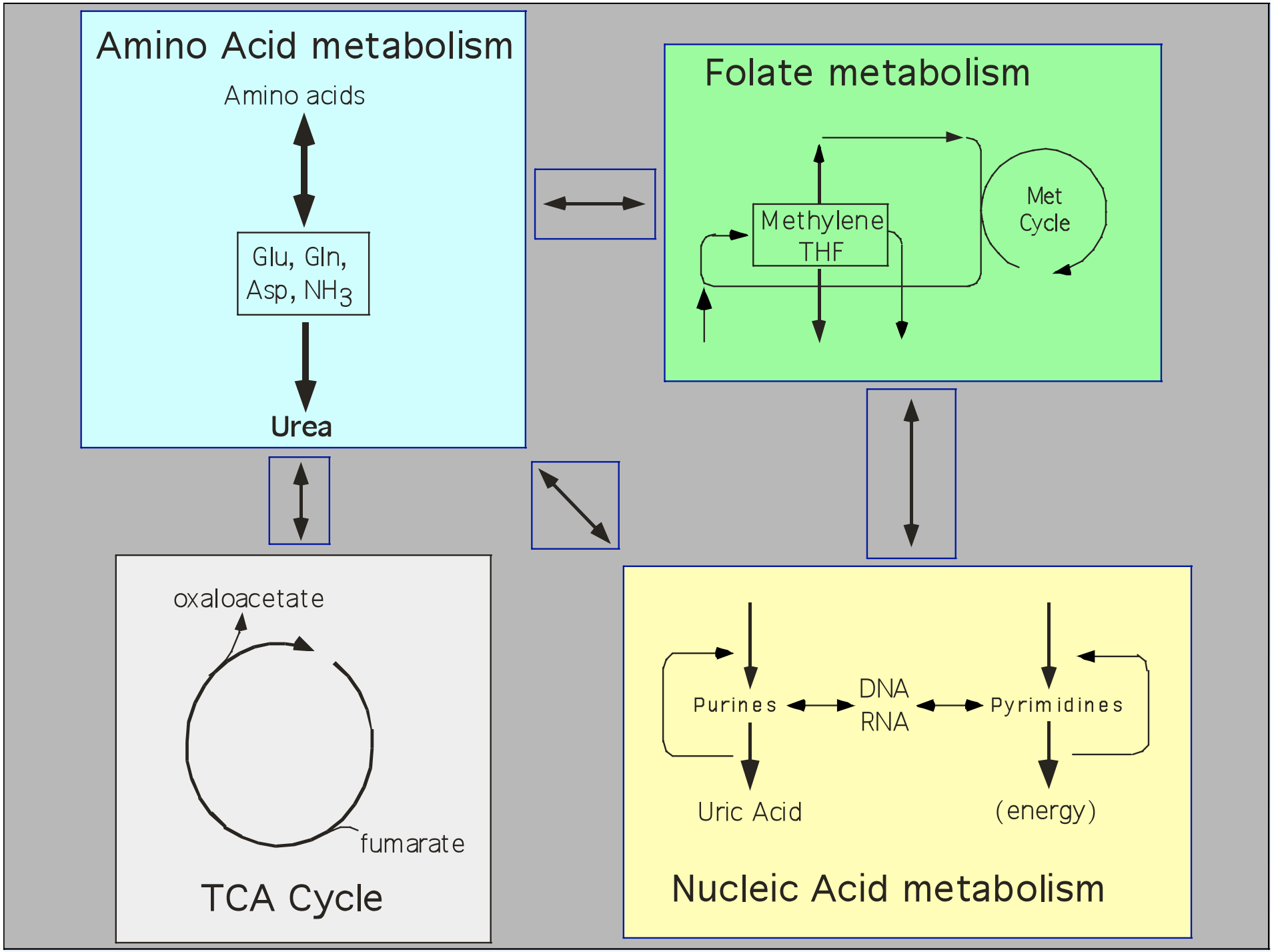
