs



Digraph



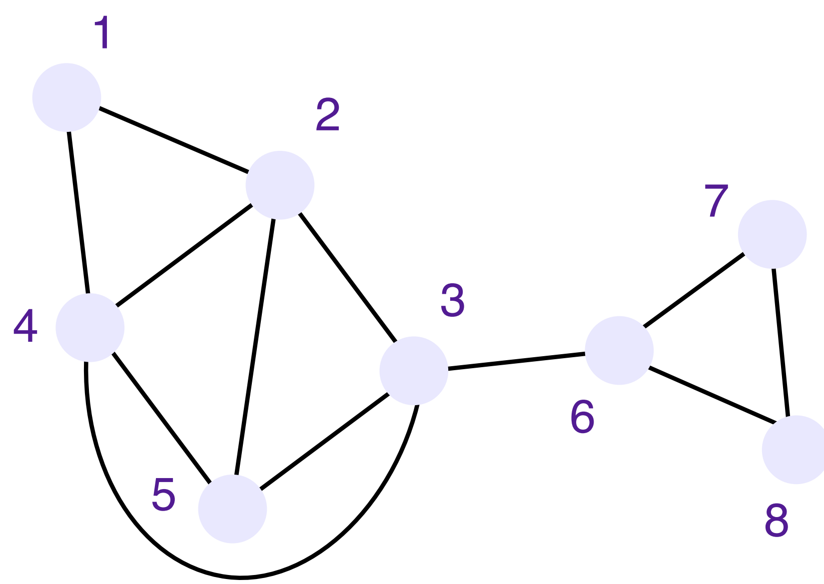
Weighted Graph



Line graph

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Graphs can be converted to matrices and polynomials



Characteristic Polynomial

$$P(G) = \det |x\mathbf{I} - \mathbf{A}|$$

$$\begin{array}{cc} & \begin{array}{cccccccc} 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 \end{array} \\ \begin{array}{c} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \\ 7 \\ 8 \end{array} & \begin{bmatrix} 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 1 & 1 & 0 & 0 \\ 1 & 1 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 \end{bmatrix} \end{array}$$

Adjacency matrix

$$\begin{array}{cc} & \begin{array}{cccccccc} 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 \end{array} \\ \begin{array}{c} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \\ 7 \\ 8 \end{array} & \begin{bmatrix} 0 & 1 & 2 & 1 & 2 & 3 & 4 & 4 \\ 1 & 0 & 1 & 1 & 1 & 2 & 3 & 3 \\ 2 & 1 & 0 & 1 & 1 & 1 & 2 & 2 \\ 1 & 1 & 1 & 0 & 1 & 2 & 3 & 3 \\ 2 & 1 & 1 & 1 & 0 & 2 & 3 & 3 \\ 3 & 2 & 1 & 2 & 2 & 0 & 1 & 1 \\ 4 & 3 & 2 & 3 & 3 & 1 & 0 & 1 \\ 4 & 3 & 2 & 3 & 3 & 1 & 1 & 0 \end{bmatrix} \end{array}$$

Distance matrix

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

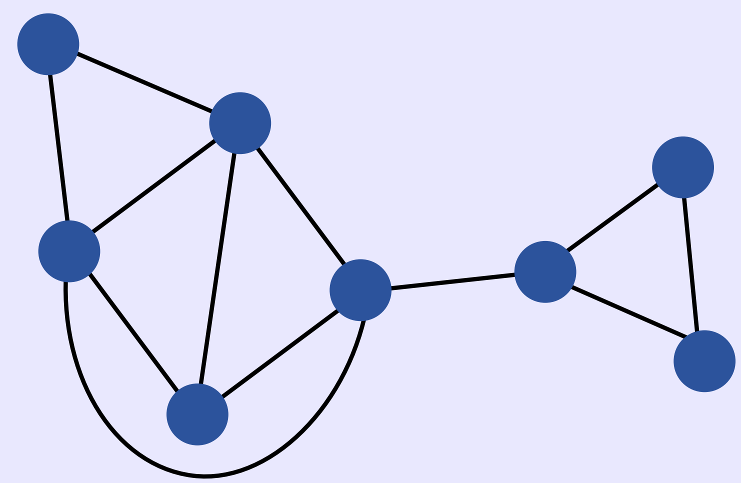
Applying graph theory to chemistry

Molecular Structures

- vertices represent atoms
- edges represent bonds
- weighted edges can represent double bonds or C–X bonds

Polymers

- vertices represent building blocks
- edges represent connections



Graph Theory

Kinetics

- vertices represent intermediates
- edges represent pathways
- frequently digraphs

And many more...

- aromaticity
- depicting orbitals and electrons
- NMR analysis
- crystals and clusters
- mapping reaction space

Bonchev, D.; Rouvray, D. H. *Chemical Graph Theory: Introduction and Fundamentals*; Gordon and Brach Science Publishers S.A.: New York, 1991.

Chemical graph theory

What is graph theory?

Historical uses of chemical graph theory

- **Isomer counting**
- **Chemical bonding**
- **Kinetics**

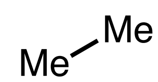
Modern uses of chemical graph theory

Isomer counting

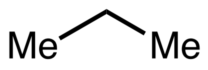
How can we go about counting the number of isomers possible for a given carbon number in a systematic fashion?

C = 1

C = 2

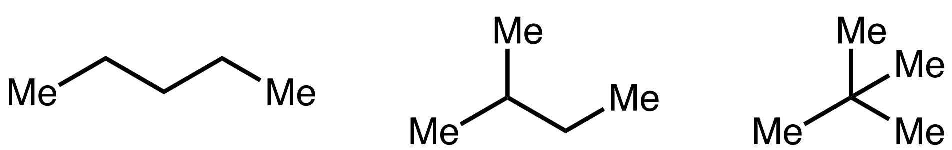


C = 3

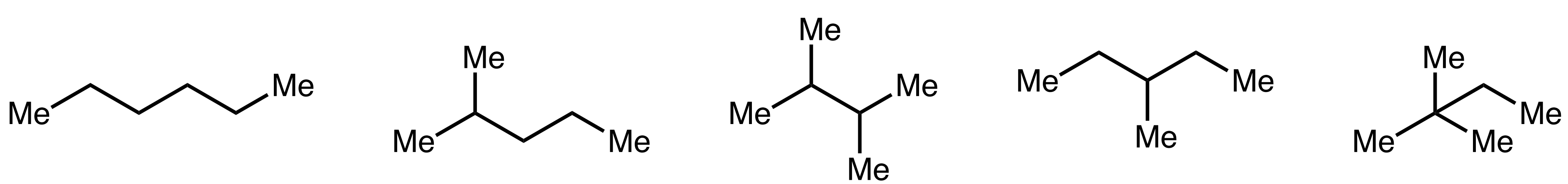


C = 4

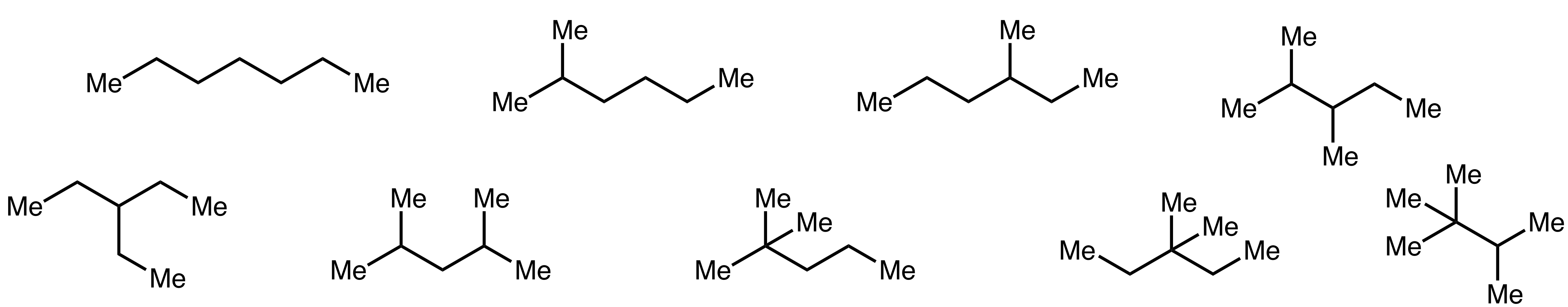
C = 5



C = 6



C = 7



Isomer counting – the Caylee approach

Recursive approach

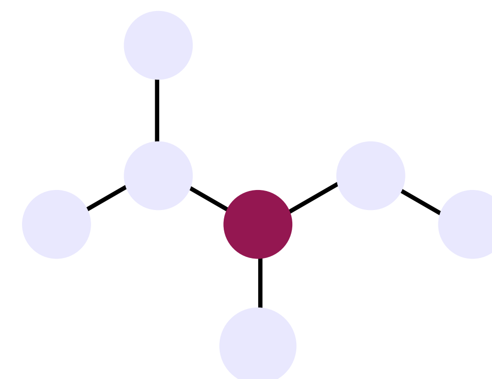
Counted the number of centric and bicentric trees

Developed methods for counting rooted and unrooted trees and then limited them to 4 vertices

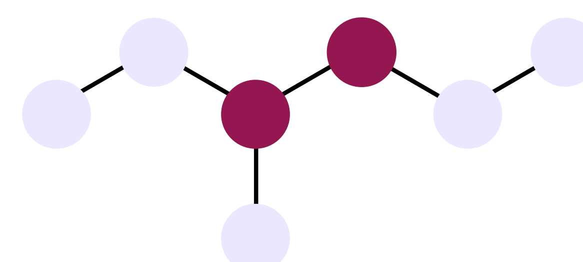
Sucessfully counted the nubmer of C1-C11 alkanes

Rather tedious process

Gave incorrect answers for C12 and C13 alkanes



centric tree



bicentric tree

Cayley, A. *Rep. Br. Assoc. Adv. Sci.*, **1875**, *45*, 257.

Isomer counting – the Henze-Blair approach

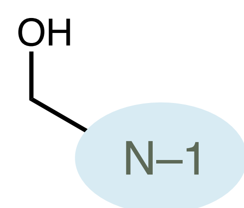
Counting the number of alcohols on acyclic alkanes

Let T_N be the number of alcohols of carbon N and p_N, s_N, and t_N be the number of primary, secondary and tertiary alcohols respectively

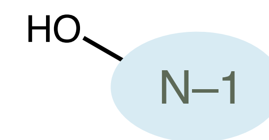
Then $T_N = p_N + s_N + t_N$

primary alcohols

$p_N = T_{N-1}$

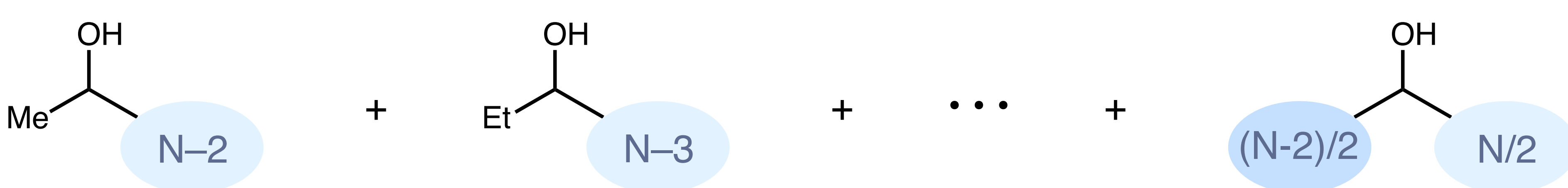


can be thought of as counting



secondary alcohols

$$s_N = \begin{cases} T_1 * T_{N-2} + T_2 * T_{N-3} + \ldots\ldots + T_{(N-2)/2} * T_{N/2} & \text{if N = even} \\ T_1 * T_{N-2} + T_2 * T_{N-3} + \ldots\ldots + T_{(N-3)/2} * T_{(N+1)/2} + (1/2) * T_{(N-1)/2} * [1 + T_{(N-1)/2}] & \text{if N = odd} \end{cases}$$

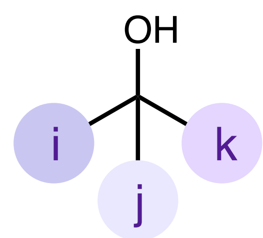


Henze, H. R.; Blair, C. M. *J. Am. Chem. Soc.* **1931**, *53*, 3042.

