OPCW

Organisation for the Prohibition of Chemical Weapons

Illuminating Chemical Reactivity

an event guaranteed to brighten up your day…

Science for Diplomats at EC-91
The Hague, 9 July 2019

Starring

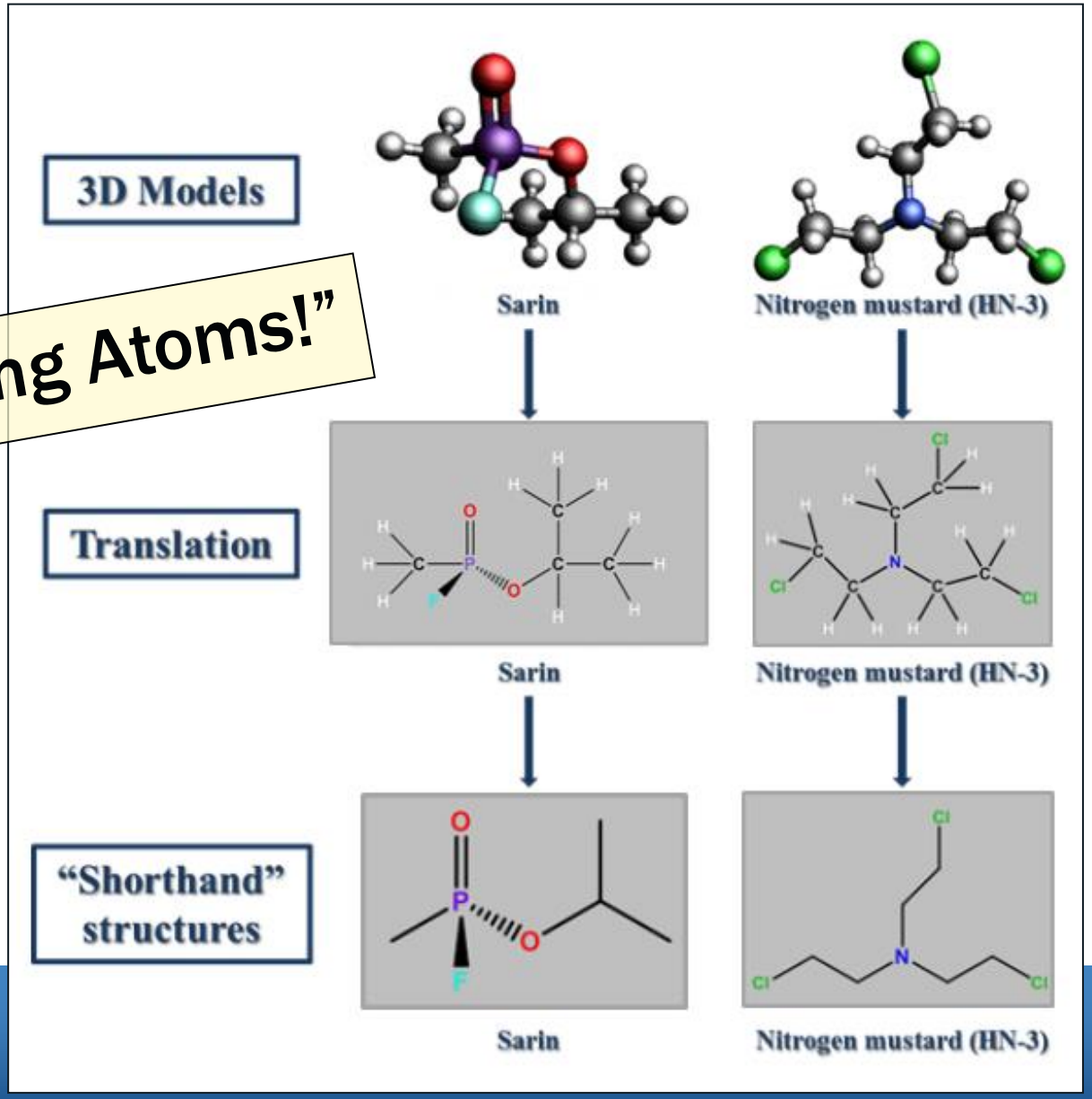
Dr Marc-Michael Blum, Head OPCW Laboratory

With supporting cast

Mr Cheng Tang (SAB Chair), Mr Lucas Benderitter (OSP), Mr Peter Brud (OSP), Dr Jonathan E. Forman (Science Policy Adviser and SAB Secretary), Ms Giovanna Pontes (OSP), Ms Ayah Wafi (OSP) and special guest Ms Andrea Dymytrova

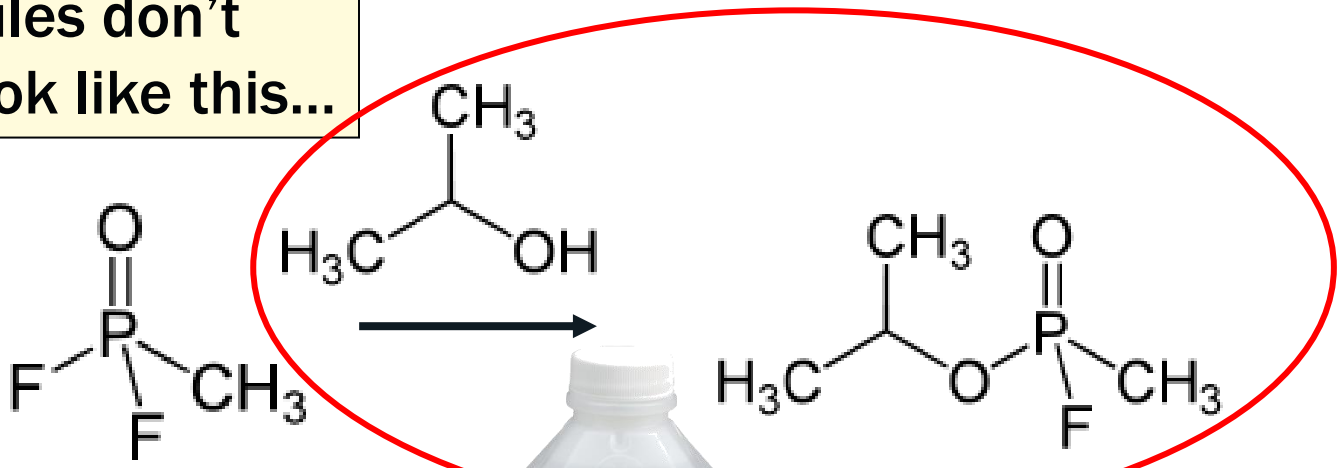
Chemistry Lessons

"Connecting Atoms!"