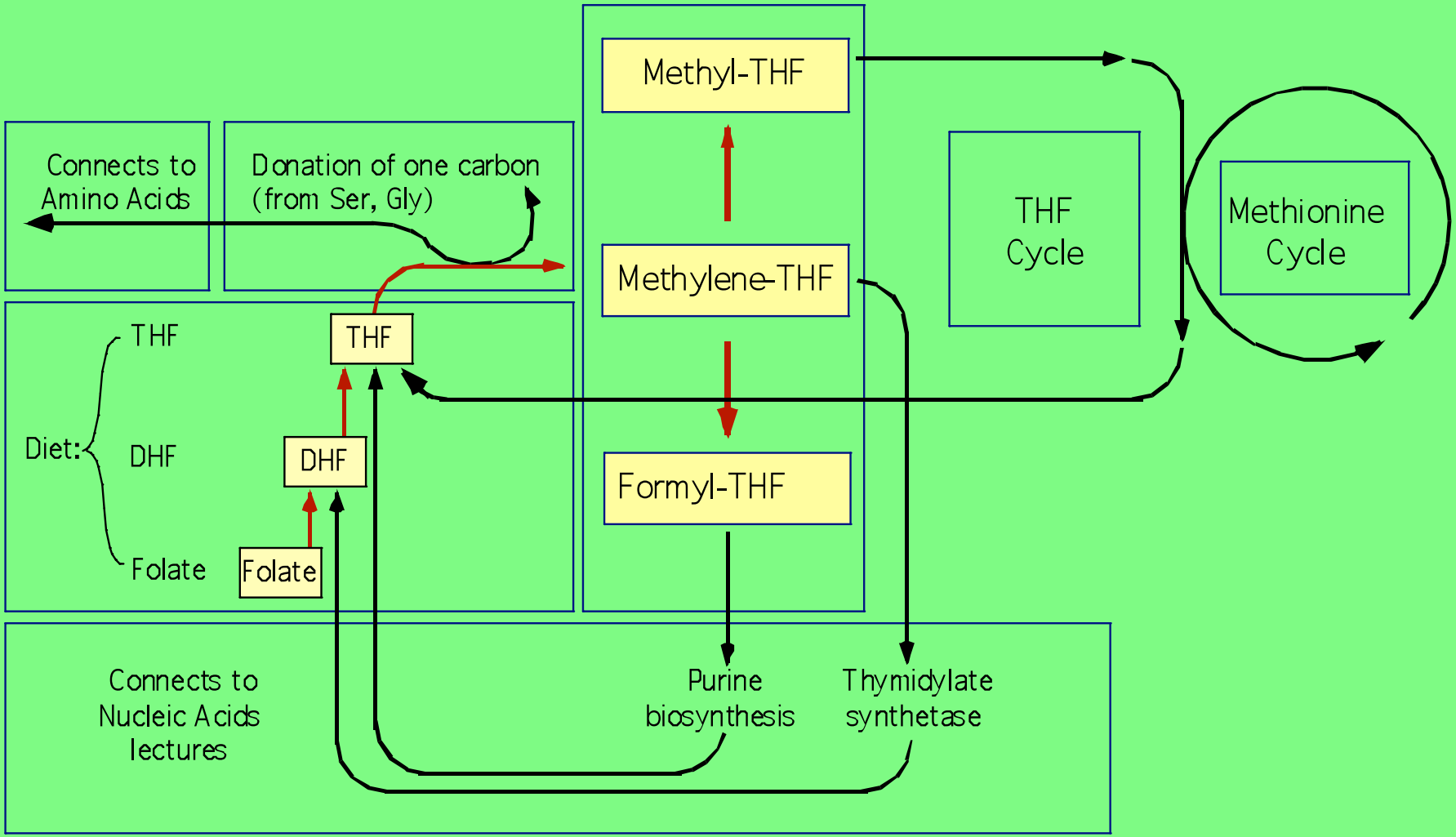
open.michigan