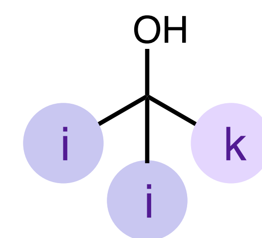
Isomer counting – the Henze-Blair approach

tertiary alcohols

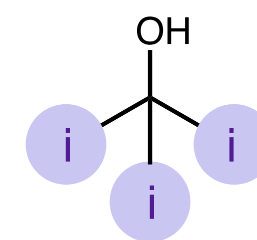
A tertiary alochol can be imagined to arise from combining 3 alkyl radicals R_i, R_j, and R_k with i, j, and k carbons respectively to the COH group



All possible permutations where i > j > k



All possible permutations where i = j and 2i + k = N - 1



All possible permutations where i = j = k and 3i = N - 1

$$t_N = \begin{cases} \Sigma\, T_i * T_j * T_k & i > j > k;\ i + j + k = N - 1 \\ + & \\ 1/2 * \Sigma\, T_i * (1 + T_i) * T_k & i = j;\ i + j + k = N - 1 \\ + & \\ 1/6 * T_i * (T_i + 1) * (T_i + 2) & i = j = k;\ i + j + k = N - 1 \end{cases}$$

This approach has been expanded to deal with structural saturated hydrocarbons, unsaturated hydrocarbons, alkynes and even stereoisomeric alcohols

Henze, H. R.; Blair, C. M. *J. Am. Chem. Soc.* **1931**, *53*, 3042.

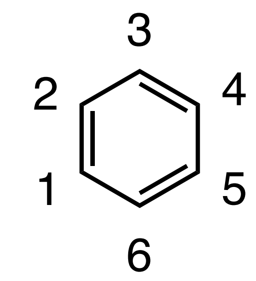
Isomer counting – the Pólya enumeration approach

Takes into account symmetry operations

Produces a polynomial that allows for isomer enumeration

f and g are equivalent if and only if there ∃ a permutation α such that α(*f*) = g

Zyklenzeiger: $Z(A) = \frac{1}{|A|} \sum_{\alpha \in A} \prod_{r} s_r^{j_r(\alpha)}$



How many ways are there to substitute a benzene ring with an R group X times?

Point group: D_6

Symmetry Operation	Permutation	Cycle index term
One identity E	(1) (2) (3) (4) (5) (6)	s_1^6
Two 6-fold rotations +/- C_6	(123456), (165432)	$2s_6^1$
Two 3-fold rotations +/- C_3	(153)(264), (135)(246)	$2s_3^2$
One vertical 2-fold rotation C_2	(14)(25)(36)	s_2^3
Three in plane binary axes C_2 that bisect 0 carbons	(16)(25)(34), (12)(36)(45), (14)(23)(56)	$3s_2^3$
Three in plane binary axes C_2 that bisect 2 carbons	(1)(4)(26)(35), (3)(6)(15)(24), (2)(5)(13)(46)	$3s_1^2 s_2^2$

Pólya, G. *Acta Math.* **1937**, *68*, 1937.

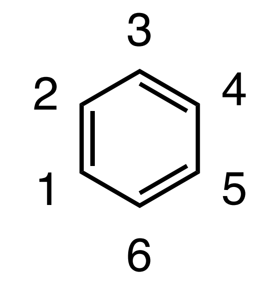
Isomer counting – the Pólya enumeration approach

Takes into account symmetry operations

Produces a polynomial that allows for isomer enumeration

f and g are equivalent if and only if there ∃ a permutation α such that α(*f*) = g

Zyklenzeiger: $Z(A) = \frac{1}{|A|} \sum_{\alpha \in A} \prod_r s_r^{j_r(\alpha)}$



How many ways are there to substitute a benzene ring with an R group X times?

Point group: D_6

$$Z(D_6) = 1/12 \{ s_1^6 + 3s_1^2 s_2^2 + 4s_2^3 + 2s_3^2 + 2s_6^1 \}$$

substituting $s_y^z = (1 + x^y)^z$

$$Z(D_6) = 1/12 [(1 + x)^6 + 3 * (1 + x)^2 * (1 + x^2)^2 + 4 * (1 + x^2)^3 + 2 * (1 + x^3)^2 + 2 * (1 + x^6)]$$

There are 3 unique isomers with 4 R substituents

$$Z(D_6) = 1 + x + 3x^2 + 3x^3 + 3x^4 + x^5 + x^6$$

Cycle index term
s_1^6
$2s_6^1$
$2s_3^2$
s_2^3
$3s_2^3$
$3s_1^2 s_2^2$

Pólya, G. *Acta Math.* **1937**, *68*, 1937.

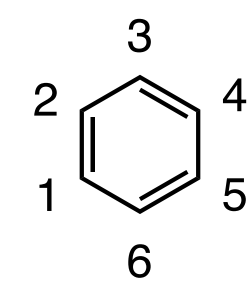
Isomer counting – the Pólya enumeration approach

Takes into account symmetry operations

Produces a polynomial that allows for isomer enumeration

f and g are equivalent if and only if there ∃ a permutation α such that α(*f*) = g

Zyklenzeiger: $Z(A) = \frac{1}{|A|} \sum_{\alpha \in A} \prod_{r} s_r^{j_r(\alpha)}$

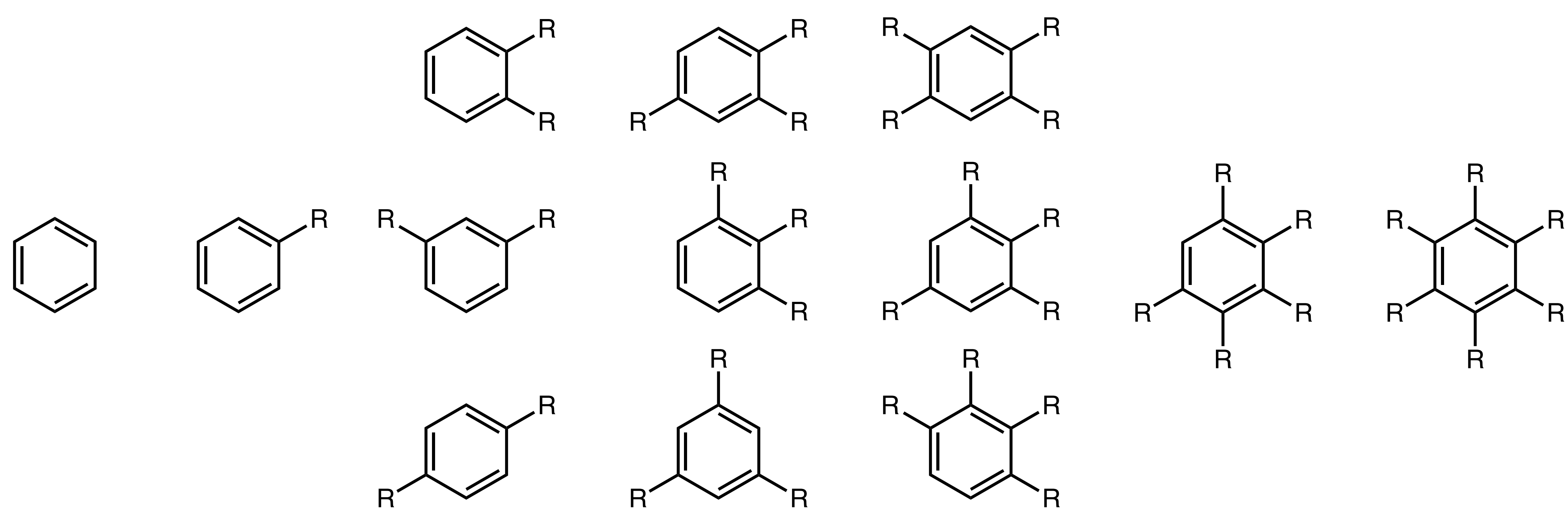


How many ways are there to substitute a benzene ring with an R group X times?

Point group: D_6

$Z(D_6) = 1 + x + 3x^2 + 3x^3 + 3x^4 + x^5 + x^6$

1 1 3 3 3 1 1



Pólya, G. *Acta Math.* **1937**, *68*, 1937.

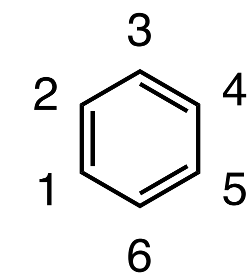
Isomer counting – the Pólya enumeration approach

Takes into account symmetry operations

Produces a polynomial that allows for isomer enumeration

f and g are equivalent if and only if there ∃ a permutation α such that α(*f*) = g

Zyklenzeiger: $Z(\mathrm{A}) = \frac{1}{|\,\mathrm{A}} \sum_{\alpha \in \mathrm{A}} \prod_{r} s_r^{j_r(\alpha)}$



How many ways are there to substitute a benzene ring with an R group X times?

Point group: D_6

This method has been extended to isotopic isomers, cyclic molecules, benzenoid hydrocarbons, porphyrins, chiral and achiral alkenes, ferrocenes, clusters, and inorganic structures, among others

Pólya, G. *Acta Math.* **1937**, *68*, 1937.