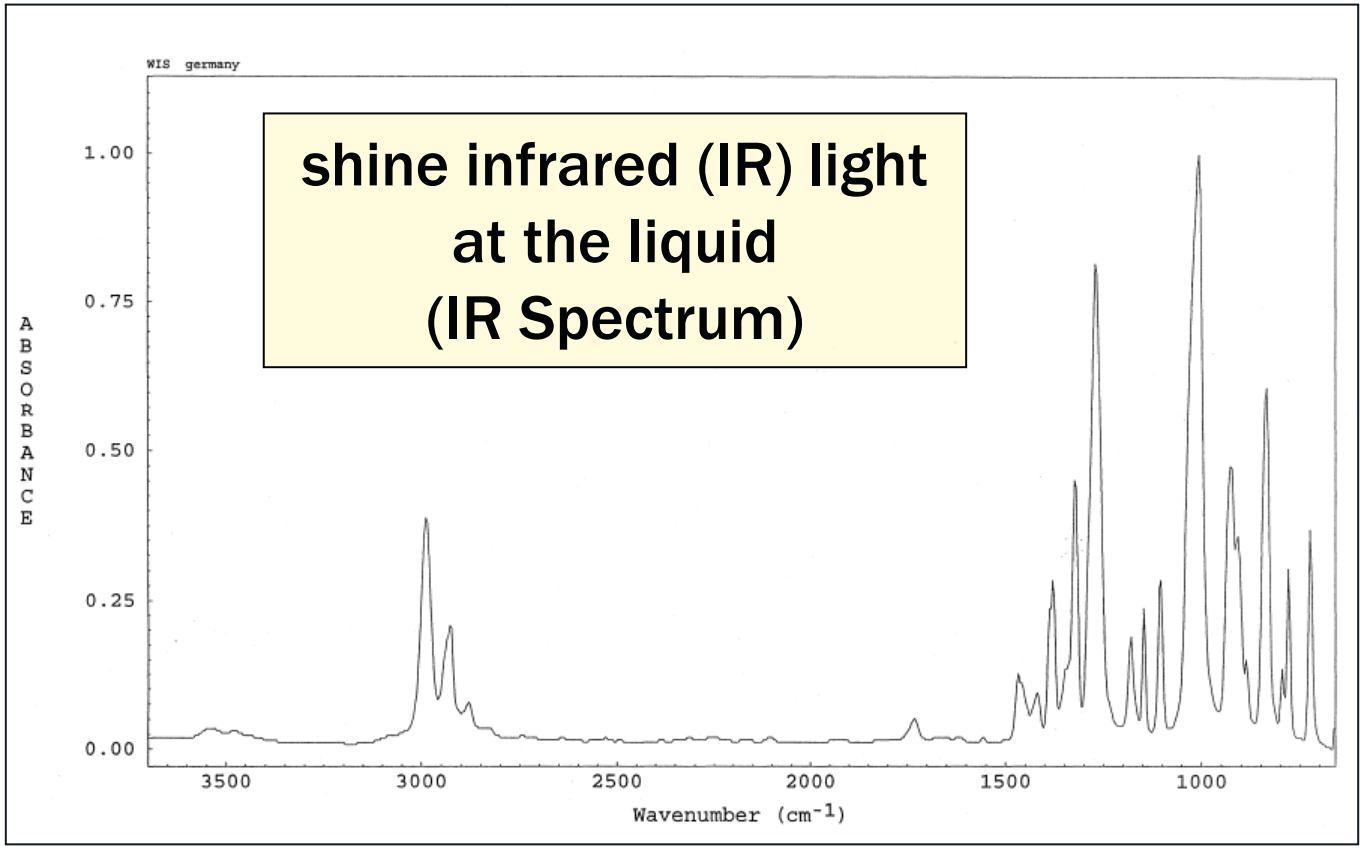
The Elephant in the Room…

molecules don't actually look like this…



colourless liquids…
How do you know which one is which?

The Elephant in the Room…



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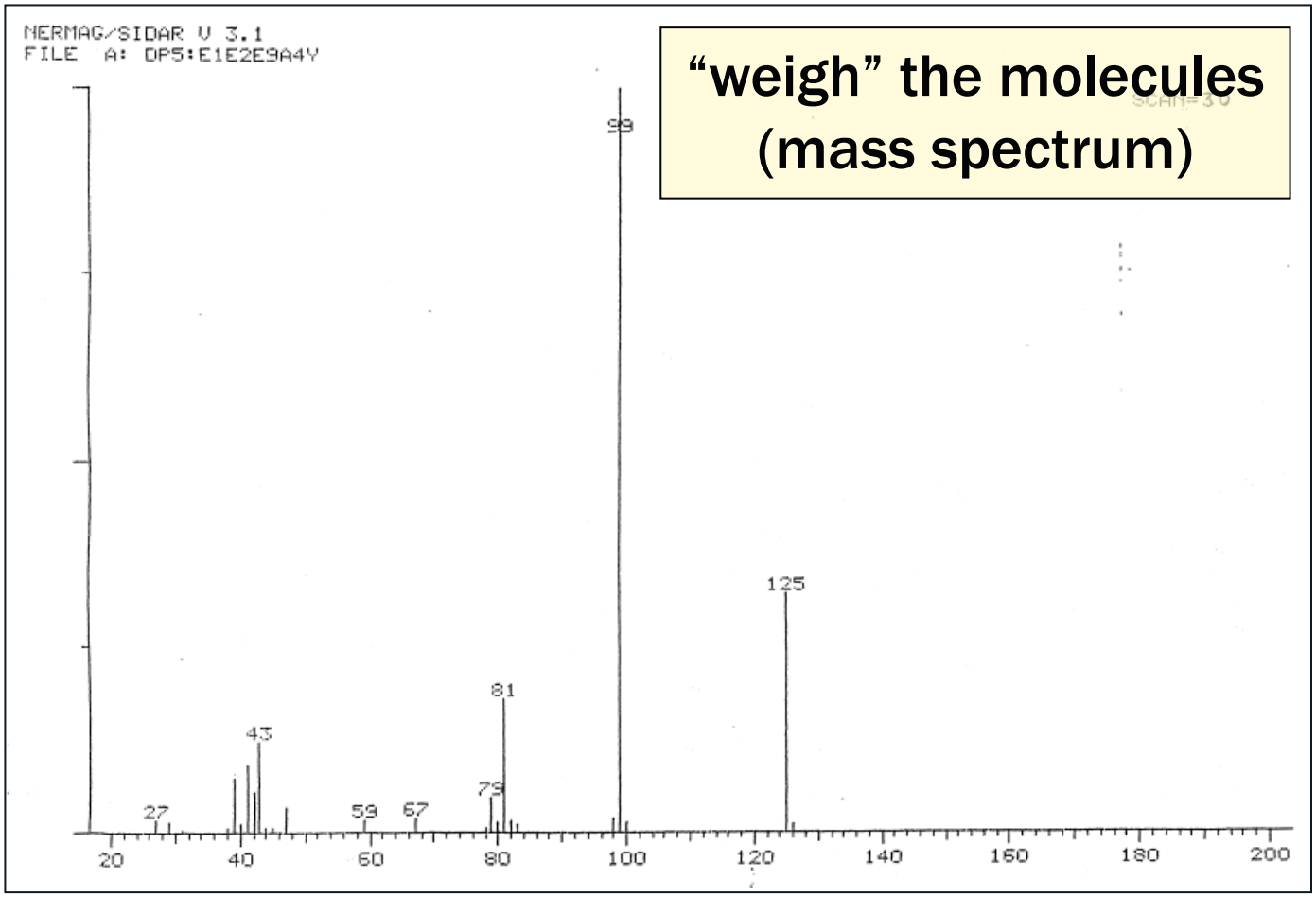

“weigh” the molecules (mass spectrum)

colourless liquids…
How do you know which one is which?