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

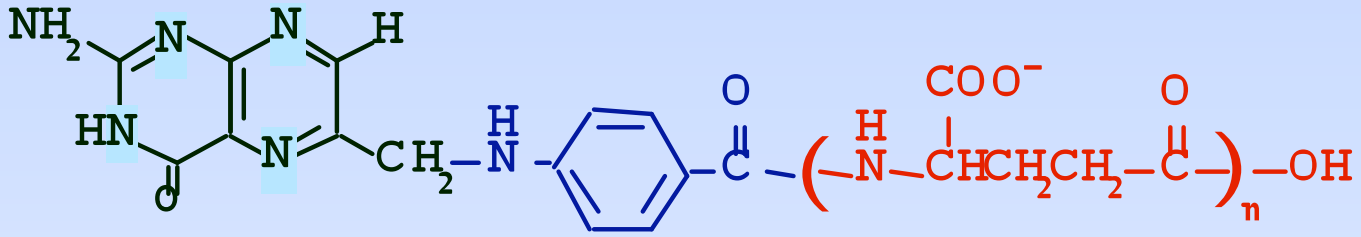
Folate ("One-Carbon") Pathways

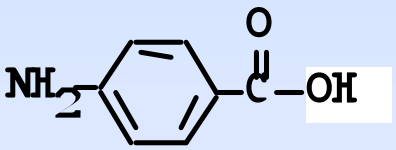
Click on any blue box to see details

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

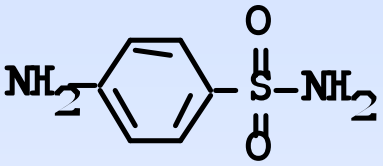


Folic Acid is Synthesized By Bacteria





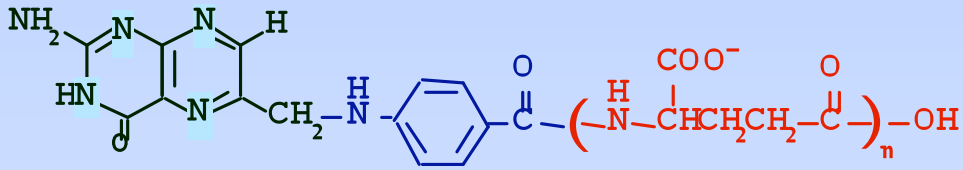
Para-aminobenzoic acid (PABA)



