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Author: Robert Lyons, Ph.D., 2008

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M1 Renal:

Folate Metabolism

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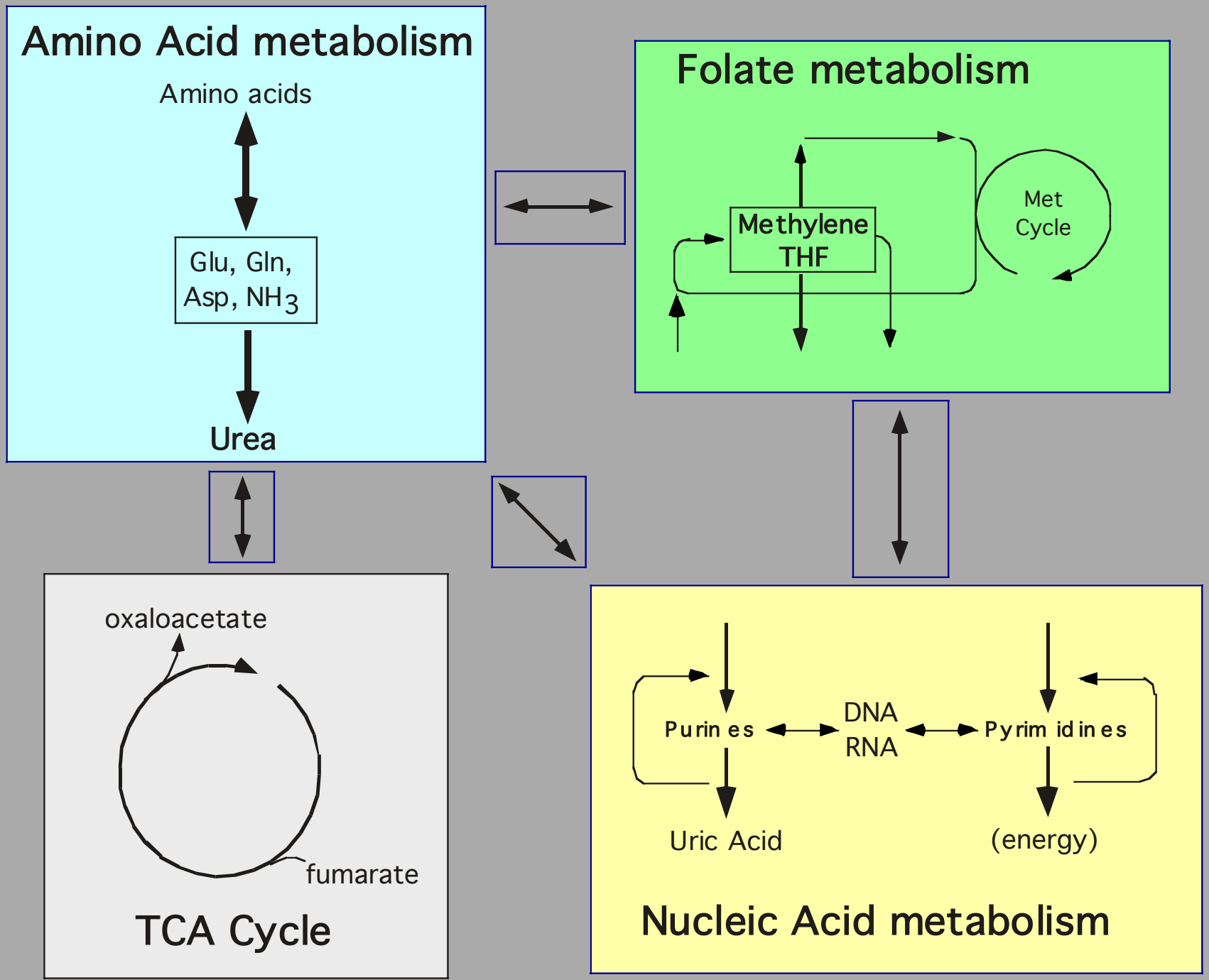
Director, DNA Sequencing Core