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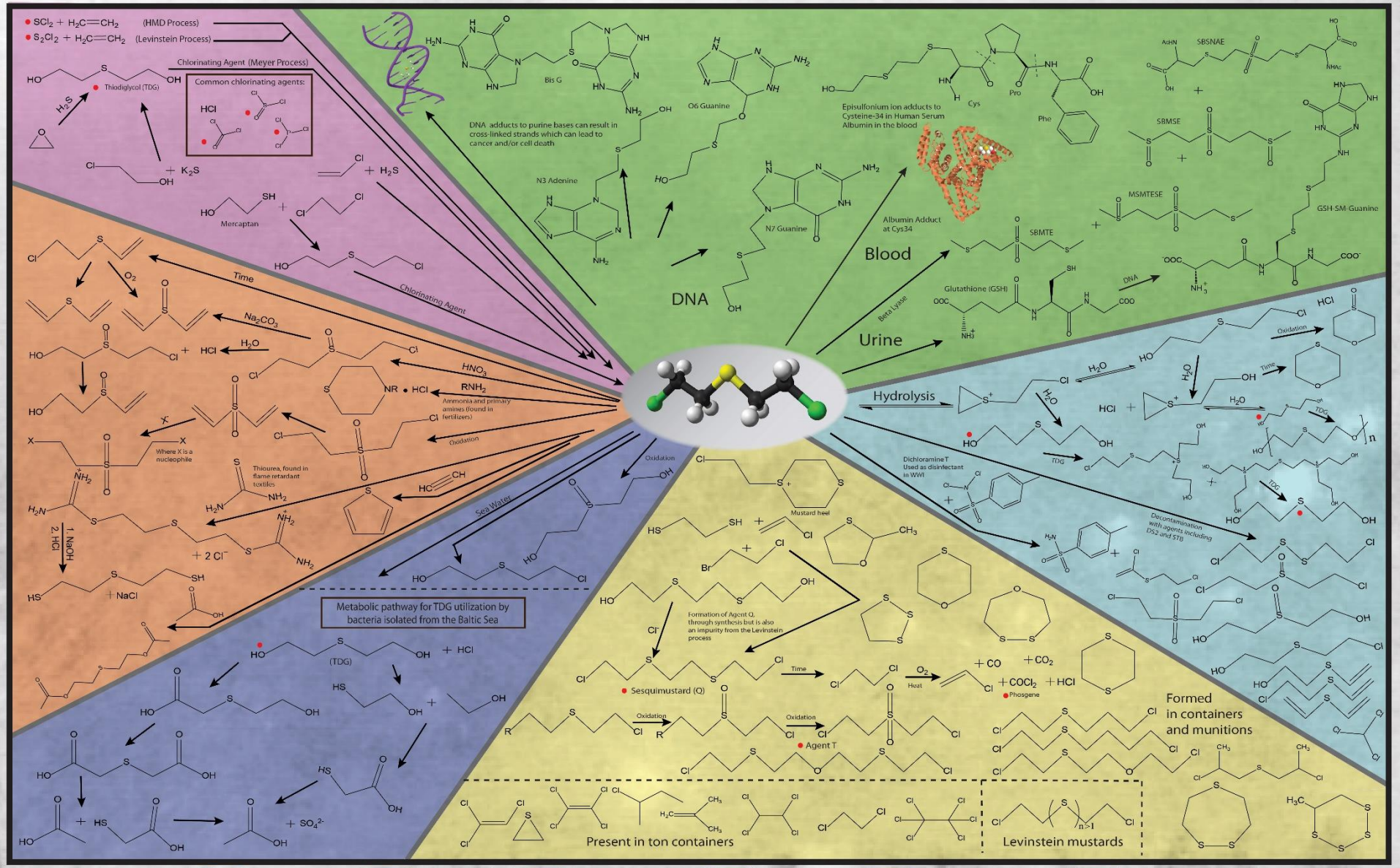
Degradation and Environmental Fate of Sulfur Mustard

Darcy van Eerten

@opcw @opcw_st /opcwonline /opcwonline /company/opcw /opcw




“mixture of chemicals”
(including “reaction products”)
“delivery device”

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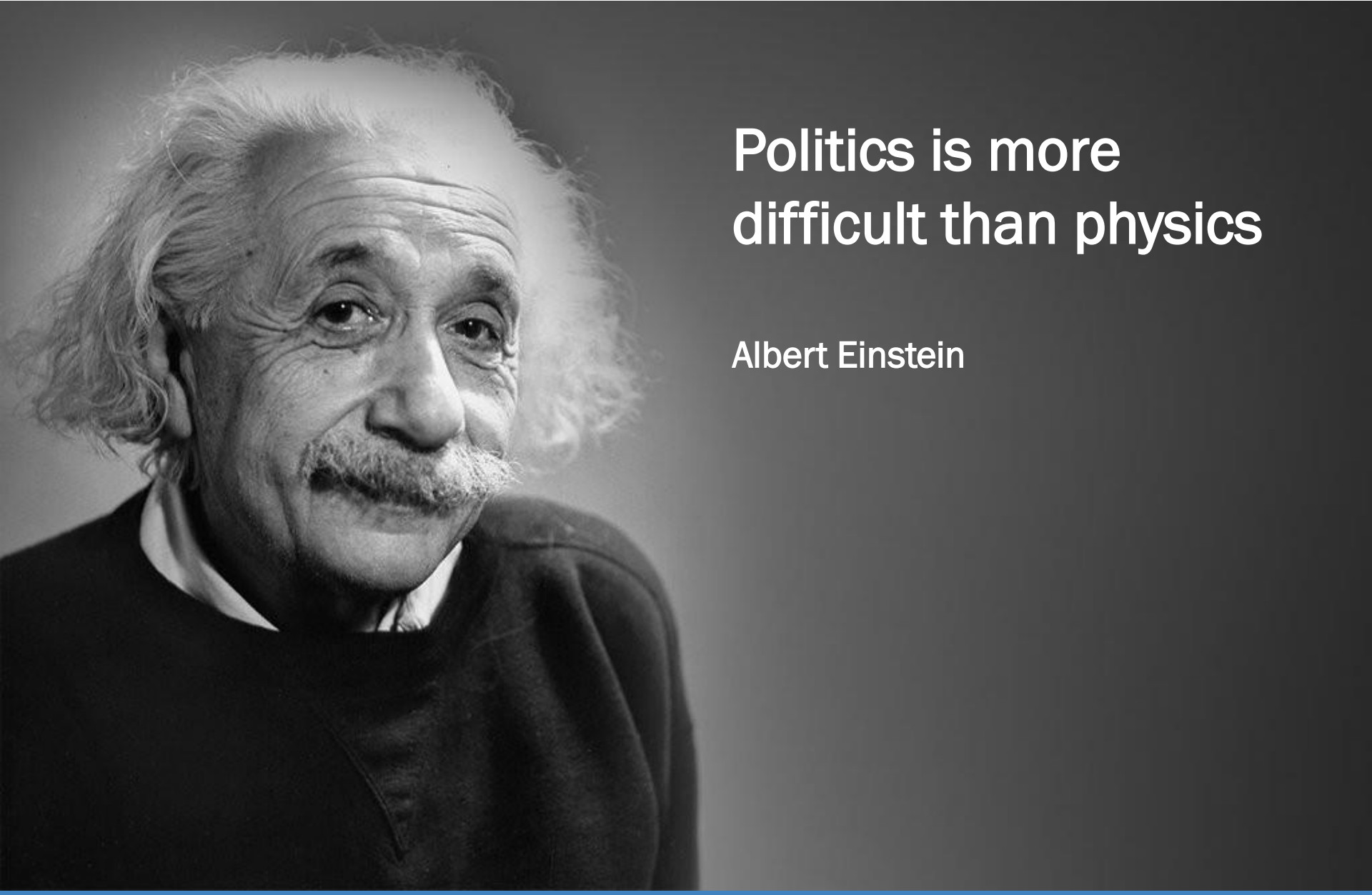
Organisation for the Prohibition of Chemical Weapons

Chemical reactivity

or why
chemistry is basically the same as politics

Marc-Michael Blum, Ph.D.
Head, OPCW Laboratory



Politics is more difficult than physics

Albert Einstein

OPCW

Chemistry is basically the same as politics

Marc-Michael Blum
Head, OPCW Laboratory

(somehow implying that Chemistry is more difficult than Physics)

Chemistry:

Chemistry is the study of matter, its properties, ***how and why substances combine or separate to form other substances***, and how substances interact with energy.