sulfanilamide

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

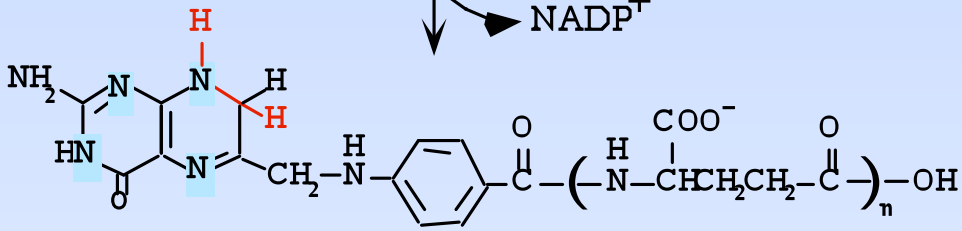
Folic acid



NADPH + H+

NADP+

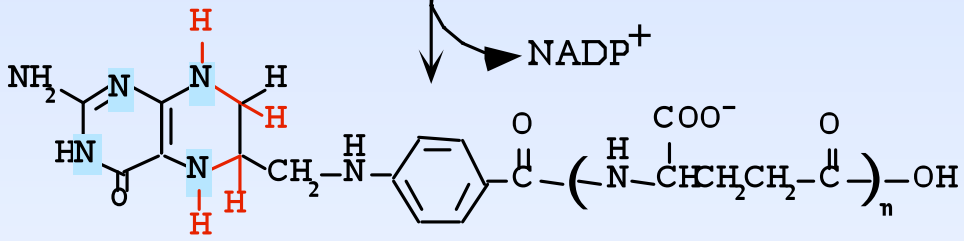
Dihydrofolate

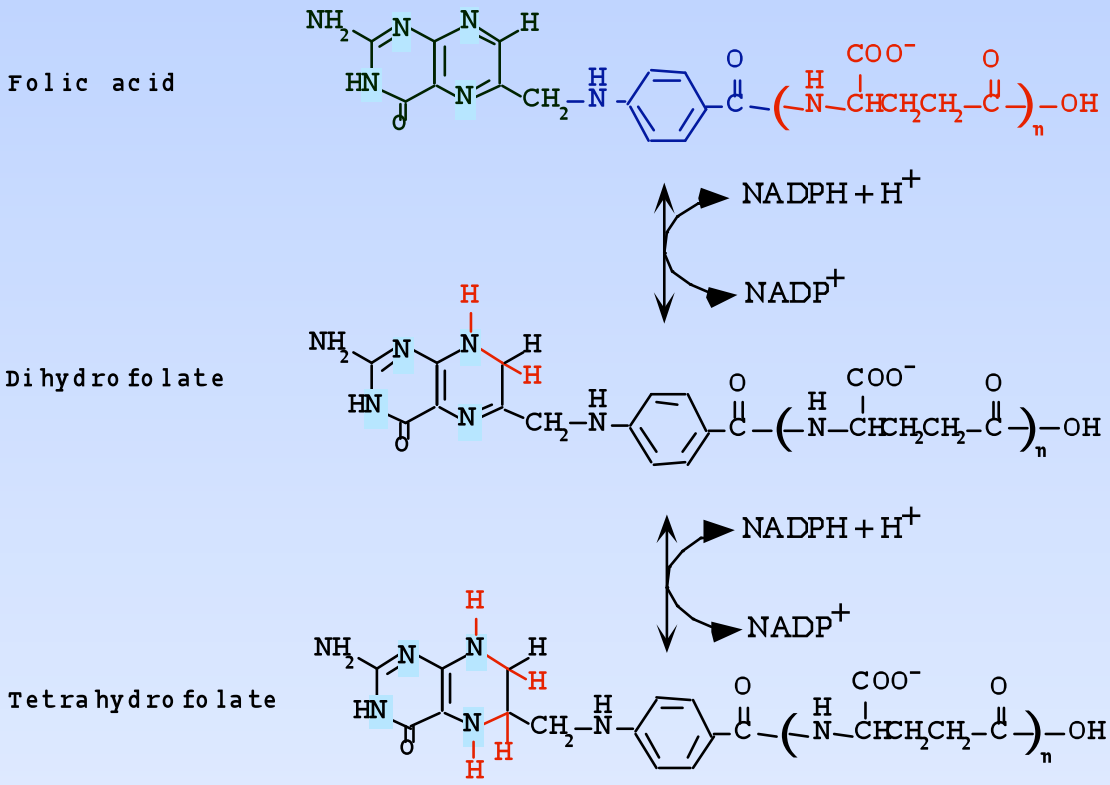


NADPH + H+

NADP+

Tetrahydrofolate



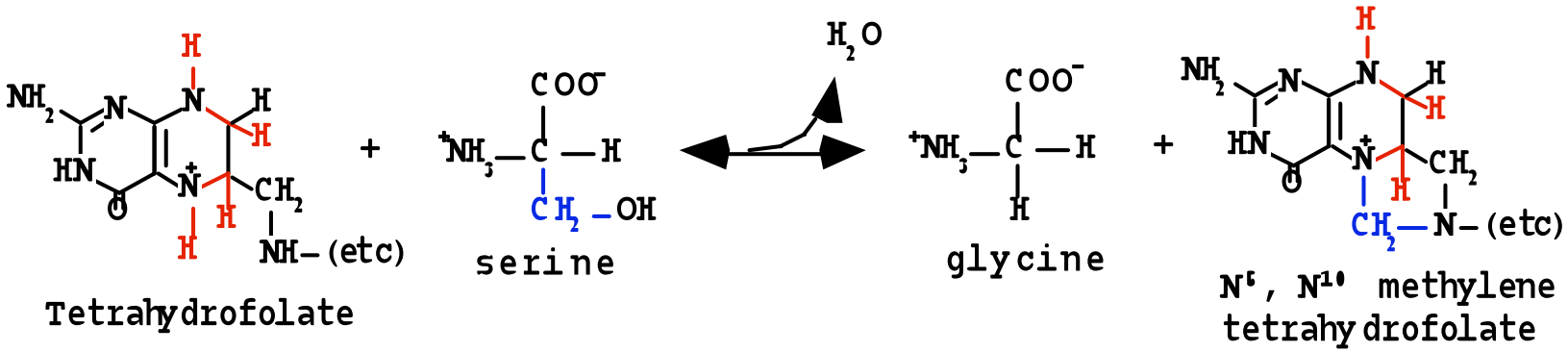


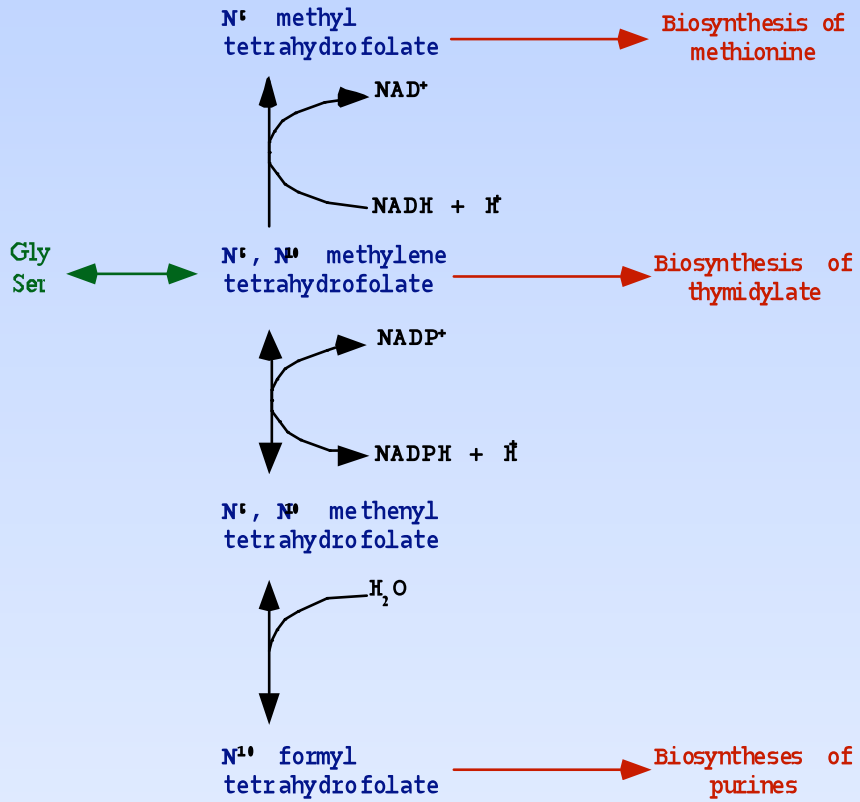
Inhibitors of DHFR are important therapeutics:

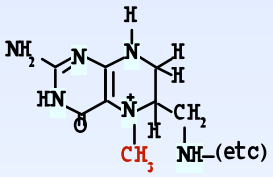
Methotrexate - chemotherapy

Trimethoprim - inhibits bacterial DHFR

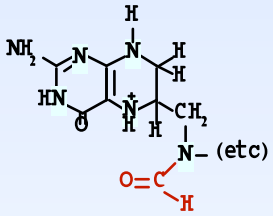
Pyrimethamine - inhibits malarial DHFR


Tetrahydrofolate
serine
glycine
N⁵, N¹⁰ methylene
tetrahydrofolate
Tetrahydrofolate
glycine
NAD⁺
NADH
N⁵, N¹⁰ methylene
tetrahydrofolate