Web: http://seqcore.brcf.med.umich.edu/mcb500

Fall 2008

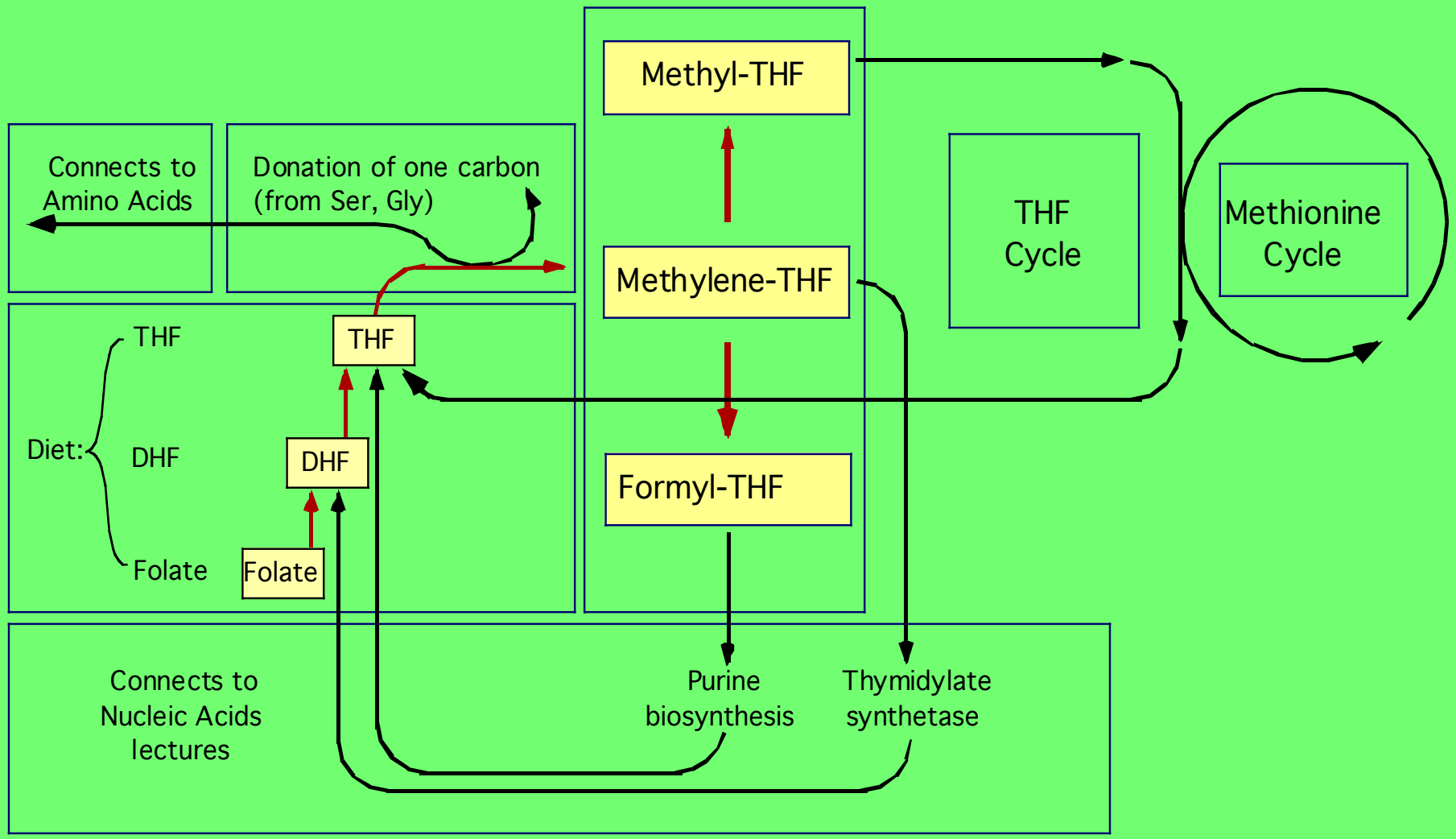
University of Michigan
Medical School


Amino Acid metabolism
Amino acids
Glu, Gln,
Asp, NH3
Urea
Folate metabolism
Methylene
THF
Met
Cycle
oxaloacetate
fumarate
TCA Cycle
Purines
DNA
RNA
Pyrimidines
Uric Acid
(energy)
Nucleic Acid metabolism

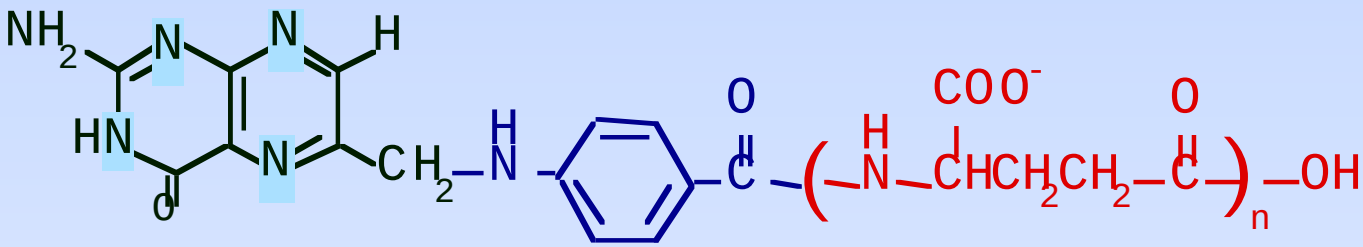
Folate ("One-Carbon") Pathways

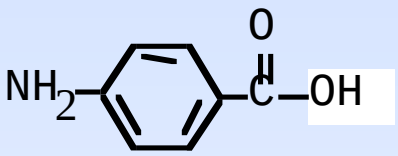
Click on any blue box to see details

(Start with the section with 'Diet' and follow the paths with red arrows)

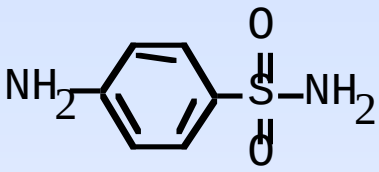


Folic Acid is Synthesized By Bacteria





Para-aminobenzoic acid (PABA)

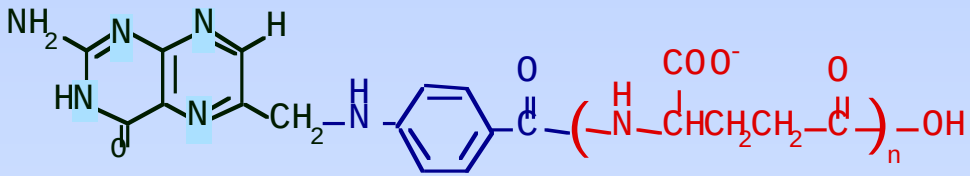


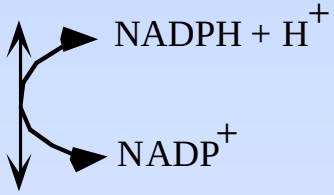
sulfanilamide

PD-INEL R. Lyons

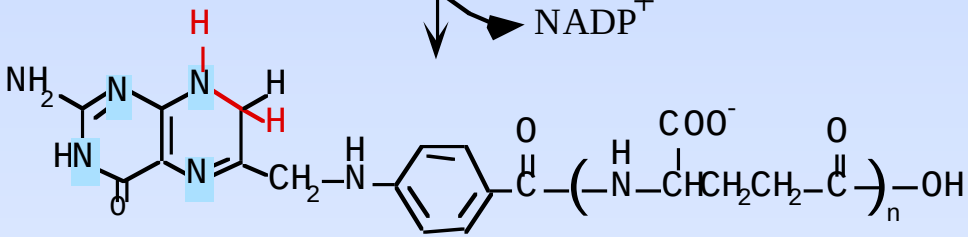
Dietary folate: folic acid (meats, green veggies)
requires the intestinal enzyme ‘Conjugase’ for absorption.