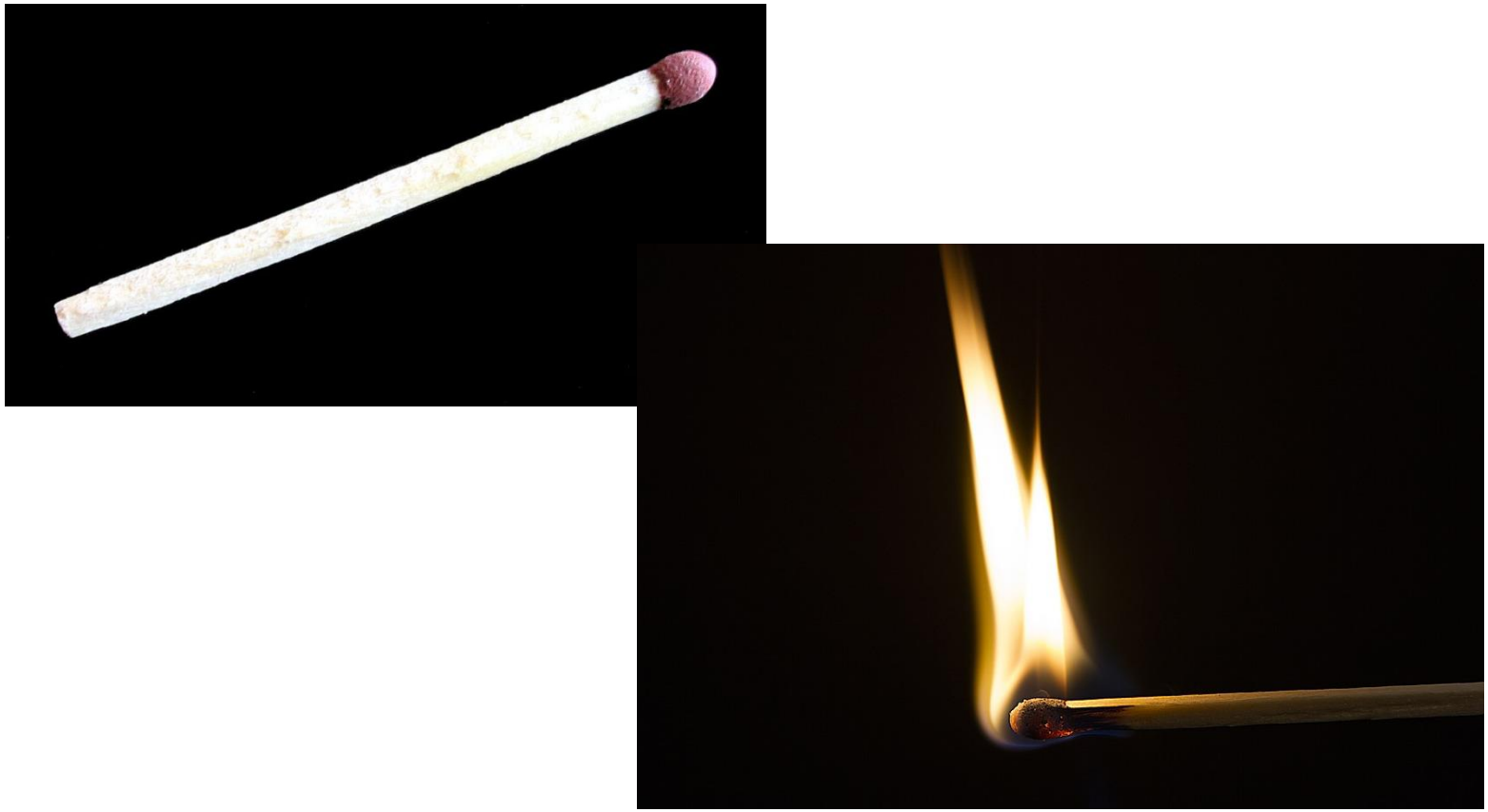
The Chemical Weapons Convention is quite focused on chemicals themselves:

- Declarations based on production, consumption and/or transfers of chemicals
- Annex on Chemicals of the CWC listing those chemicals for which special verification measures are in place
- Sampling & Analysis is conducted to confirm the presence or absence of a CWC relevant chemical
- …

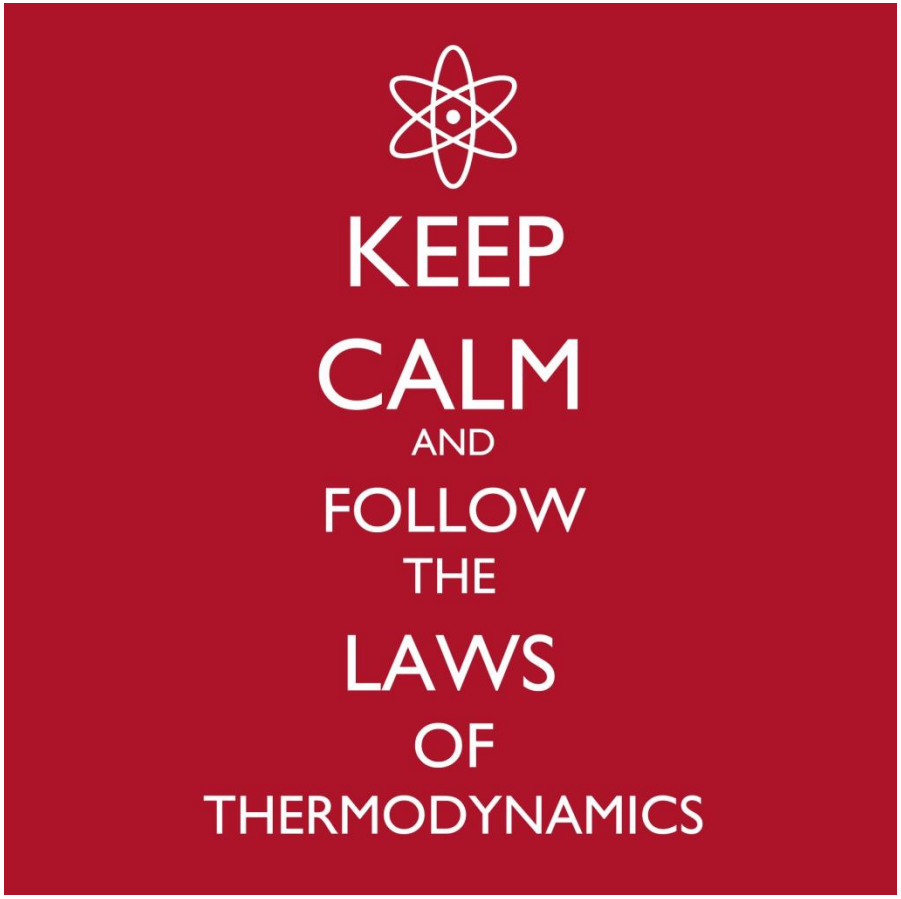
But we also deal with REACTIONS of chemicals:

- We discuss the meaning of “production by synthesis”
- We discuss the the productions of DOCs via biomediated processes
- Sampling & Analysis is looking for precursors and degradation products of chemical agents in IAUs
- Reaction products of agents with biomolecules (“adducts”) are valuable biomarkers and important in biomedical verification
- …

So why do chemicals react with each other?



What are the laws that determine in what direction a chemical reaction is proceeding?

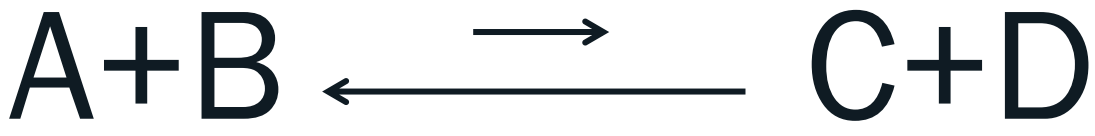


The first law of thermodynamics is a version of the law of conservation of energy, adapted for thermodynamic systems. The law of conservation of energy states that the total energy of an isolated system is constant; energy can be transformed from one form to another, but can be neither created nor destroyed.