Isomer counting – the N-tuple code

Assigns each tree a unique code

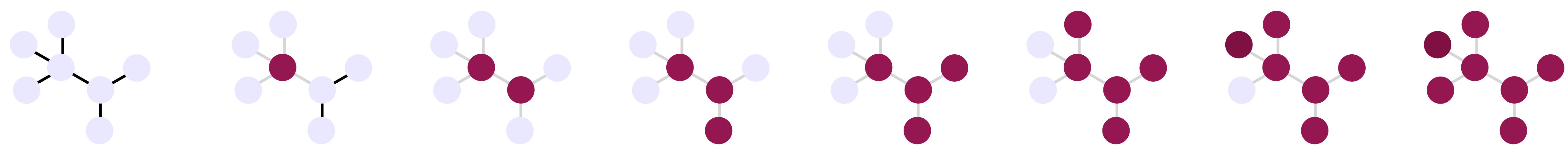
Isomorphic compounds have the same code

Have been used for generation and enumeration of acyclic graphs

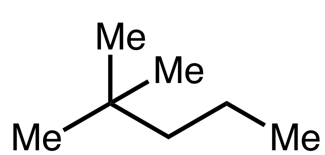
Start from most substituted vertice

Remove vertex and incident edges, then examine the subtrees

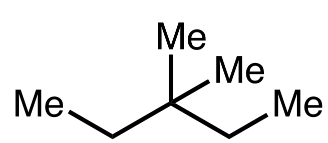
Produce the lexicographically largest code



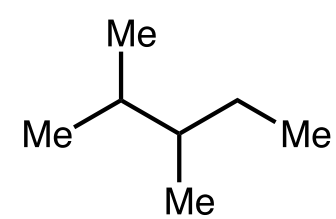
{4,2,0,0,0,0,0} 4 2 0 0 0 0 0



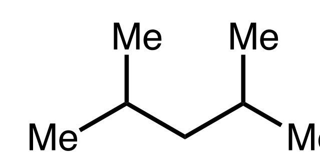
{4,1,1,0,0,0,0}



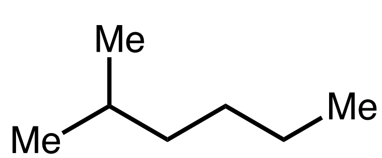
{4,1,0,1,0,0,0}



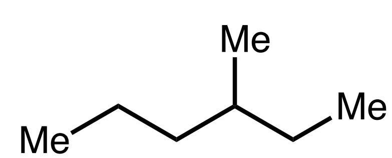
{3,2,1,0,0,0,0}



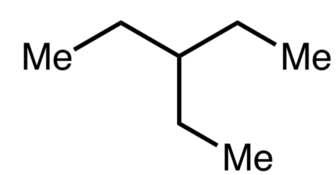
{3,1,2,0,0,0,0}



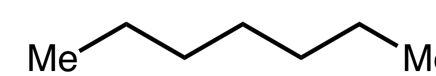
{3,1,1,1,0,0,0}



{3,1,1,0,1,0,0}



{3,1,0,1,0,1,0}



{2,1,1,1,1,0,0}

Knop, J. V.; Müller, W. R.; Jeričević, Ž.; Trinajstić, N. *J. Chem. Inf. Comput. Appl. Chem.* **1981**, *21*, 94.

Chemical graph theory

What is graph theory?

Historical uses of chemical graph theory

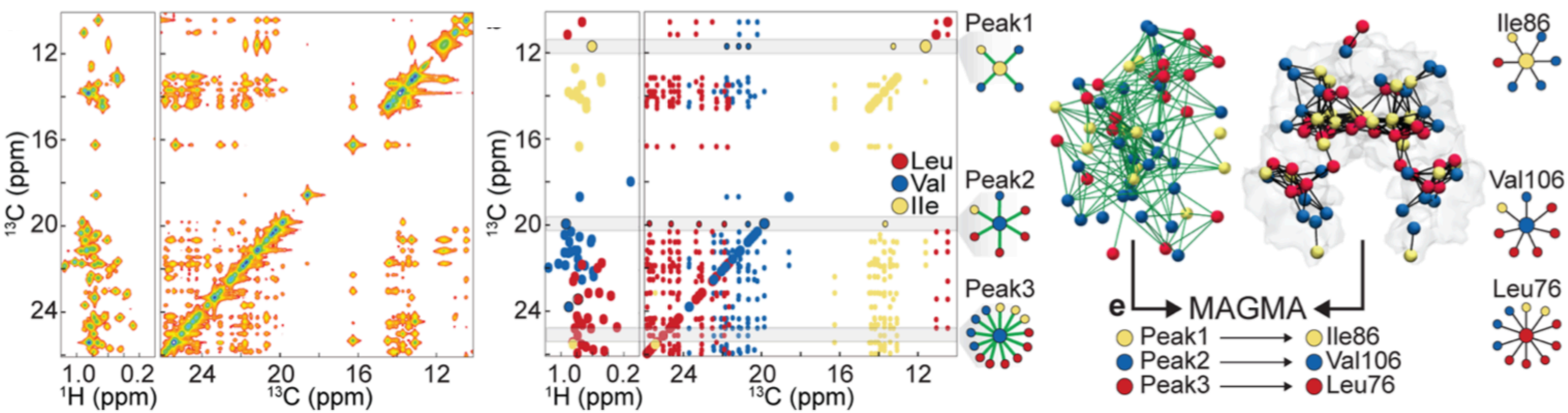
- **Isomer counting**
- **Chemical bonding**
- **Kinetics**

Modern uses of chemical graph theory

NMR assignment of methyl peaks in large molecules via MAGMA

- NMR spectroscopy can probe both structure and dynamics of biomolecules at atomic resolutions
- Methyl-TROSY can be utilized to study protein complexes up to 1 MDa in molecular weight
- A major challenge to this approach is the need to match resonances in the NMR with specific atoms
- Generally obtained by either monitoring assignments from smaller in tact proteins or individually changing residues and observing the NMR perturbations

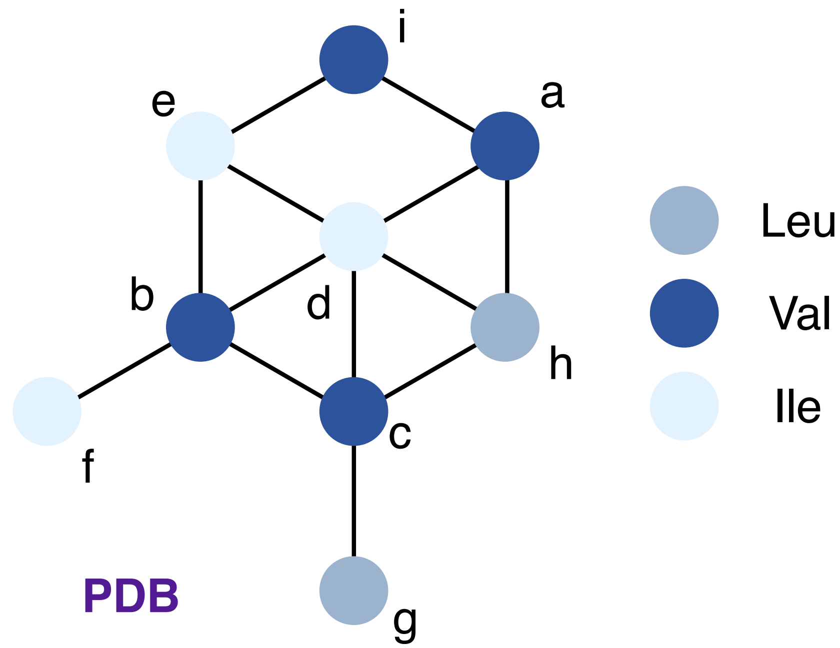
Would it be possible to use graph theory to simplify this process?

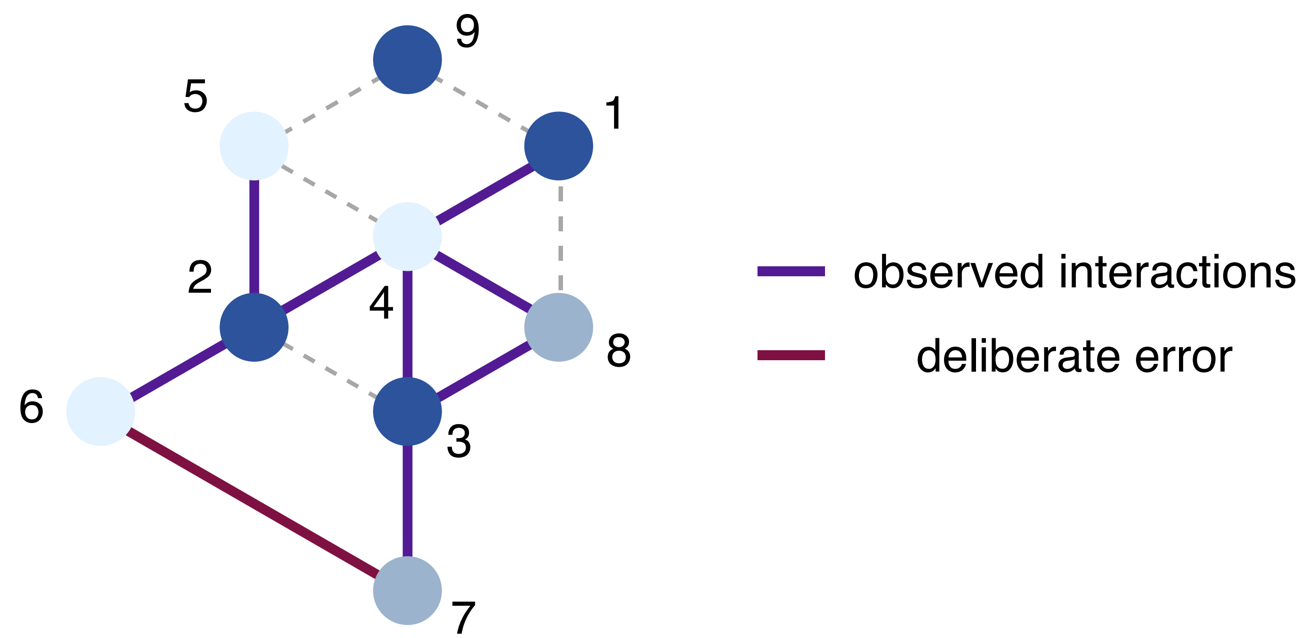


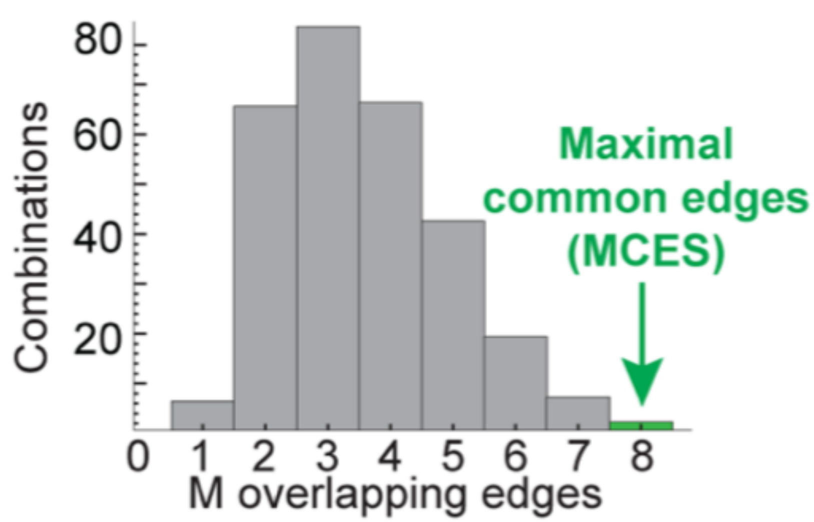
Methyl Assignment by Graph MAtching

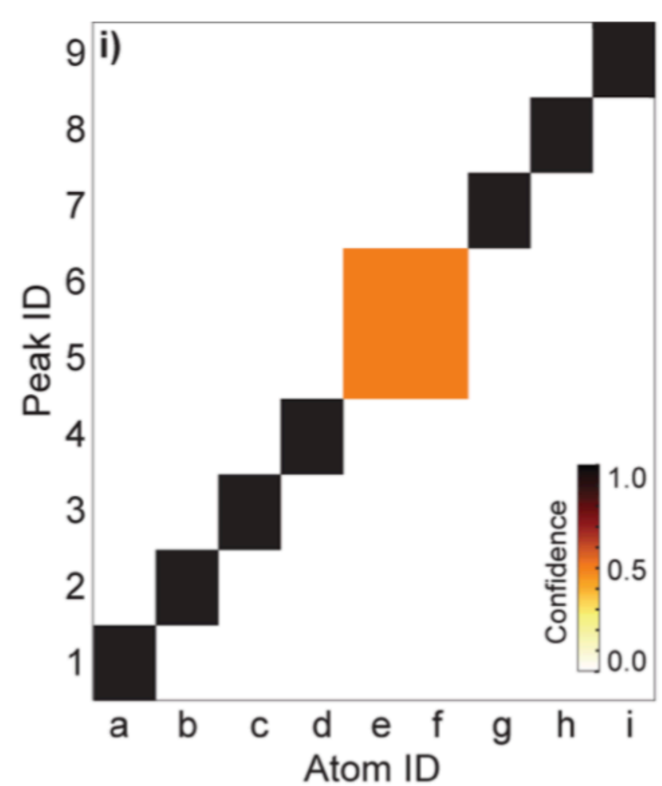
Pritišanac, I.; Degiacomi, M. T.; Alderson, T. R.; Carneiro, M. G.; AB, E.; Siegal, G.; Baldwin, A. J. *J. Am. Chem. Soc.* **2017**, *139*, 9523.