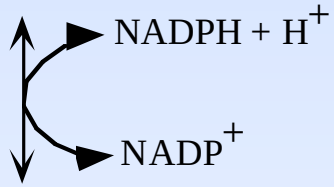
Folic acid



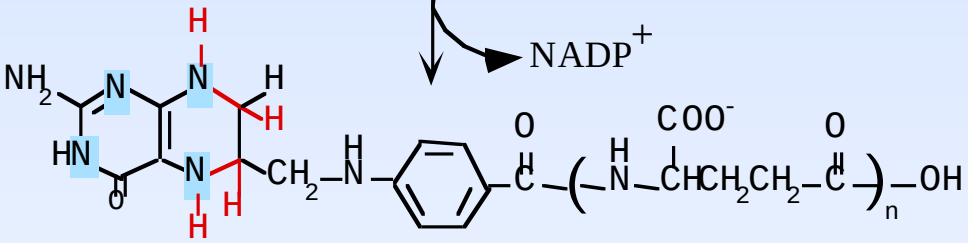


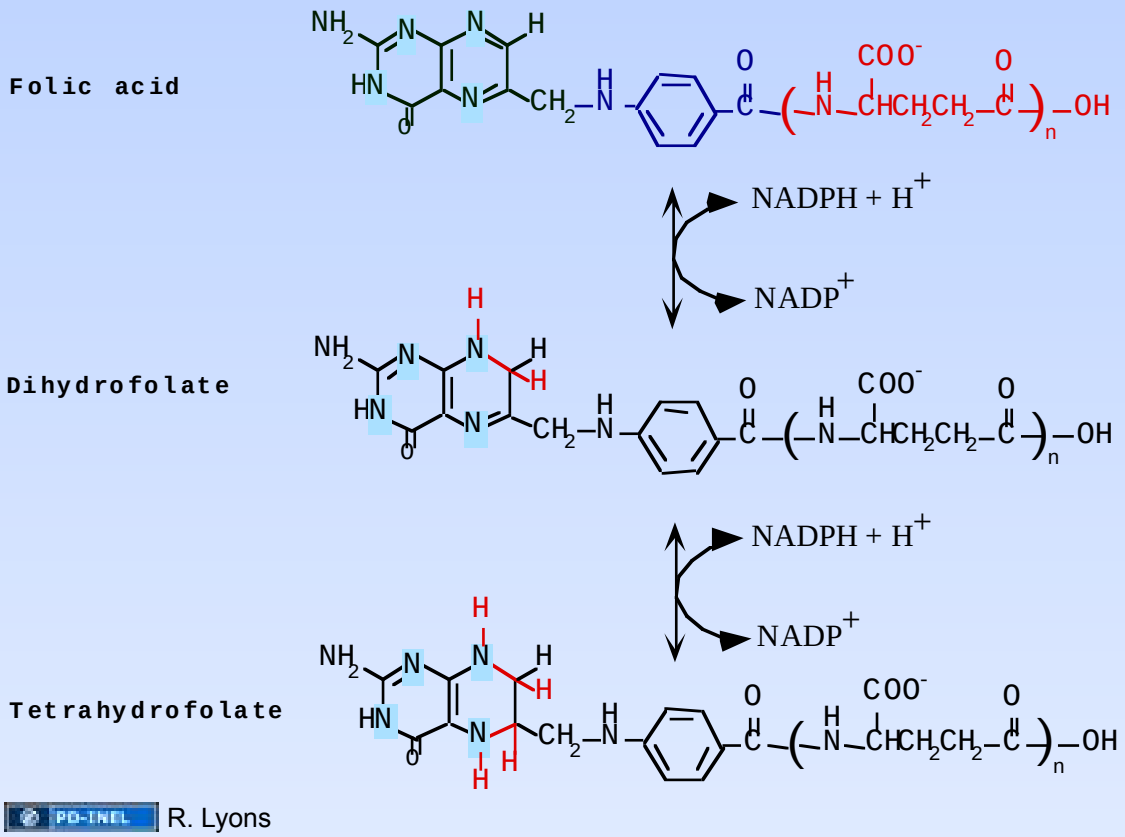
Dihydrofolate





Tetrahydrofolate



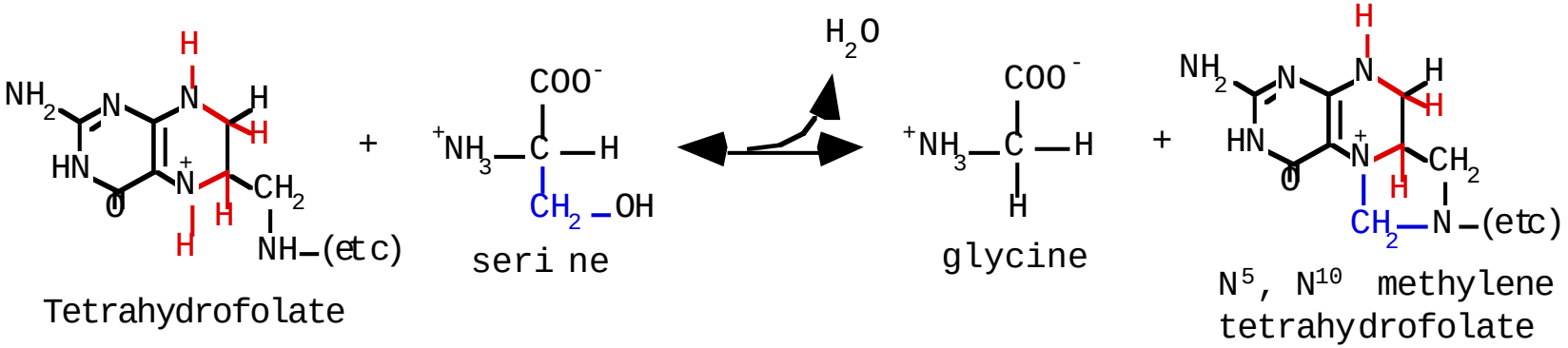


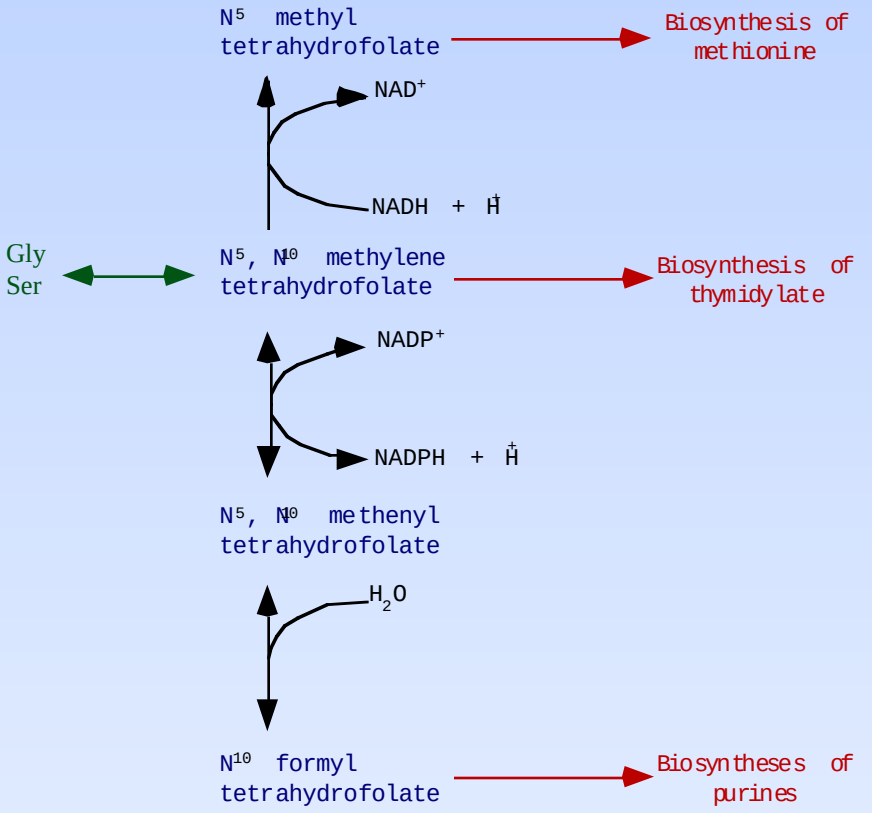
Inhibitors of DHFR are important therapeutics:

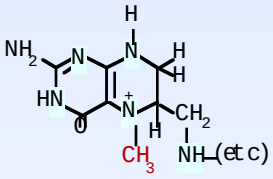
Methotrexate - chemotherapy

Trimethoprim - inhibits bacterial DHFR

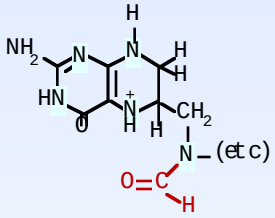
Pyrimethamine - inhibits malarial DHFR


Tetrahydrofolate
seri ne
glycine
N5, N10 methylene
tetrahydrofolate
Tetrahydrofolate
glycine
NAD+
NH4+
CO2
NADH
N5, N10 methylene
tetrahydrofolate