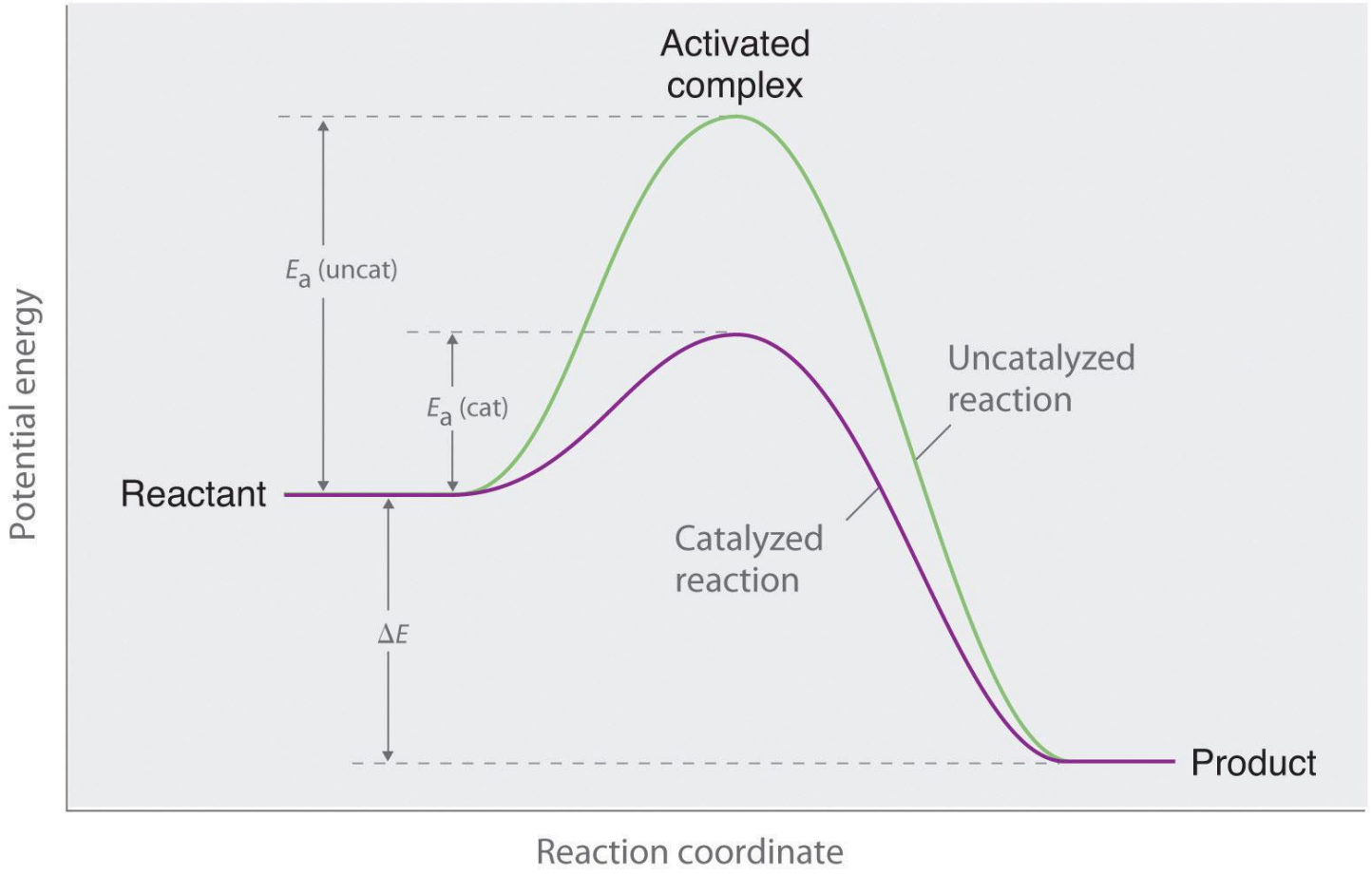
The second law of thermodynamics states that the total entropy of an isolated system can never decrease over time. The total entropy of a system and its surroundings can remain constant in ideal cases where the system is in thermodynamic equilibrium. In all processes that occur, including spontaneous processes, the total entropy of the system and its surroundings increases and the process is irreversible in the thermodynamic sense. The increase in entropy accounts for the irreversibility of natural processes, and the asymmetry between future and past.

Chemical equilibrium

Thermodynamics determine if A and B or C and D are the favoured products and where the equilibrium is located. It does NOT determine reaction rates.



Activation Energy and reaction rates



Fritz Haber (1868-1934)

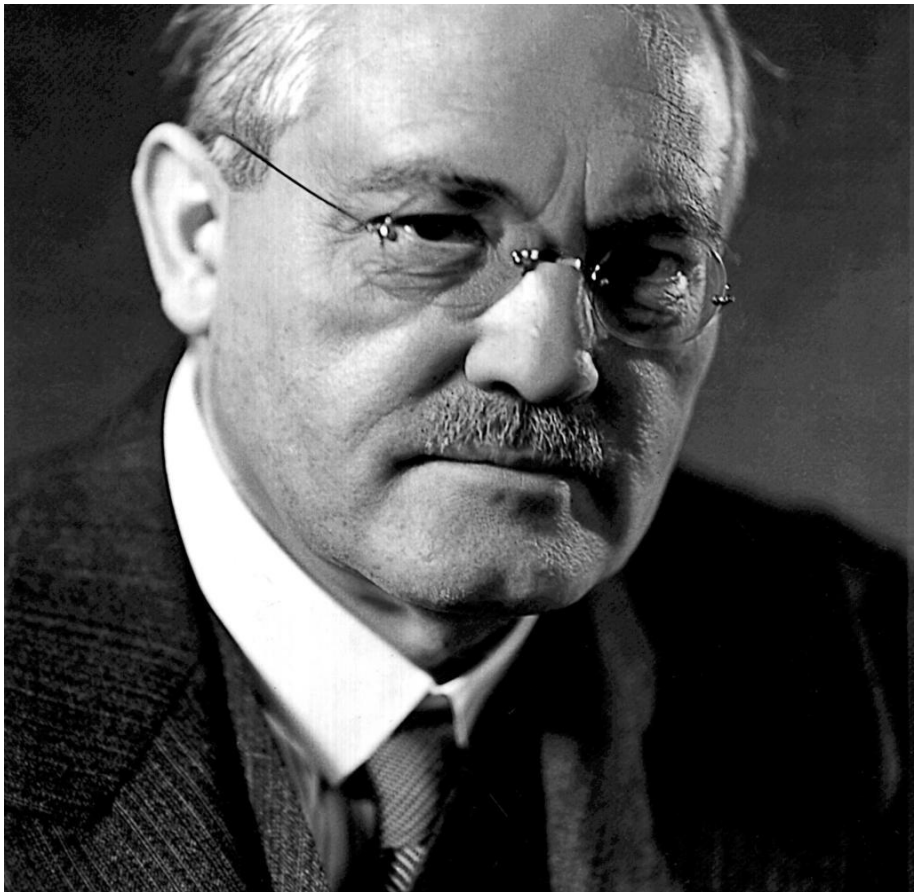
"Father" of chemical warfare in World War I

But also Nobel Laureate in Chemistry 1918

Carl Bosch (1874-1940)