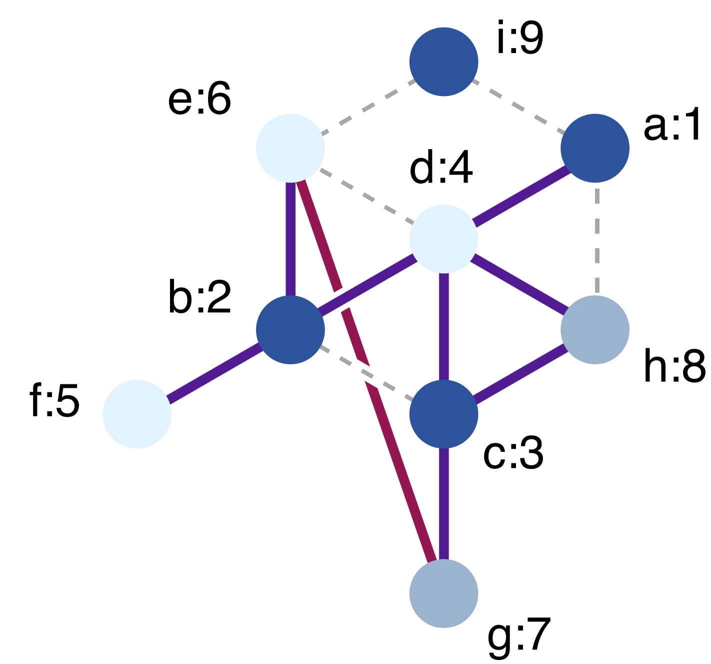
NMR assignment of methyl peaks in large molecules via MAGMA





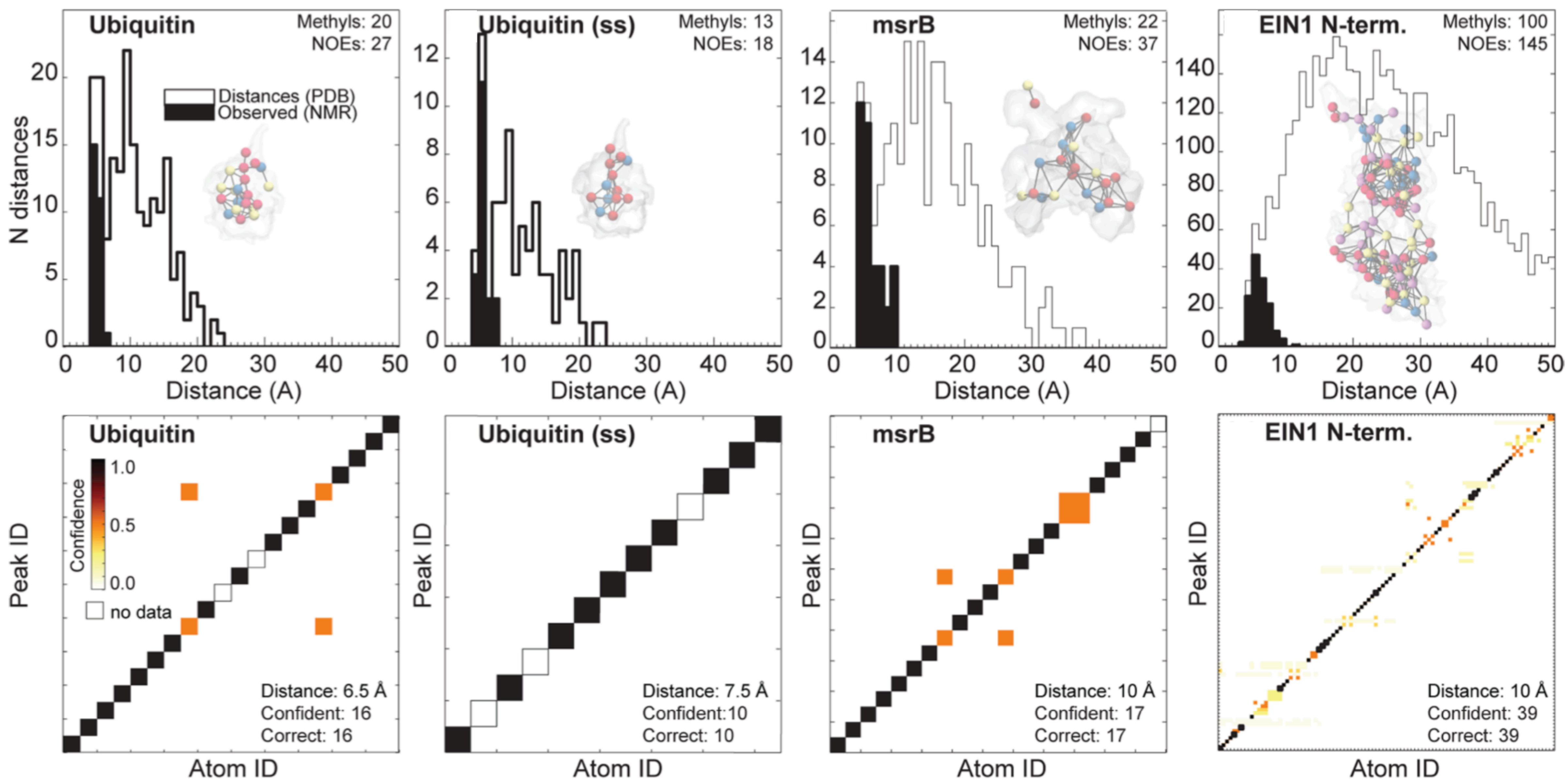






Pritišanac, I.; Degiacomi, M. T.; Alderson, T. R.; Carneiro, M. G.; AB, E.; Siegal, G.; Baldwin, A. J. *J. Am. Chem. Soc.* **2017**, *139*, 9523.

NMR assignment of methyl peaks in large molecules via MAGMA

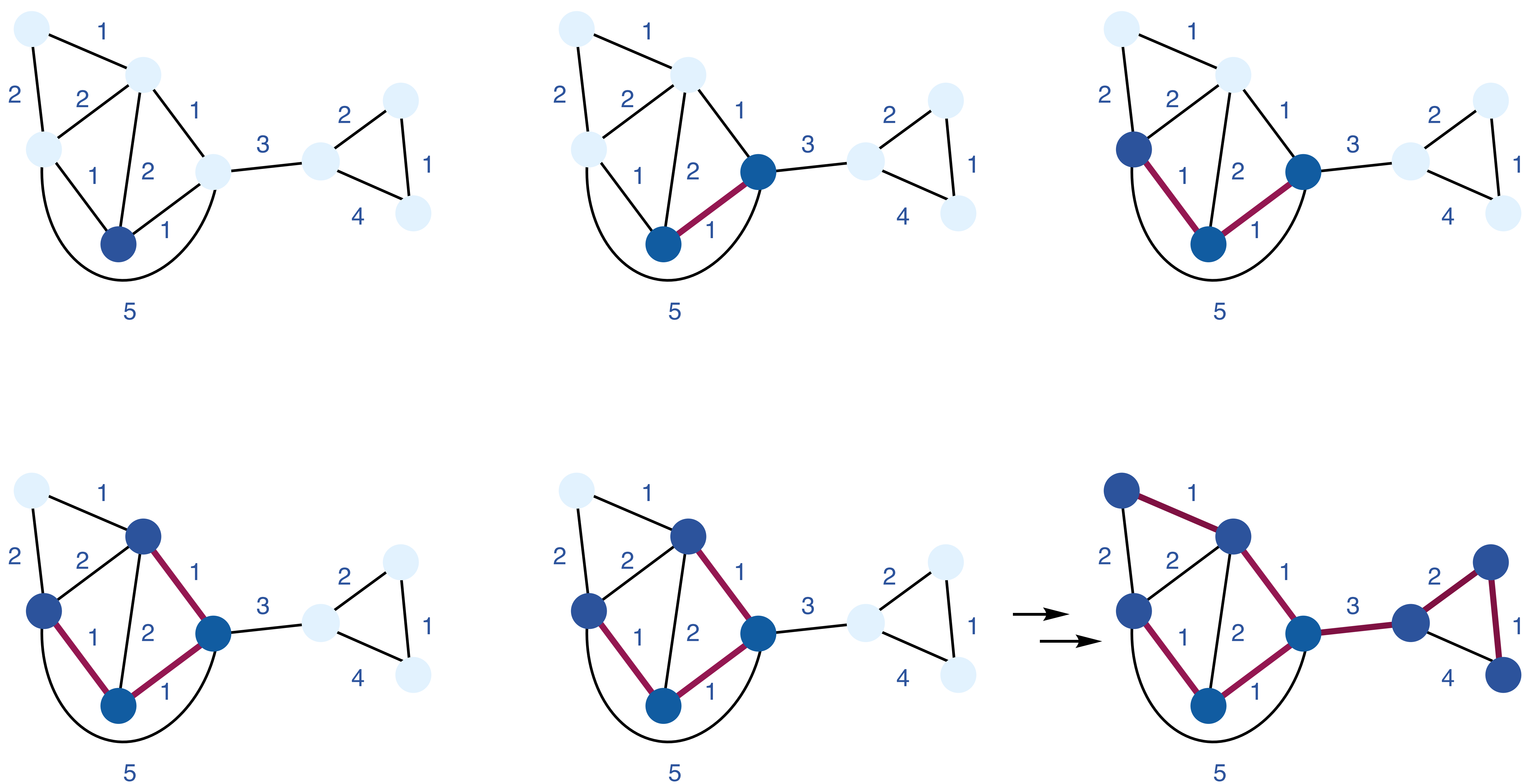


Pritišanac, I.; Degiacomi, M. T.; Alderson, T. R.; Carneiro, M. G.; AB, E.; Siegal, G.; Baldwin, A. J. *J. Am. Chem. Soc.* **2017**, *139*, 9523.