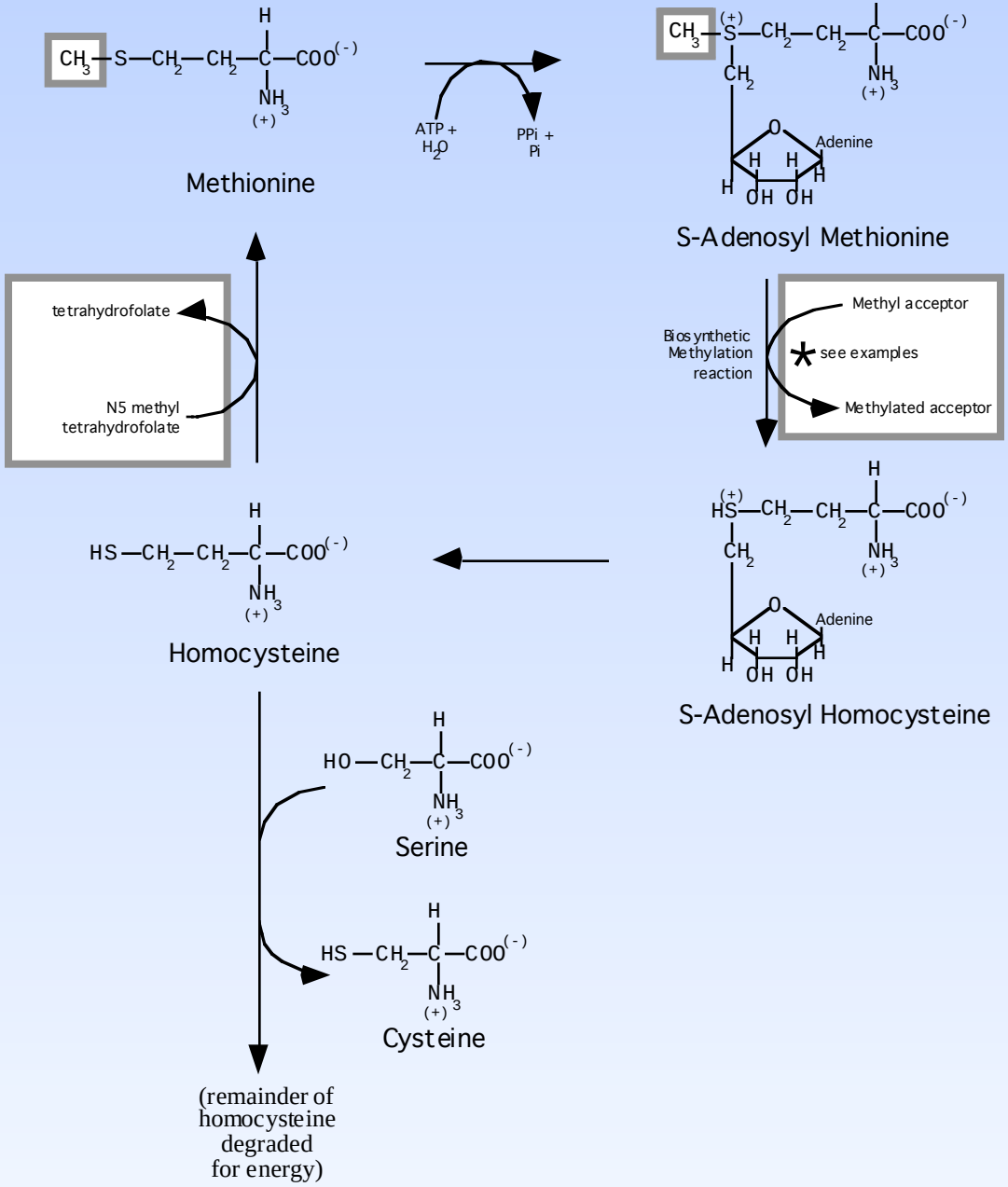


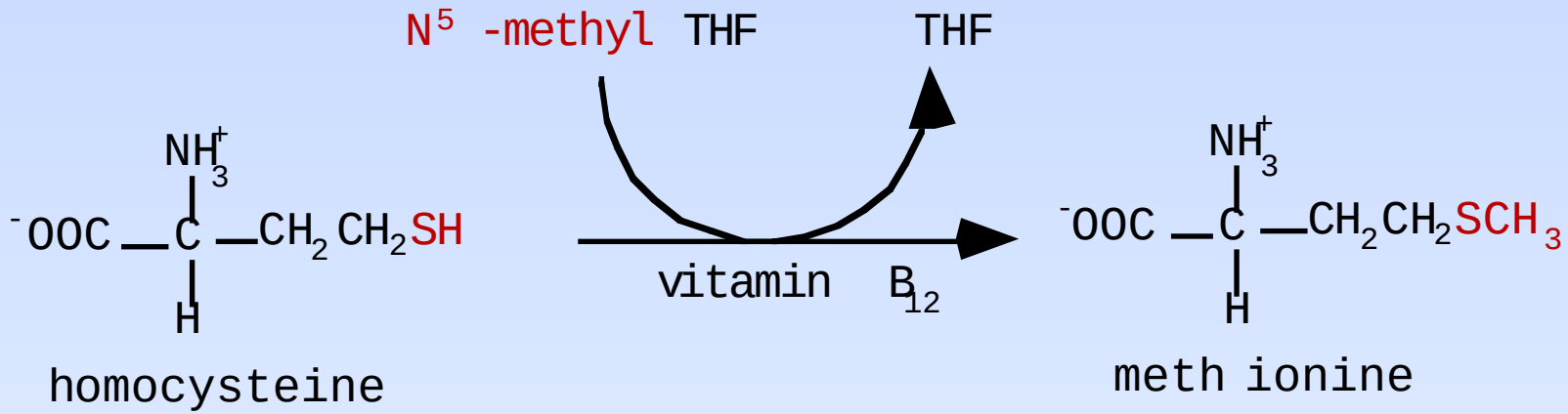
N5- methyl tetrahydrofolate



N10- formyl tetrahydrofolate

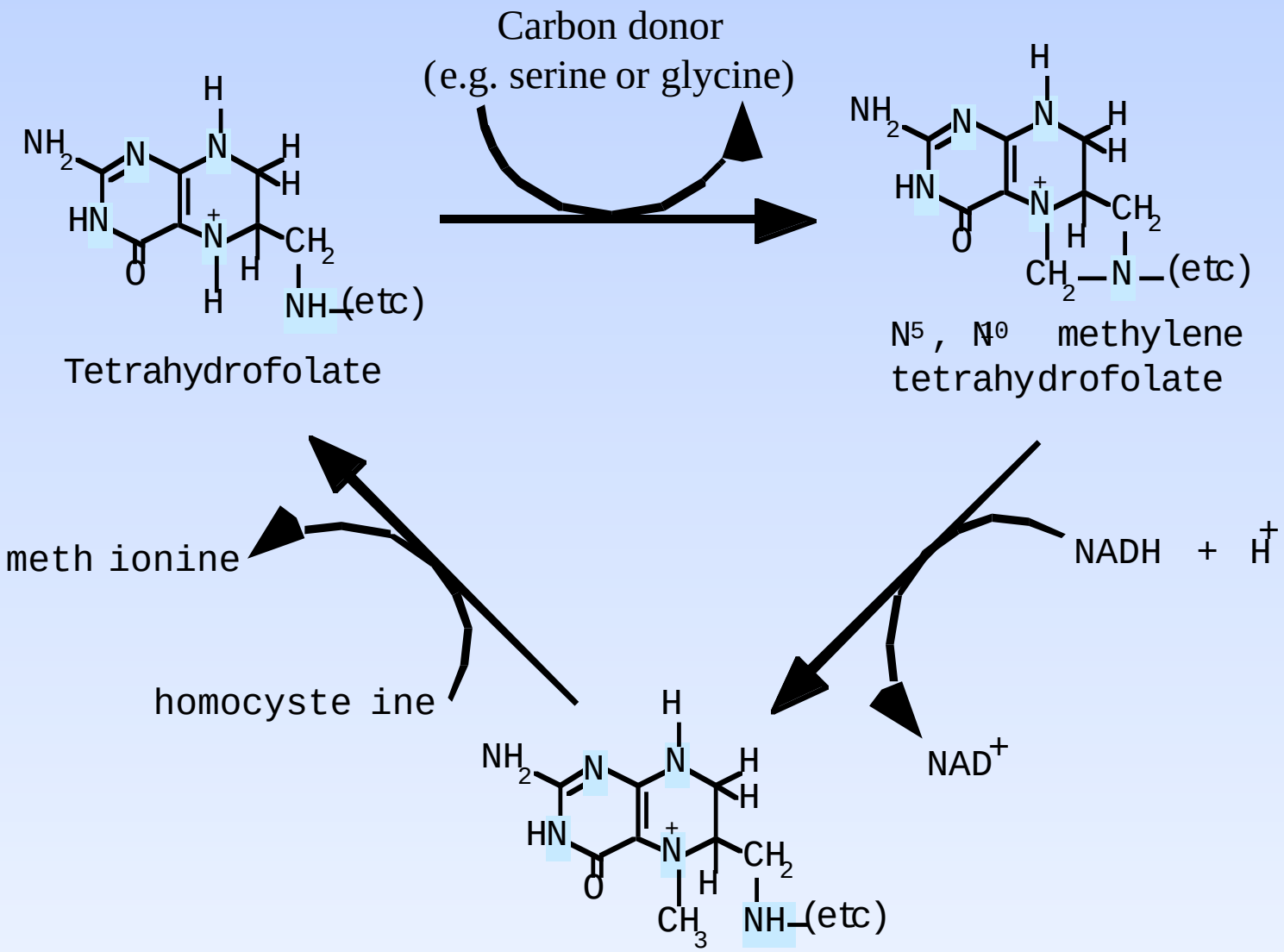
Methionine Cycle And Biological Methyl Groups

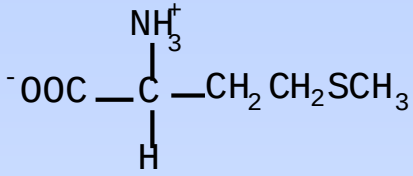




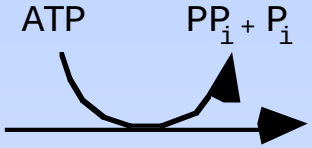
homocysteine

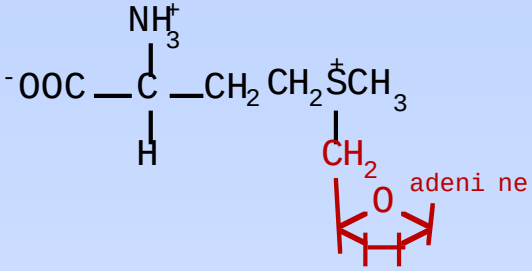
meth ionine


Carbon donor
(e.g. serine or glycine)
Tetrahydrofolate
N5, N10 methylene
tetrahydrofolate
meth ionine
homocyste ine
NADH + H+
NAD+
N5 methyl
tetrahydrofolate