Chemist and Industrialist

Nobel Laureate in Chemistry 1931



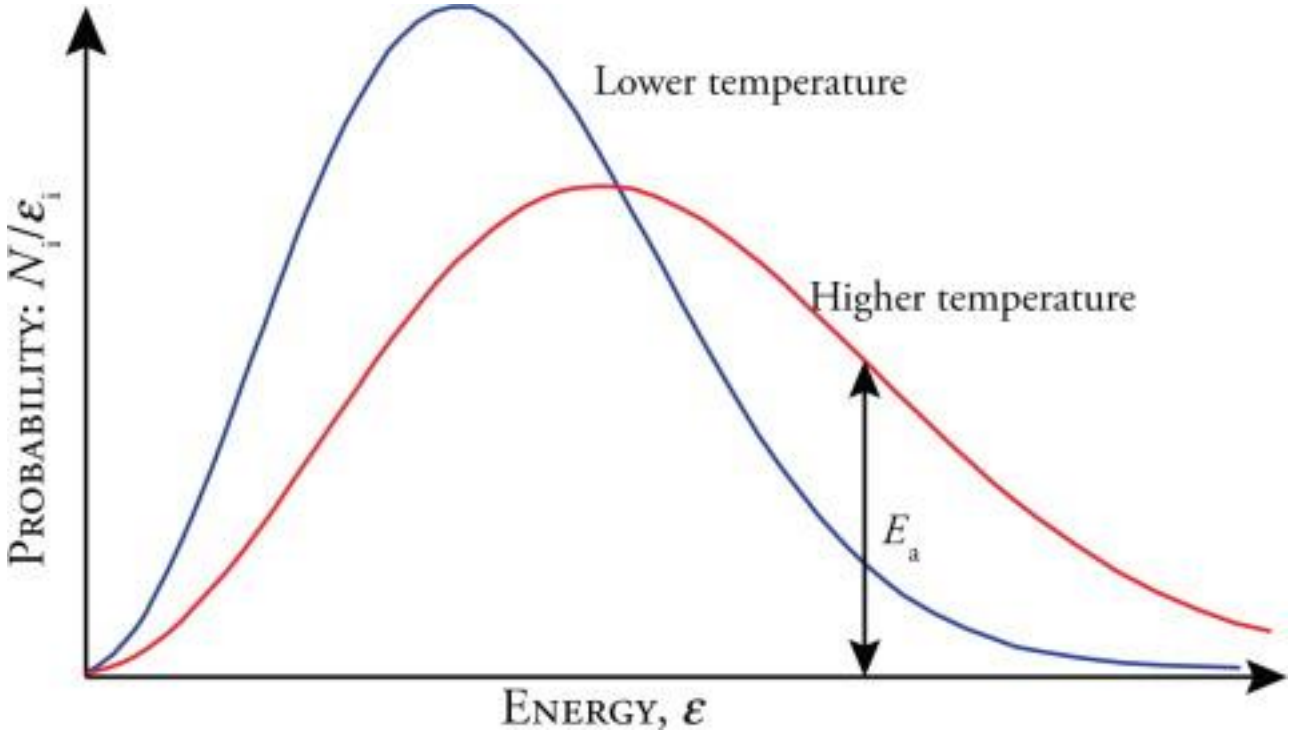
The Haber-Bosch process

Making ammonia with nitrogen from the air

$$N_2 + 3\,H_2 \rightleftharpoons 2\,NH_3$$

- Nitrogen is a very stable and unreactive molecule.
- Process has high activation barrier.
- Raising the temperature makes reaction faster but shifts equilibrium from ammonia towards starting products

Reaction rate and temperature



The Haber-Bosch process

The solution:

- Lowering activation energy a using metal catalyst
- Temperature for reasonable reaction rates now lower but still favouring the starting products
- Shifting the equilibrium towards ammonia by applying high pressure.

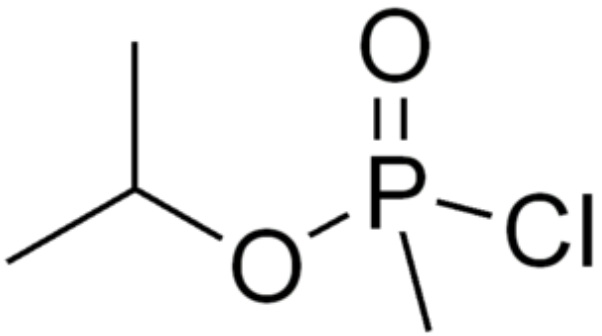
The Haber-Bosch process

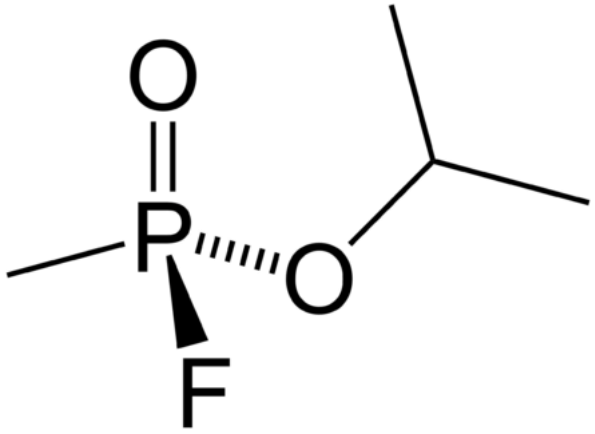
Major technological breakthrough (high pressure reactions in industry). Uses about 1-2% of world energy consumption.

- Enabled Imperial Germany to continue to fight World War I despite being blocked from accessing natural nitrate deposits Enabled the mass production of nitrogen fertilizers
- Enabling massive growth of agricultural production
- Without the Haber process the current world population would not be possible
- About half of all nitrogen atoms in the human body are derived from air nitrogen via the Haber process.

Chemical warfare and reactivity

- Nerve agents should have high reactivity with the biological target (Acetylcholinesterase) but low reactivity towards water (hydrolytic stability). Fluoridates better than chloridates.





But back to Chemistry and Politics....

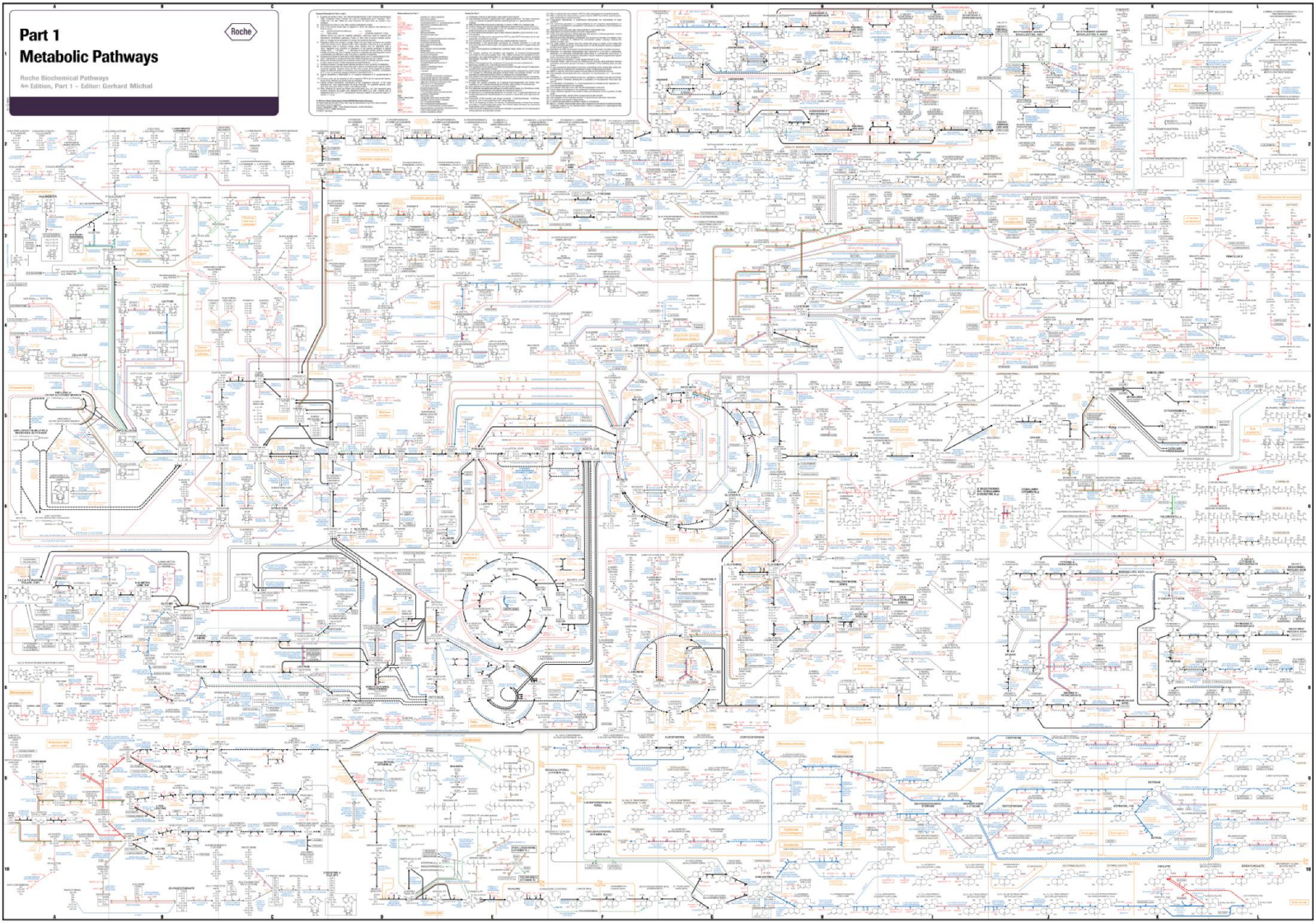
How can this be similar to politics? Clearly defined start and end states? Predictable reaction rates and equilibrium? No room for negotiations?