Kinetic Analysis with Prim's algorithm

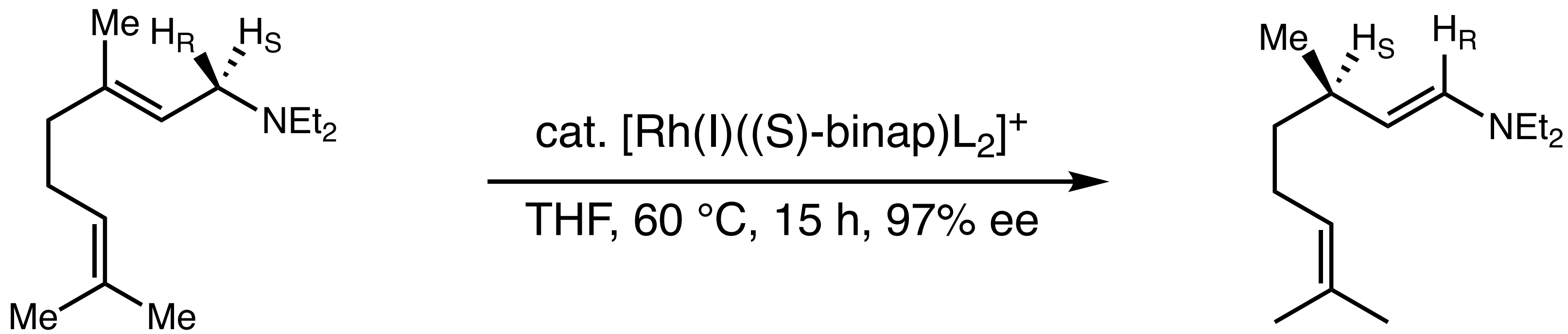
Minimum spanning tree – a subset of edges that connect a graph together with the minimal possible weight

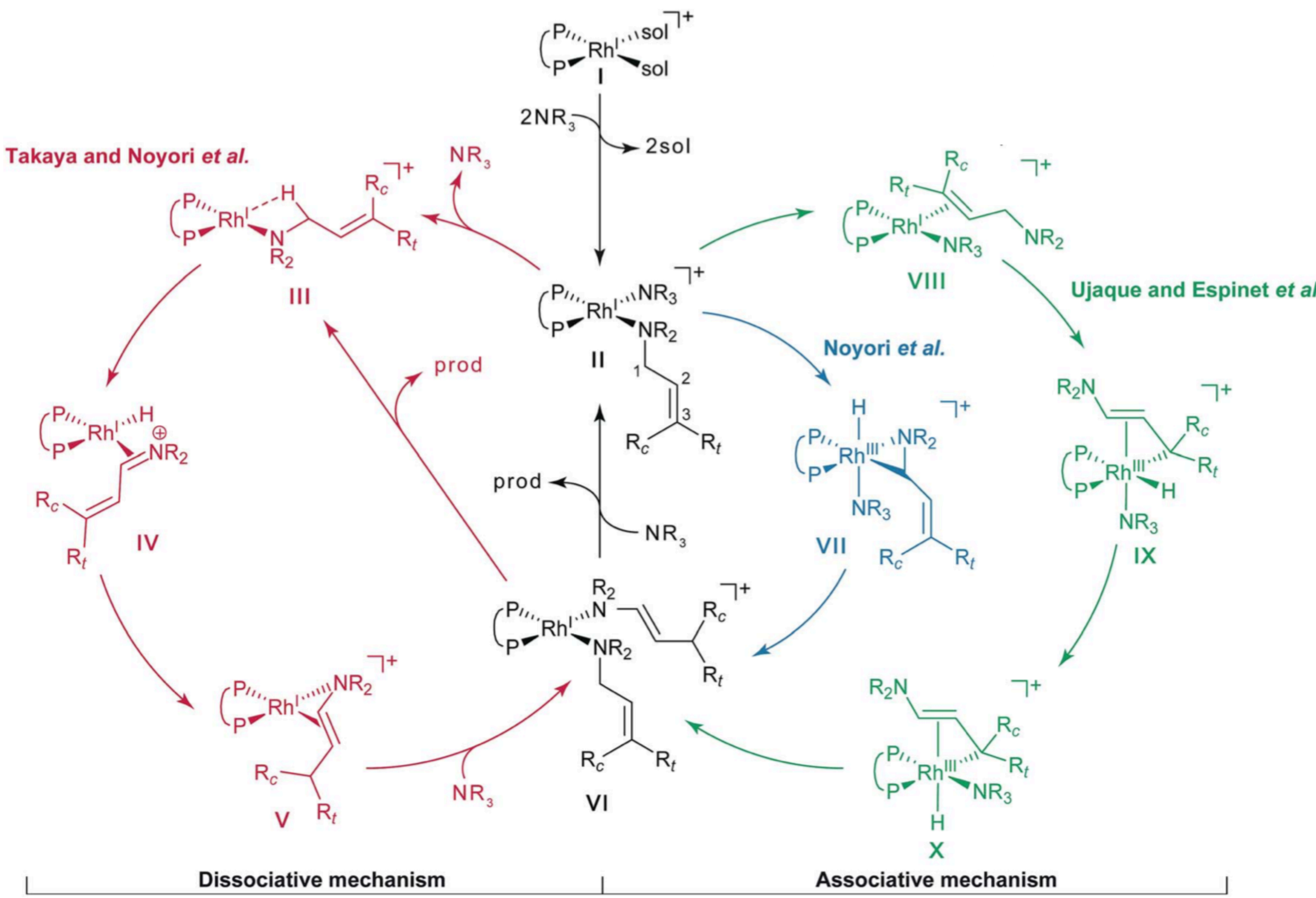
Prim's algorithm finds minimum spanning by repeatedly adding the cheapest vertice to the spanning tree



Yoshimura, T.; Maeda, S.; Taketsugu, T.; Sawamura, M.; Morokuma, K.; Mori, S. *Chem. Sci.* **2017**, *8*, 4475.

Kinetic Analysis with Prim's algorithm

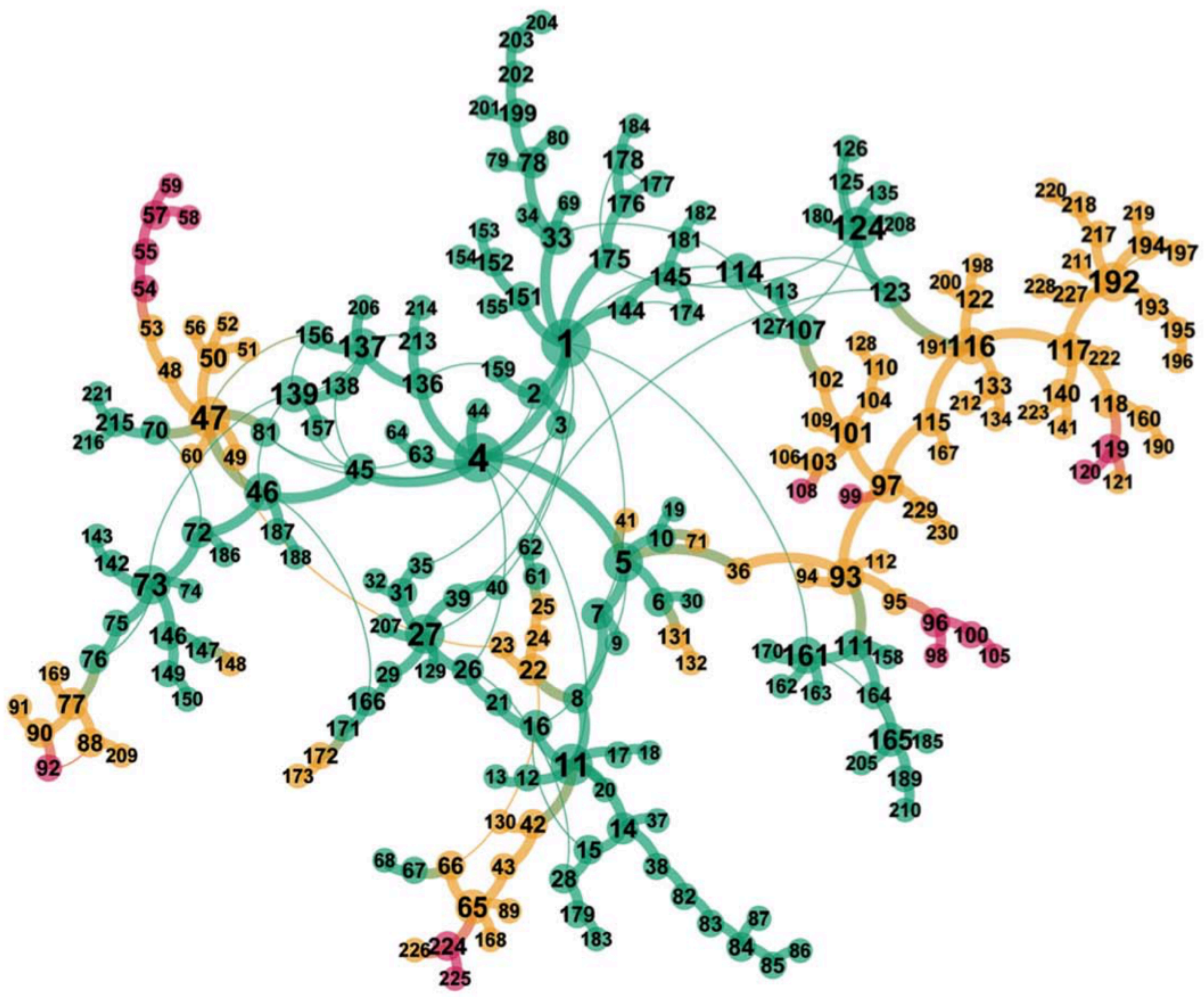




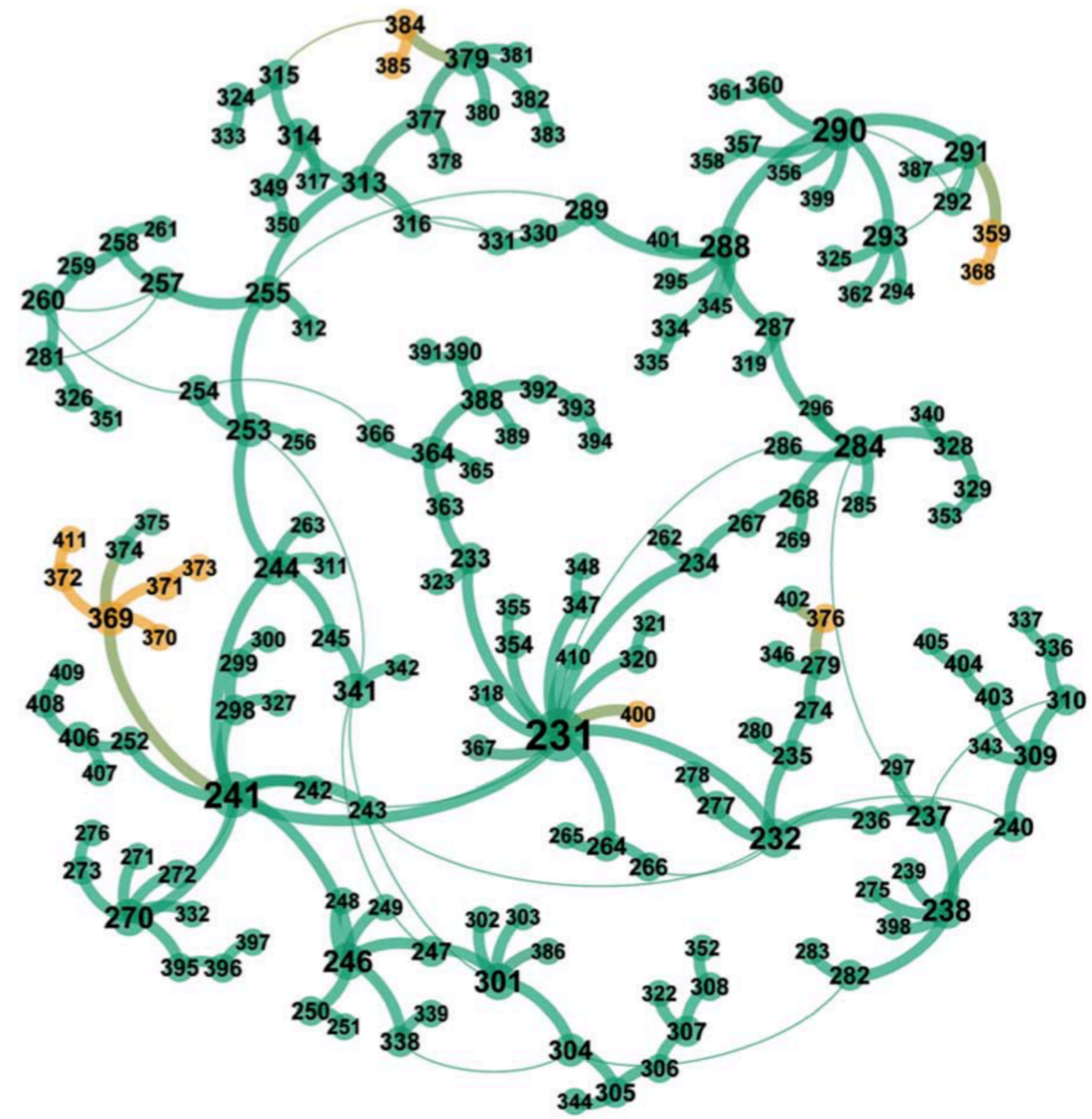
Yoshimura, T.; Maeda, S.; Taketsugu, T.; Sawamura, M.; Morokuma, K.; Mori, S. *Chem. Sci.* **2017**, *8*, 4475.