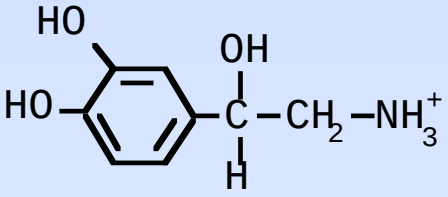


Methionine

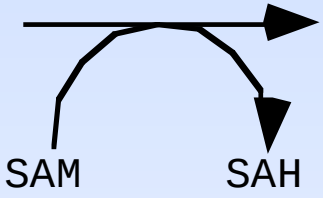


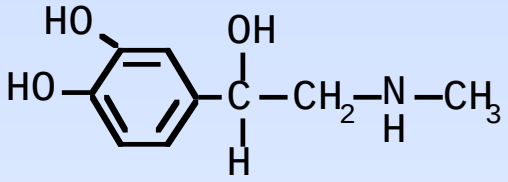


S-Adenosyl methionine



Norepinephrine

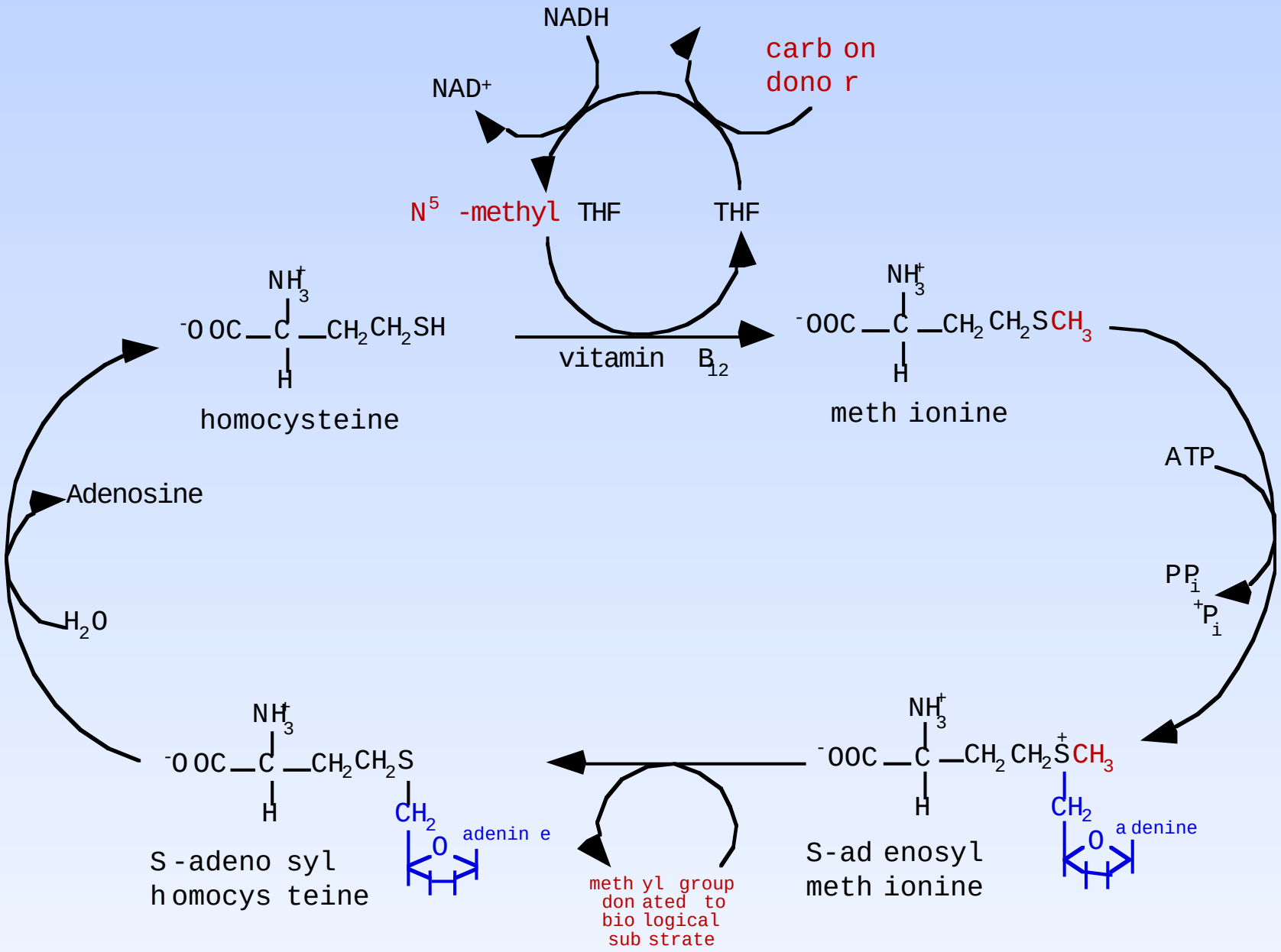


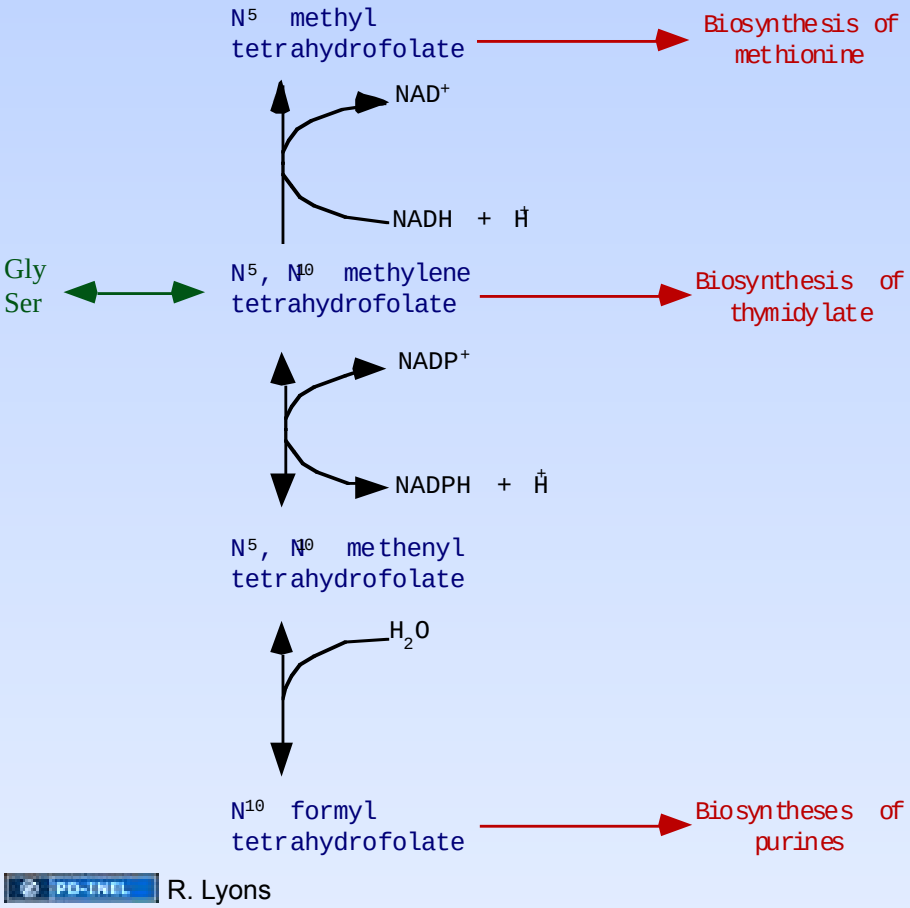


Epinephrine

Other methyl acceptors:

- DNA (“CpG Islands”)
- RNA


NADH
NAD+
carb on
dono r
N5 -methyl THF
THF
vitamin B12
homocysteine
meth ionine
ATP
PPi
+Pi
Adenosine
H2O
S-adeno syl
h omocys teine
adenin e
meth yl group
don ated to
bio logical
sub strate
S-ad enosyl
meth ionine
a denine



Folate Deficiencies: Symptom: megaloblastic anemia

Dietary deficiency:

Common especially in developing countries, lower socioeconomic classes

Folate deficiency secondary to bowel irritation:

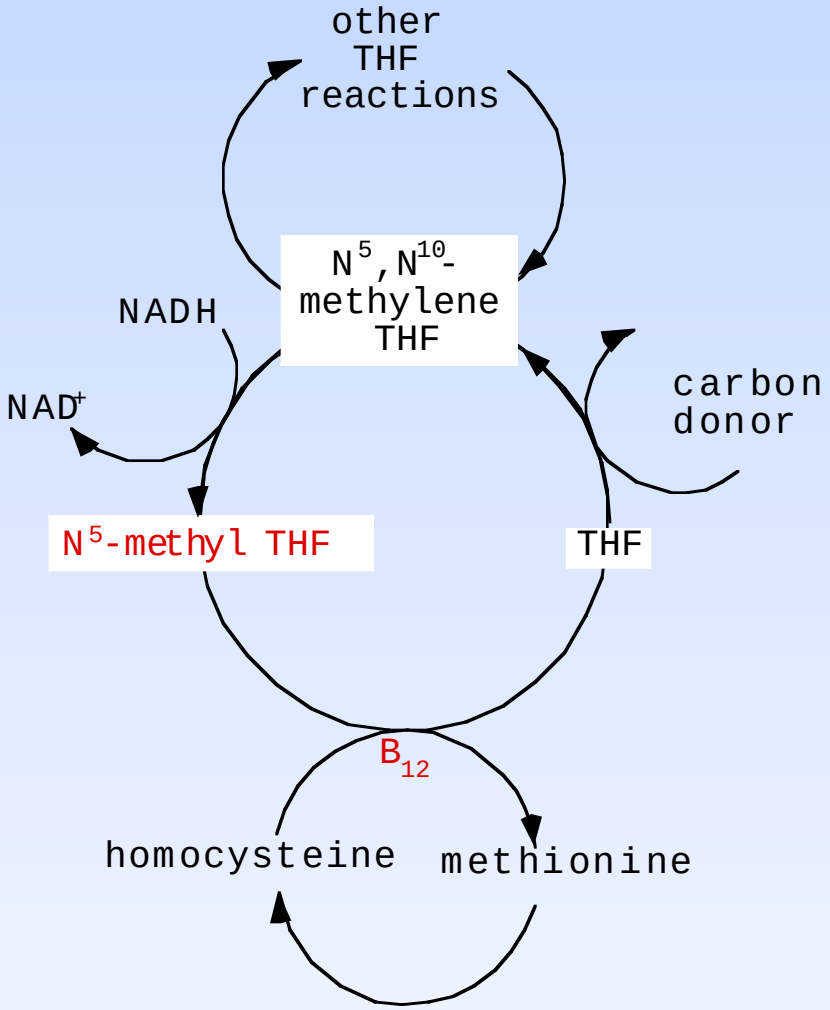
- Conjugase is essential for adequate absorption of dietary folates

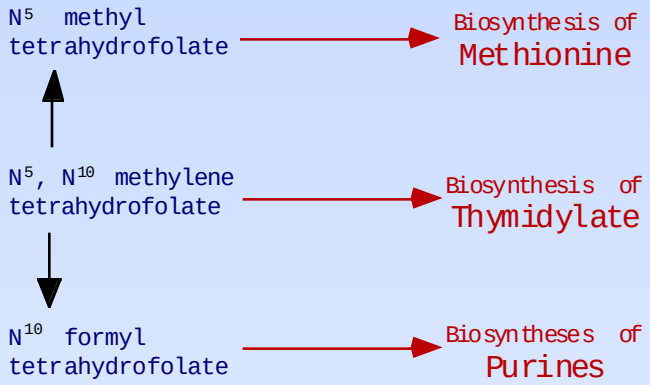
- Conjugase production may be compromised by bowel irritation:

  'Tropical Sprue' - bowel irritation probably arising from bacterial origin, causes intestinal inflamation and malabsorption.

  'Celiac Sprue' - similar outcome, but the original irritation is due to an allergic response, for example to gliaden (a component in gluten)

Folate Deficiency Secondary to B12 deficiency: the ‘methyl trap’ hypothesis





B12 is also critical in other reactions, ones for which the deficiency has serious neurological consequences.

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