Chemistry can be a little bit more complicated.....

Part 1
Metabolic Pathways

Roche

Roche Biochemical Pathways
4th Edition, Part 1 – Editor: Gerhard Michal



Part 1
Metabolic Pathways

Roche

Roche Biochemical Pathways
4th Edition, Part 1 – Editor: Gerhard Michal

Nucleotide Metabolism
Purines

Nucleotide Metabolism
NAD, NADP

Antibiotics
Penicillin, Cephalosporin

Carbohydrate Metabolism
Acidic Carbohydrate Derivatives

Amino Acid Metabolism
Histidine

Carbo-
hydrate
Meta-
bolism
Inositol

Carbohydrate
Metabolism
Pentoses and
Pentose Cycle

Amino Acid Metabolism
Lysine

Bacterial
Meta-
bolism
Penicillin,
Cephalos-
porin

Amino Acid Metabolism
Serine, Threonine, Cysteine, Methionine

Carbohydrate Metabolism
Di- and Polysaccharides

Carbohydrate Metabolism
Amino Sugar Derivatives

Bacterial
Metabolism
Butanol/
Butyrate,
Fermentation

Carbohydrate
Metabolism
Nucleotide Sugars

Bacterial
Metabolism
Methane Oxidation

Carbohydrate
Metabolism
Pyruvate Turnover

Citrate and
Glyoxalate Cycle

Tetrapyrrole Metabolism
Porphyrins, Cobalamin

Tetrapyrrole Metabolism
Heme, Cytochromes, Chlorophyll

Carbohydrate Metabolism
Glycolysis and Gluconeogenesis

C1-Metabolism

Lipid Metabolism
Glyco- and Phospholipids

Lipid Metabolism
Fatty Acids

Amino Acid
Metabolism
Urea Cycle

Amino Acid Metabolism
Glutamate, Proline, Hydroxyproline

Nucleotide Metabolism
Pyrimidines

Bacterial
Metabolism
Methanogenesis

Lipid Metabolism
Sphingolipids

Bacterial Metabolism
Alkane Oxidation

Amino Acid Metabolism
Leucine, Isoleucine, Valine

Lipid Metabolism
Carotenoids and Isoprenoids

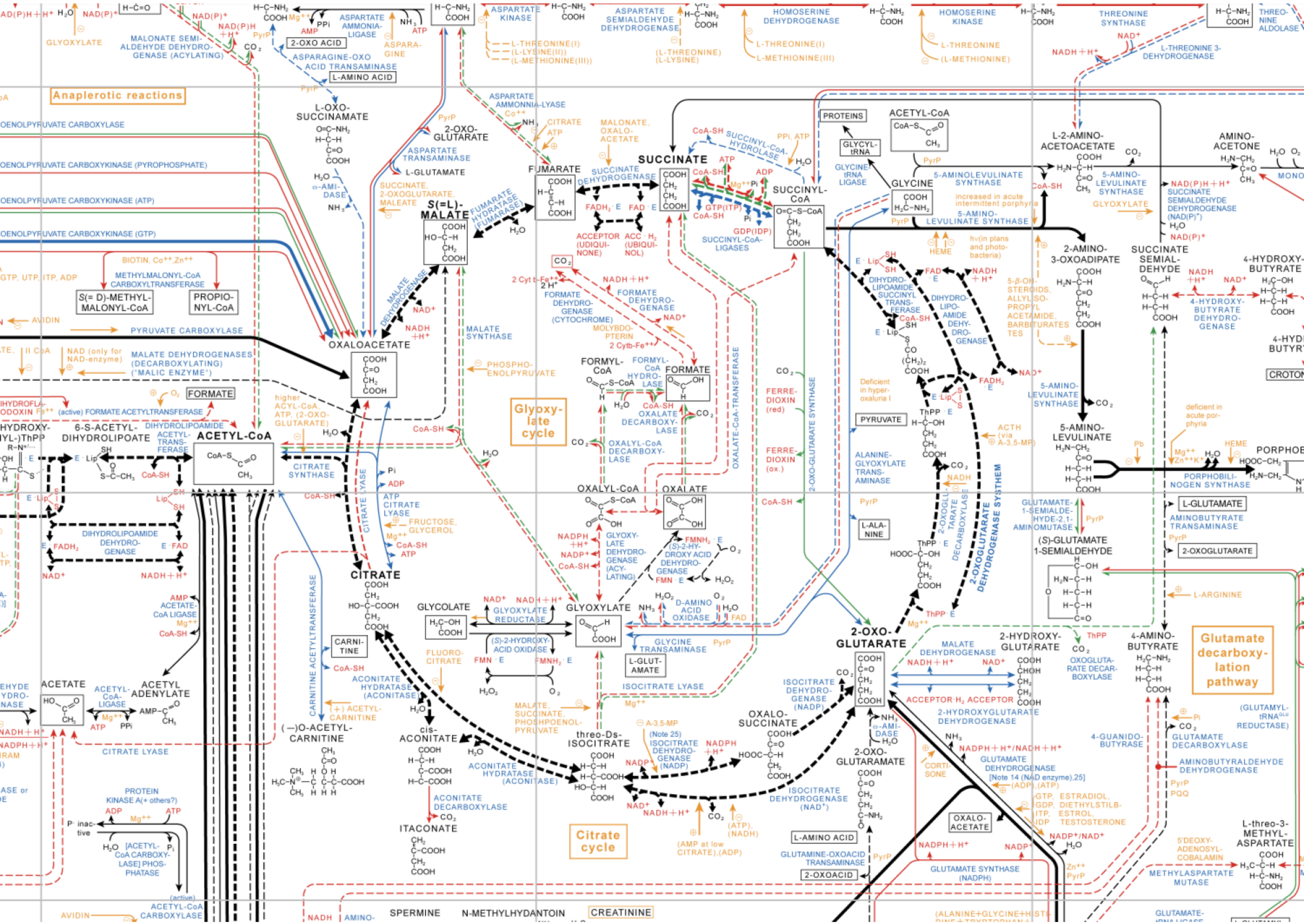
Steroid Metabolism
Mineralocorticoids and Glucocorticoids