Kinetic analysis with Prim's algorithm

Dissociative



Associative

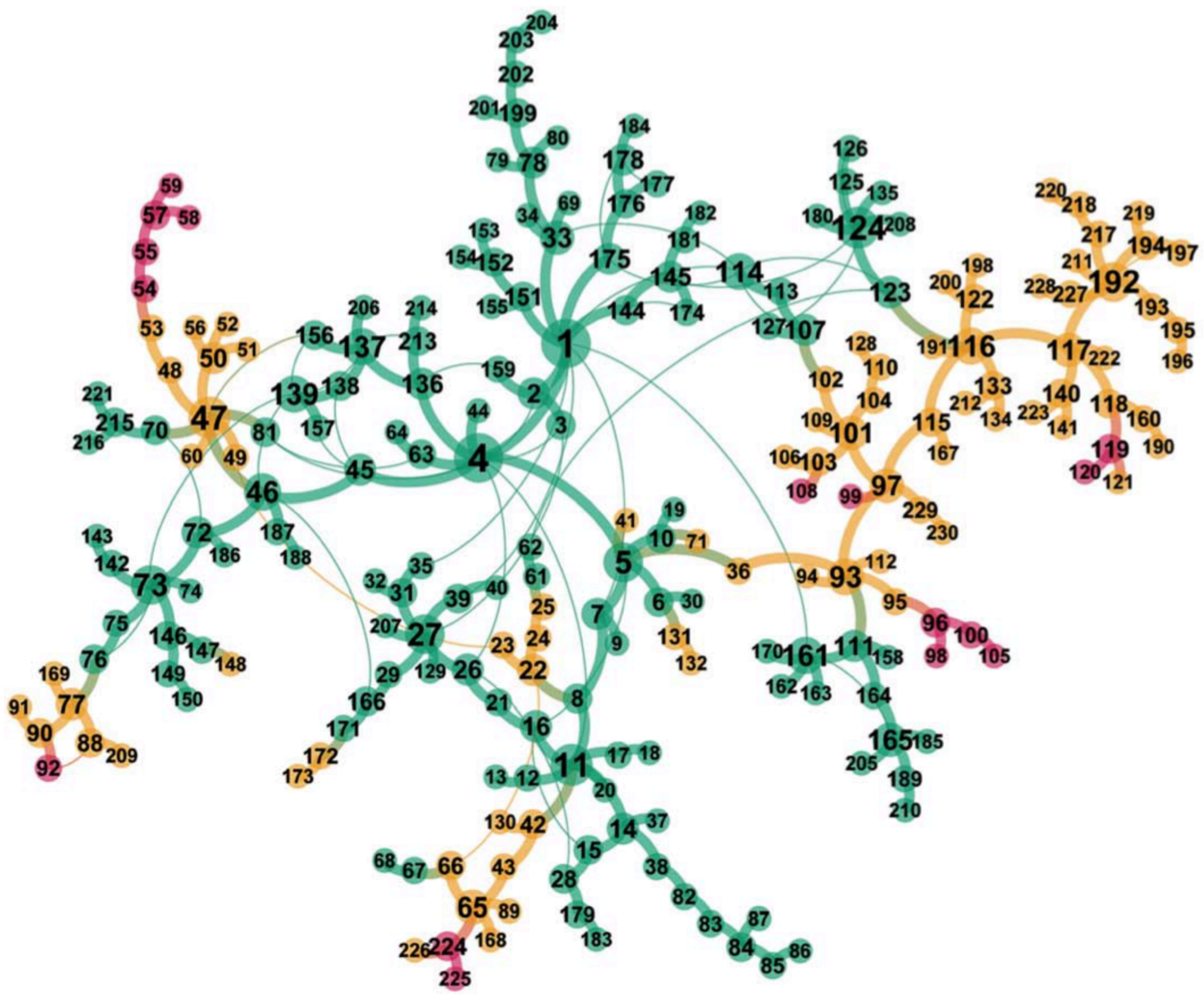


- Bolded edges are part of the spanning tree
- Green paths represent earlier in the pathway and red later

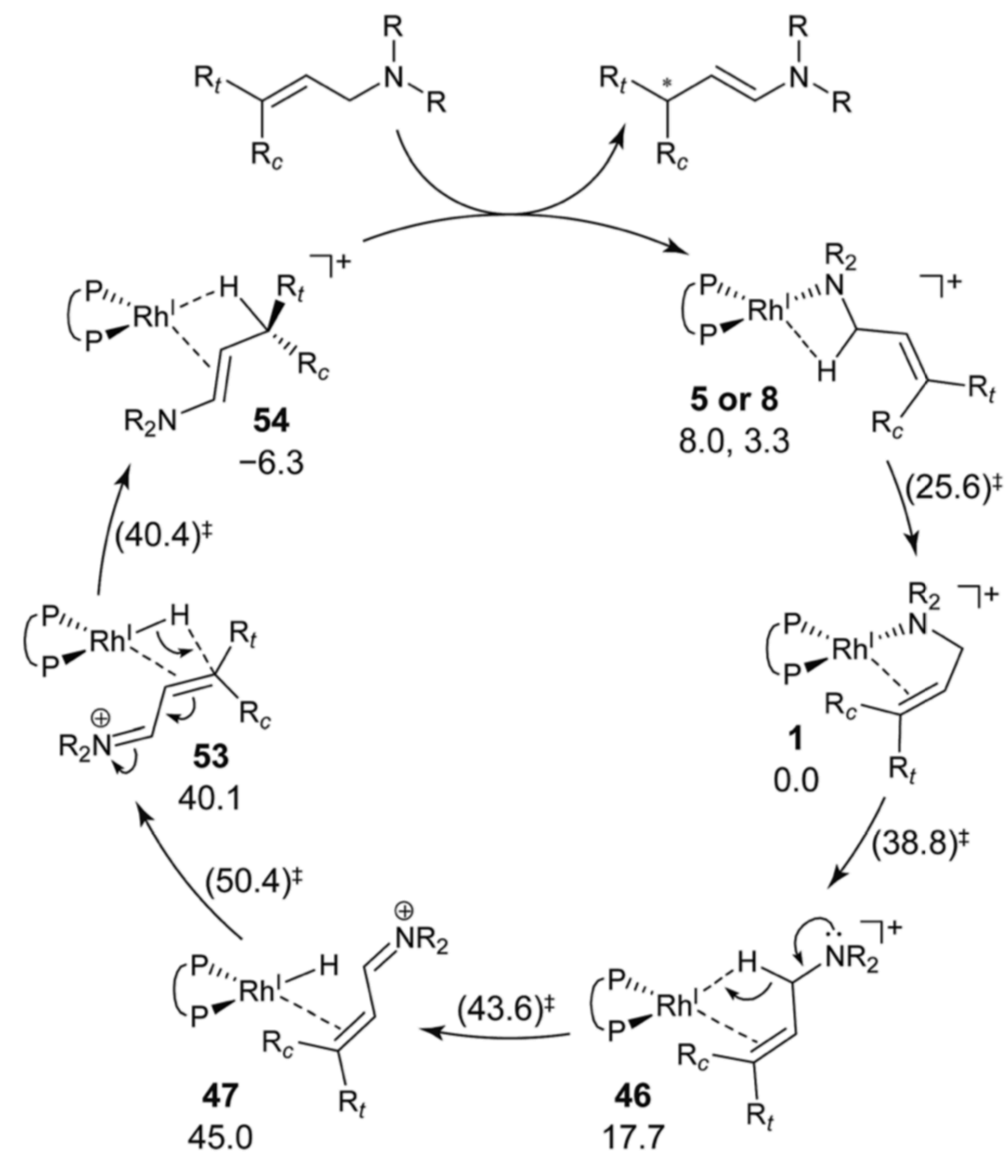
Yoshimura, T.; Maeda, S.; Taketsugu, T.; Sawamura, M.; Morokuma, K.; Mori, S. *Chem. Sci.* **2017**, *8*, 4475.

Kinetic analysis with Prim's algorithm

Dissociative



Proposed mechanism



- Bolded edges are part of the spanning tree
- Green paths represent earlier in the pathway and red later

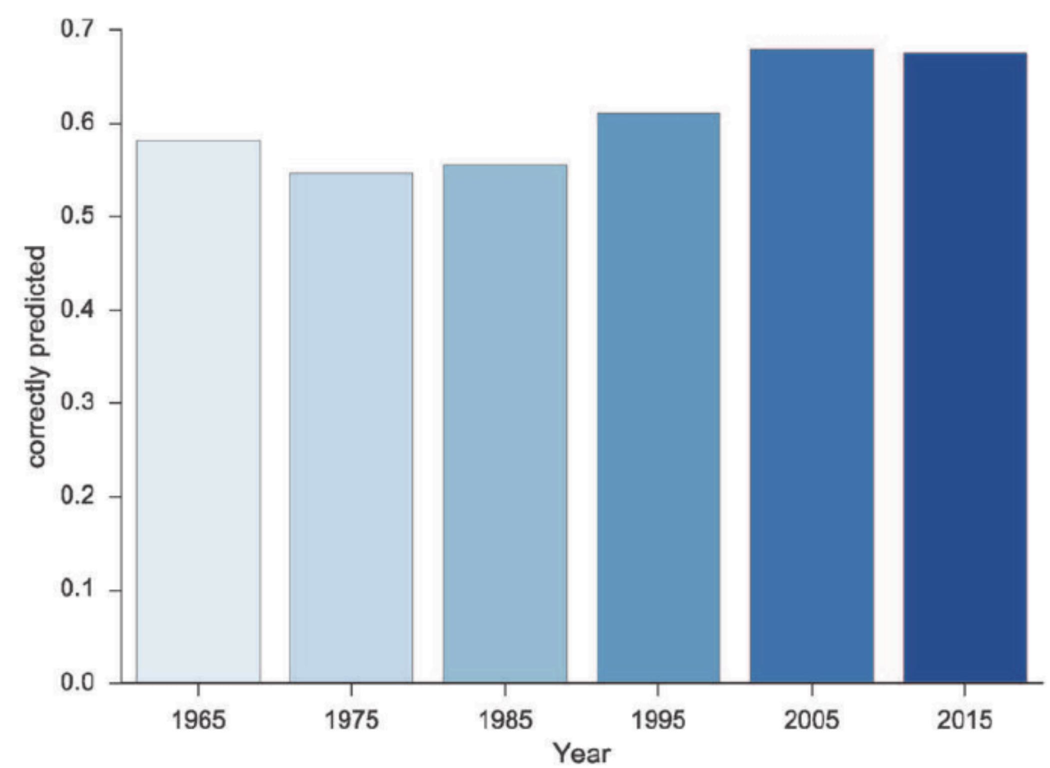
Yoshimura, T.; Maeda, S.; Taketsugu, T.; Sawamura, M.; Morokuma, K.; Mori, S. *Chem. Sci.* **2017**, *8*, 4475.

Can we use graph theory to predict reactions?

High-throughput computer-based reaction predictions (HTRP) can be used for *de novo* drug design, virtual chemical space exploration, and to predict if retrosynthesis disconnections are feasible

Can we use this to predict reactions?

- Constructed a knowledge graph from 14.4 million reactants and 8.2 million binary reactions
- Vertices represent reactants and reaction conditions with edges connecting reactants to reaction conditions and other reactants
- Predict reactions, products and reaction conditions
- Correctly predicted the right product with 67.5% accuracy on 180,000 reactions that were withheld from the data set
- Able to predict the products and reaction conditions of 'novel' reactions with decent efficiency



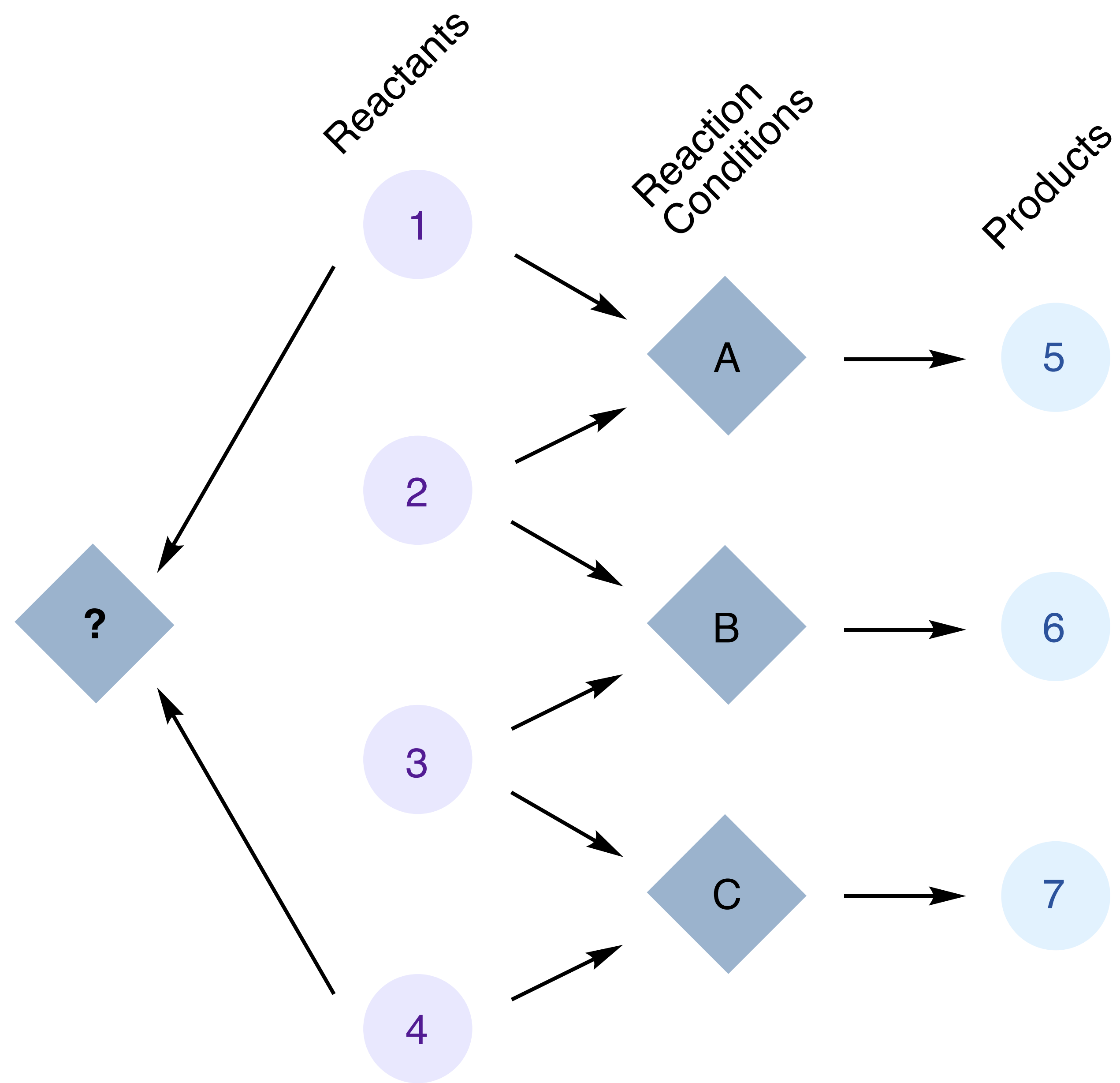
Segler, M. H. S.; Waller, M. P.; *Chem. Eur. J.* **2017**, *23*, 6118.

Can we use graph theory to predict reactions?

High-throughput computer-based reaction predictions (HTRP) can be used for *de novo* drug design, virtual chemical space exploration, and to predict if retrosynthesis disconnections are feasible

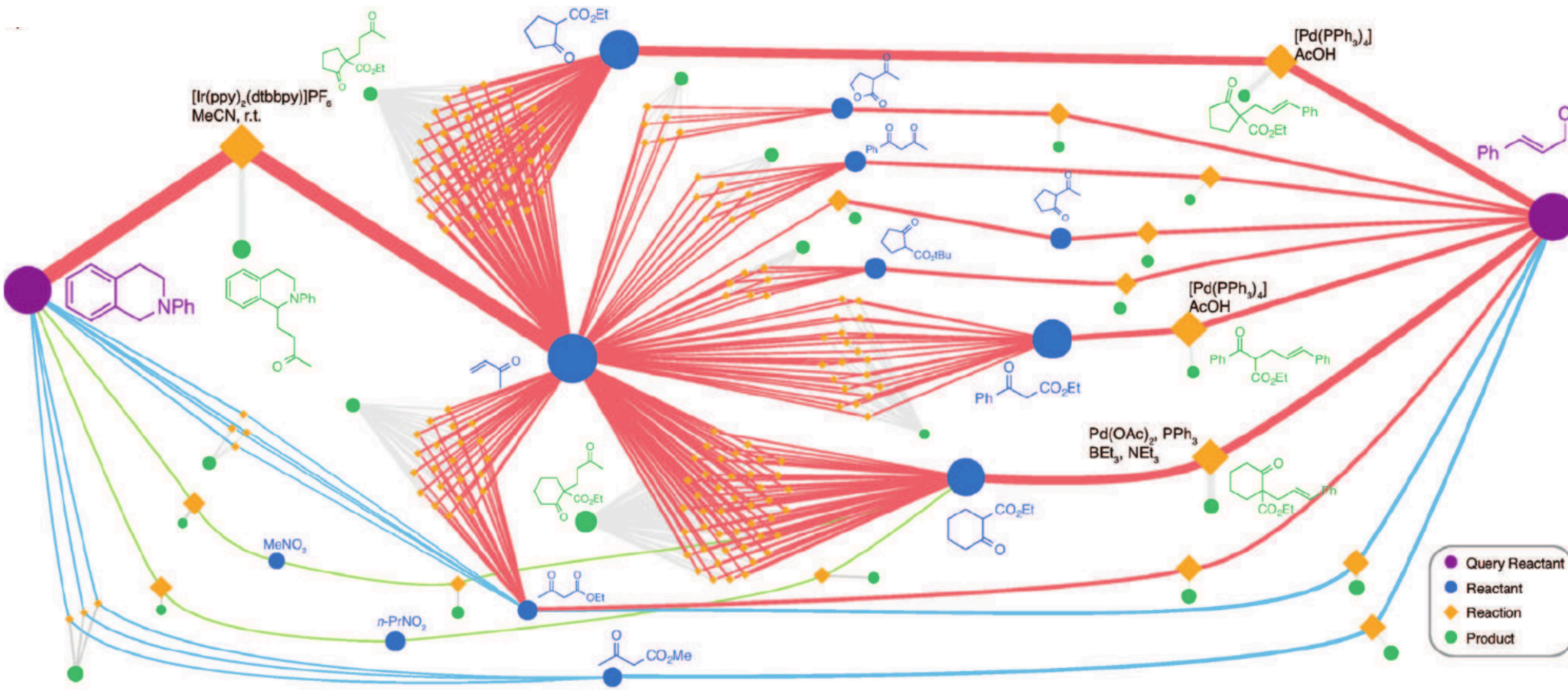
Can we use this to predict reactions?