Steroid
Metabolism
Phytosteroles

Steroid Metabolism
Androgens and Estrogens

Steroid Metabolism
Cholesterol Synthesis

Cofactors and Vitamines
Coenzyme A



GLYOXYLATE
MALONATE SEMI-ALDEHYDE DEHYDROGENASE (ACYLATING)
ASPARTATE AMMONIA-LIGASE
2-OXO ACID
ASPARAGINE-OXO ACID TRANSAMINASE
L-AMINO ACID
ASPARAGINE
ASPARTATE KINASE
L-THREONINE(I)
(L-LYSINE(III))
(L-METHIONINE(III))
ASPARTATE SEMIALDEHYDE DEHYDROGENASE
(L-THREONINE)
(L-LYSINE)
HOMOSERINE DEHYDROGENASE
L-THREONINE(I)
L-METHIONINE(III)
HOMOSERINE KINASE
L-THREONINE
(L-METHIONINE)
THREONINE SYNTHASE
THREONINE ALDOLASE
L-THREONINE 3-DEHYDROGENASE
Anaplerotic reactions
PHOSPHOENOLPYRUVATE CARBOXYLASE
PHOSPHOENOLPYRUVATE CARBOXYKINASE (PYROPHOSPHATE)
PHOSPHOENOLPYRUVATE CARBOXYKINASE (ATP)
PHOSPHOENOLPYRUVATE CARBOXYKINASE (GTP)
L-OXO-SUCCINAMATE
ω-AMIDASE
2-OXO-GLUTARATE
ASPARTATE TRANSAMINASE
L-GLUTAMATE
SUCCINATE, 2-OXOGLUTARATE, MALEATE
ASPARTATE AMMONIA-LYASE
CITRATE
MALONATE, OXALOACETATE
FUMARATE
S(=L)-MALATE
FUMARATE HYDRATASE (FUMARASE)
SUCCINATE DEHYDROGENASE
ACCEPTOR (UDIQUINONE)
ACC·H₂ (UBIQUINOL)
SUCCINATE
SUCCINYL-CoA HYDROLASE
SUCCINYL-CoA
SUCCINYL-CoA LIGASES
PROTEINS
GLYCYL-tRNA
GLYCINE-tRNA LIGASE
ACETYL-CoA
GLYCINE
5-AMINOLEVULINATE SYNTHASE
increased in acute intermittent porphyria
5-AMINO-LEVULINATE SYNTHASE
L-2-AMINO-ACETOACETATE
AMINO-ACETONE
5-AMINO-LEVULINATE SYNTHASE
GLYOXYLATE
SUCCINATE SEMIALDEHYDE DEHYDROGENASE
BIOTIN, Co⁺⁺,Zn⁺⁺
METHYLMALONYL-CoA CARBOXYLTRANSFERASE
S(= D)-METHYLMALONYL-CoA
PROPIONYL-CoA
AVIDIN
PYRUVATE CARBOXYLASE
MALATE DEHYDROGENASE
MALATE SYNTHASE
OXALOACETATE
MALATE DEHYDROGENASES (DECARBOXYLATING) ("MALIC ENZYME")
NAD (only for NAD-enzyme)
FORMATE
(active) FORMATE ACETYLTRANSFERASE
higher ACYL-CoA, ATP, (2-OXOGLUTARATE)
PHOSPHOENOLPYRUVATE
Glyoxylate cycle
FORMATE DEHYDROGENASE (CYTOCHROME)
MOLYBDOPTERIN
FORMATE DEHYDROGENASE
FORMYL-CoA
FORMYL-CoA HYDROLASE
FORMATE
OXALATE DECARBOXYLASE
OXALYL-CoA DECARBOXYLASE
OXALATE-CoA-TRANSFERASE
2-OXO-GLUTARATE SYNTHASE
FERREDOXIN (red)
FERREDOXIN (ox.)
PYRUVATE
ALANINE-GLYOXYLATE TRANSAMINASE
L-ALANINE
DIHYDROLIPOAMIDE SUCCINYLTRANSFERASE
DIHYDROLIPOAMIDE DEHYDROGENASE
5-β-OH-STEROIDS, ALLYLISOPROPYL ACETAMIDE, BARBITURATES
Deficient in hyperoxaluria I
2-OXOGLUTARATE DECARBOXYLASE
2-OXOGLUTARATE DEHYDROGENASE SYSTEM
2-AMINO-3-OXOADIPATE
5-AMINO-LEVULINATE SYNTHASE
5-AMINO-LEVULINATE
deficient in acute porphyria
PORPHOBILINOGEN SYNTHASE
PORPHOBILINOGEN
4-HYDROXYBUTYRATE
4-HYDROXYBUTYRATE DEHYDROGENASE
CROTON
HYDROXYETHYL-ThPP
6-S-ACETYL-DIHYDROLIPOATE
DIHYDROLIPOAMIDE ACETYLTRANSFERASE
ACETYL-CoA
CITRATE SYNTHASE
ATP CITRATE LYASE
FRUCTOSE, GLYCEROL
DIHYDROLIPOAMIDE DEHYDROGENASE
OXALYL-CoA
OXALATE
GLYOXYLATE DEHYDROGENASE (ACYLATING)
(S)-2-HYDROXY ACID DEHYDROGENASE
D-AMINO ACID OXIDASE
GLUTAMATE-1-SEMIALDEHYDE-2,1-AMINOMUTASE
(S)-GLUTAMATE 1-SEMIALDEHYDE
L-GLUTAMATE
AMINOBUTYRATE TRANSAMINASE
2-OXOGLUTARATE
L-ARGININE
AMP ACETATE-CoA LIGASE
CITRATE
CARNITINE ACETYLTRANSFERASE
CARNITINE
GLYCOLATE
GLYOXYLATE REDUCTASE
(S)-2-HYDROXY-ACID OXIDASE
GLYOXYLATE
GLYCINE TRANSAMINASE
L-GLUTAMATE
ISOCITRATE LYASE
2-OXO-GLUTARATE
MALATE DEHYDROGENASE
2-HYDROXY-GLUTARATE
OXOGLUTARATE DECARBOXYLASE
4-AMINO-BUTYRATE
Glutamate decarboxylation pathway
ACETATE
ACETYL-CoA LIGASE
ACETYL ADENYLATE
FLUOROCITRATE
ACONITATE HYDRATASE (ACONITASE)
(+) ACETYL-CARNITINE
(−)-O-ACETYL-CARNITINE
cis-ACONITATE
MALATE, SUCCINATE, PHOSPHOENOLPYRUVATE
threo-Ds-ISOCITRATE
ISOCITRATE DEHYDROGENASE (NADP)
OXALO-SUCCINATE
ISOCITRATE DEHYDROGENASE (NADP)
ACCEPTOR·H₂ ACCEPTOR
2-HYDROXYGLUTARATE DEHYDROGENASE
4-GUANIDOBUTYRASE
GLUTAMATE DECARBOXYLASE
(GLUTAMYL-tRNA REDUCTASE)
AMINOBUTYRALDEHYDE DEHYDROGENASE
CITRATE LYASE
PROTEIN KINASE A(+ others?)
[ACETYL-CoA CARBOXYLASE] PHOSPHATASE
ACONITATE HYDRATASE (ACONITASE)
ACONITATE DECARBOXYLASE
ITACONATE
Citrate cycle
(AMP at low CITRATE),(ADP)
ISOCITRATE DEHYDROGENASE (NAD⁺)
2-OXO-GLUTARAMATE
ω-AMIDASE
CORTISONE
GLUTAMATE DEHYDROGENASE [Note 14 (NAD enzyme),25]
GTP, ESTRADIOL, GDP, DIETHYLSTILBESTROL, ITP, ESTROL, IDP, TESTOSTERONE
OXALO-ACETATE
L-AMINO ACID
GLUTAMINE-OXOACID TRANSAMINASE
2-OXOACID
GLUTAMATE SYNTHASE (NADPH)
5'DEOXY-ADENOSYL-COBALAMIN
METHYLASPARTATE MUTASE
L-threo-3-METHYL-ASPARTATE
AVIDIN
ACETYL-CoA CARBOXYLASE
SPERMINE
N-METHYLHYDANTOIN
CREATININE
(ALANINE+GLYCINE+HISTIDINE+TRYPTOPHAN+

OPCW

منظمة حظر الأسلحة الكيميائية

禁止化学武器组织

Organisation for the Prohibition of Chemical Weapons

Organisation pour l'Interdiction des Armes Chimiques

Организация по запрещению химического оружия

Organización para la Prohibición de las Armas Químicas