- Constructed a knowledge graph from 14.4 million reactants and 8.2 million binary reactions
- Vertices represent reactants and reaction conditions with edges connecting reactants to reaction conditions and other reactants
- Predict reactions, products and reaction conditions
- Correctly predicted the right product with 67.5% accuracy on 180,000 reactions that were withheld from the data set
- Able to predict the products and reaction conditions of 'novel' reactions with decent efficiency



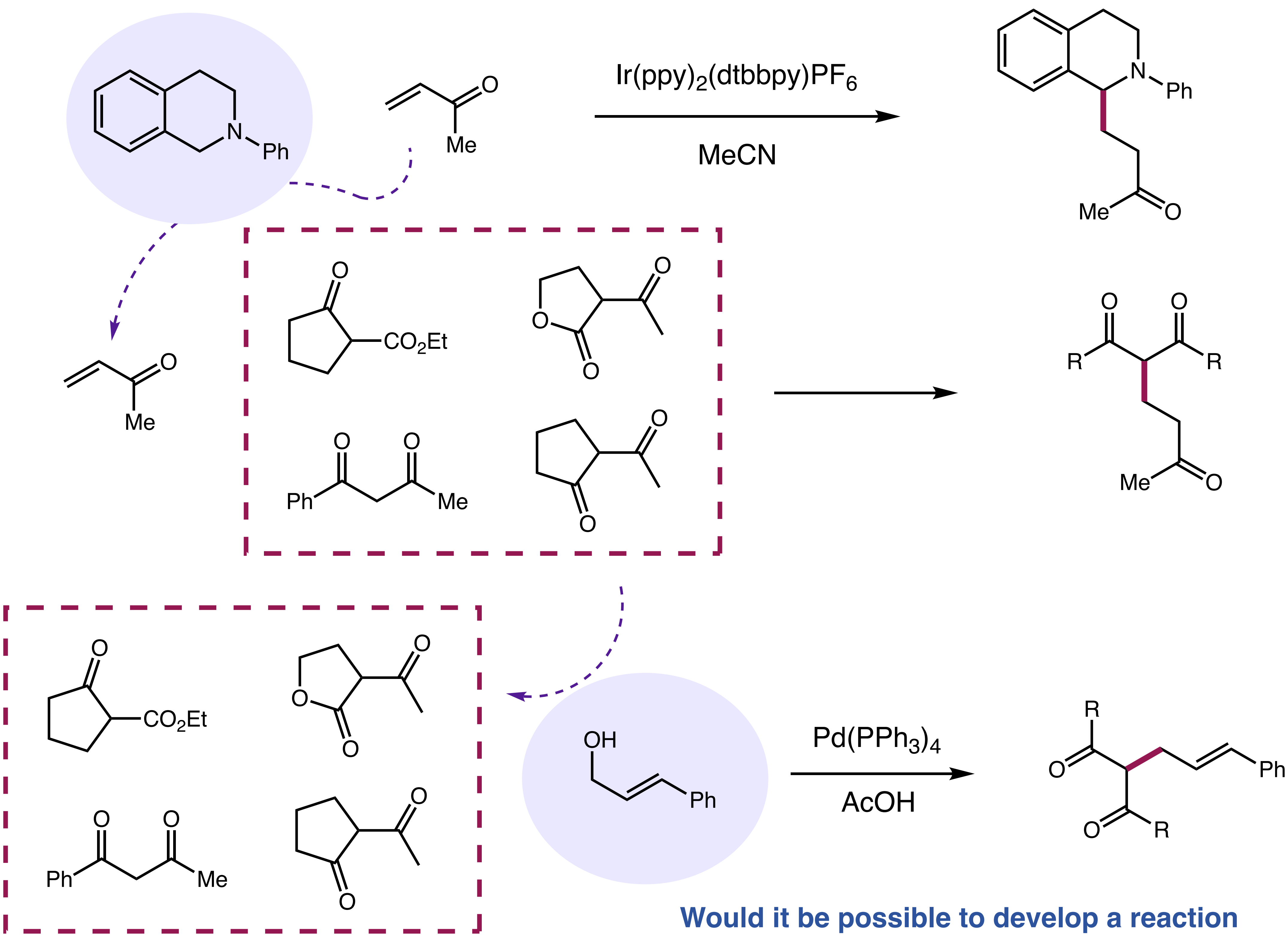
Segler, M. H. S.; Waller, M. P.; *Chem. Eur. J.* **2017**, *23*, 6118.

Can we use graph theory to predict reactions?



Segler, M. H. S.; Waller, M. P.; *Chem. Eur. J.* **2017**, *23*, 6118.

Can we use graph theory to predict reactions?

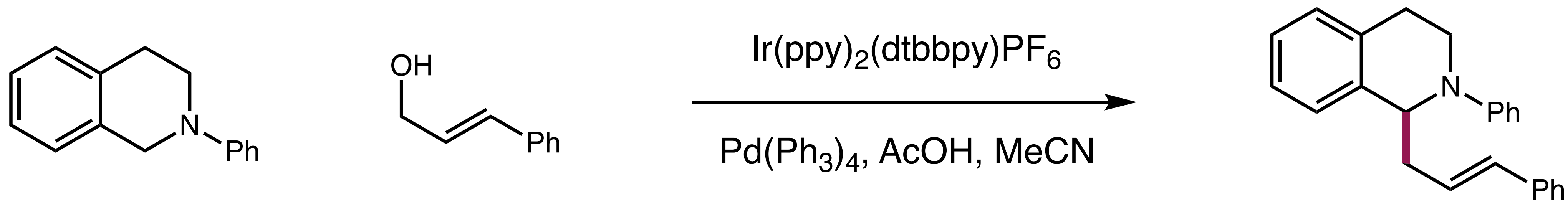


Would it be possible to develop a reaction between these 2 components?

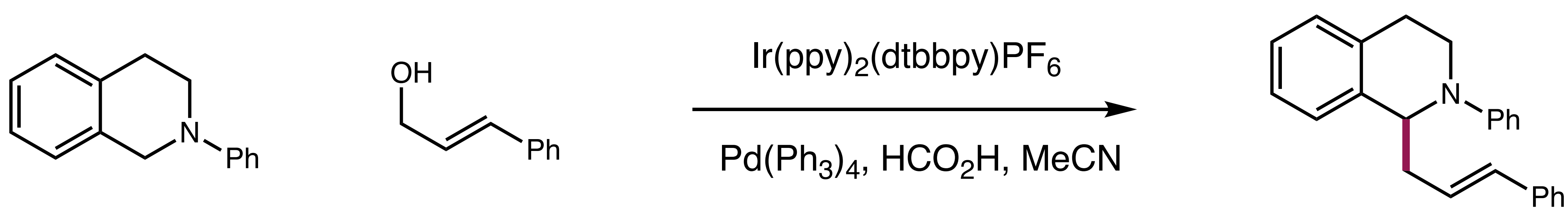
Segler, M. H. S.; Waller, M. P.; *Chem. Eur. J.* **2017**, *23*, 6118.

Can we use graph theory to predict reactions?

Predicted



Discovered



Xuan, J.; Zeng, T.-T.; Feng, Z.-J.; Deng, Q.-H.; Chen, J.-R.; Lu, L.-Q.; Xiao, J. X.; Alper, H. *Angew. Chem. Int. Ed.* **2015**, *54*, 1625

Segler, M. H. S.; Waller, M. P.; *Chem. Eur. J.* **2017**, *23*, 6118.

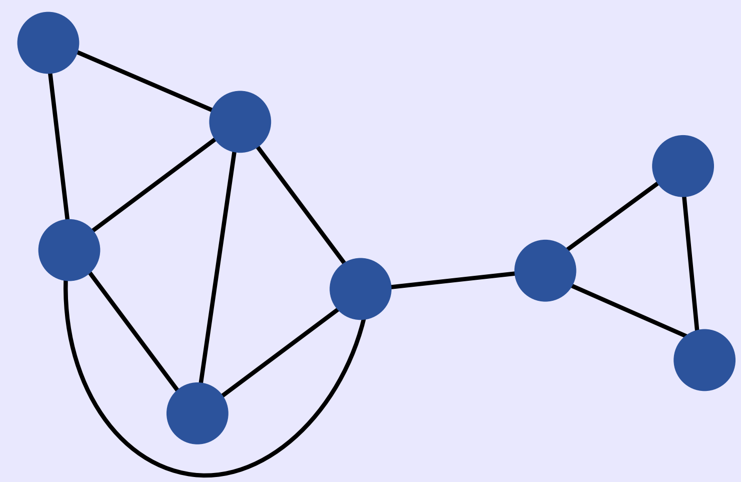
Applying graph theory to chemistry

Molecular Structures

- vertices represent atoms
- edges represent bonds
- weighted edges can represent double bonds or C–X bonds

Polymers

- vertices represent building blocks
- edges represent connections



Graph Theory

Kinetics

- vertices represent intermediates
- edges represent pathways
- frequently digraphs

And many more…

- aromaticity
- depicting orbitals and electrons
- NMR analysis
- crystals and clusters
- mapping reaction space

Questions

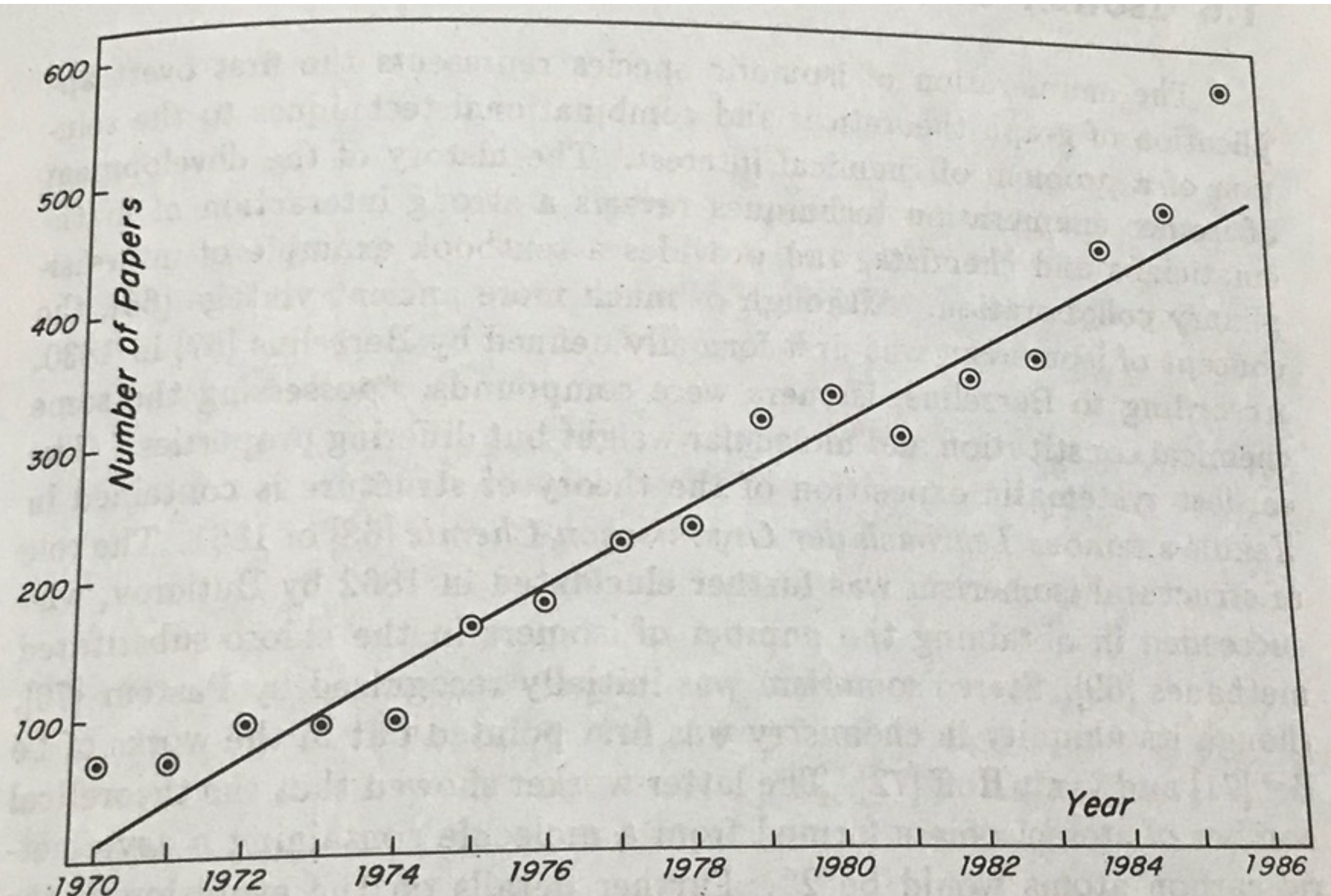


Figure 13. A plot showing the annual number of papers published in the area of chemical graph theory for the years 1970-1986. Note the annual growth rate of around 25% for this period.