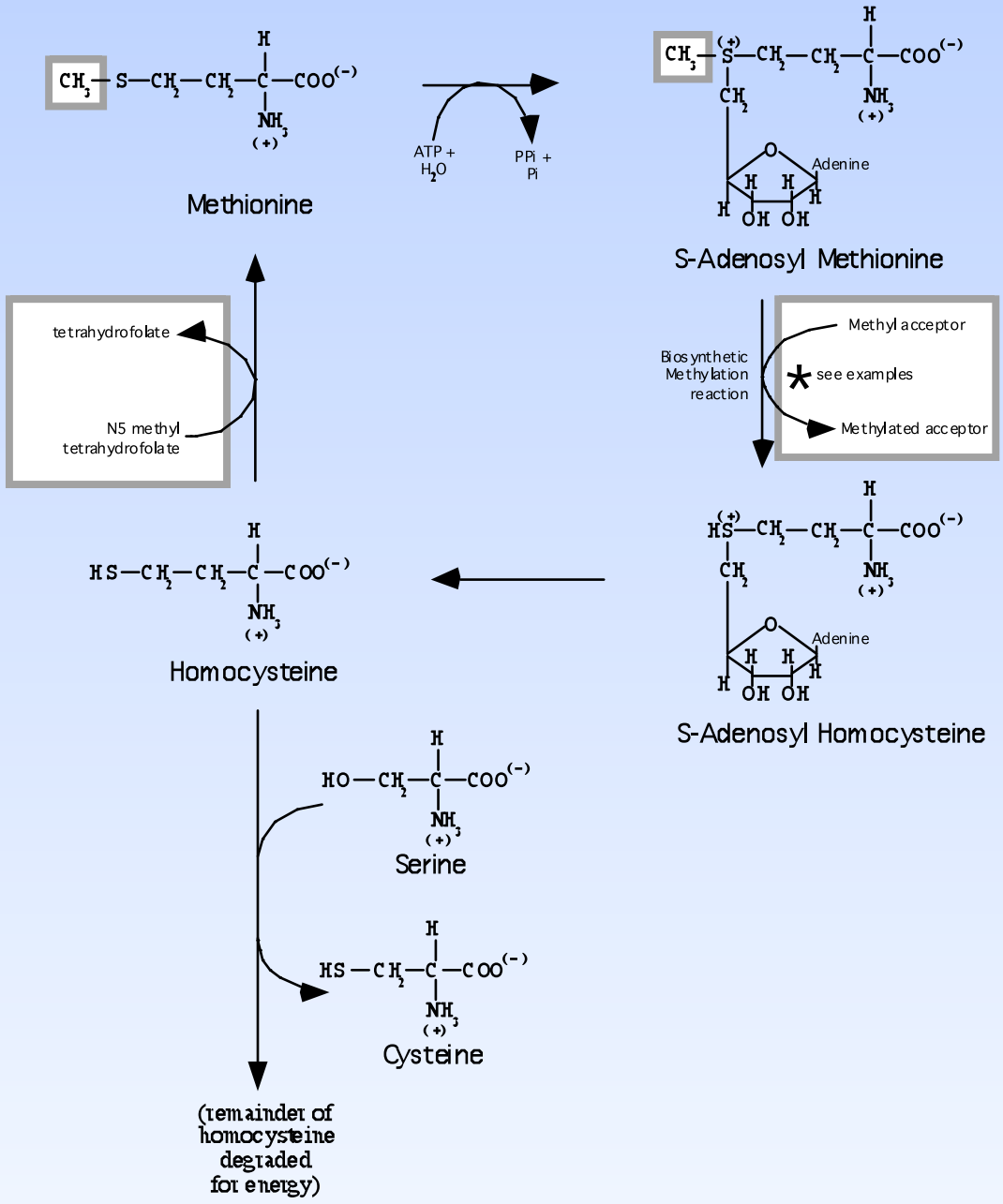


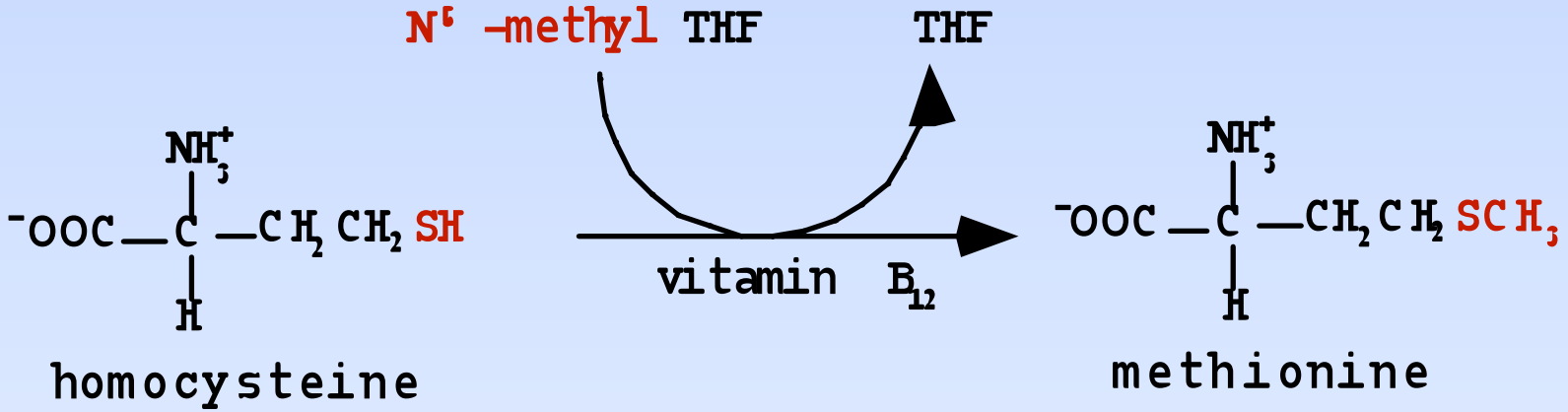
N5- methyl tetrahydrofolate

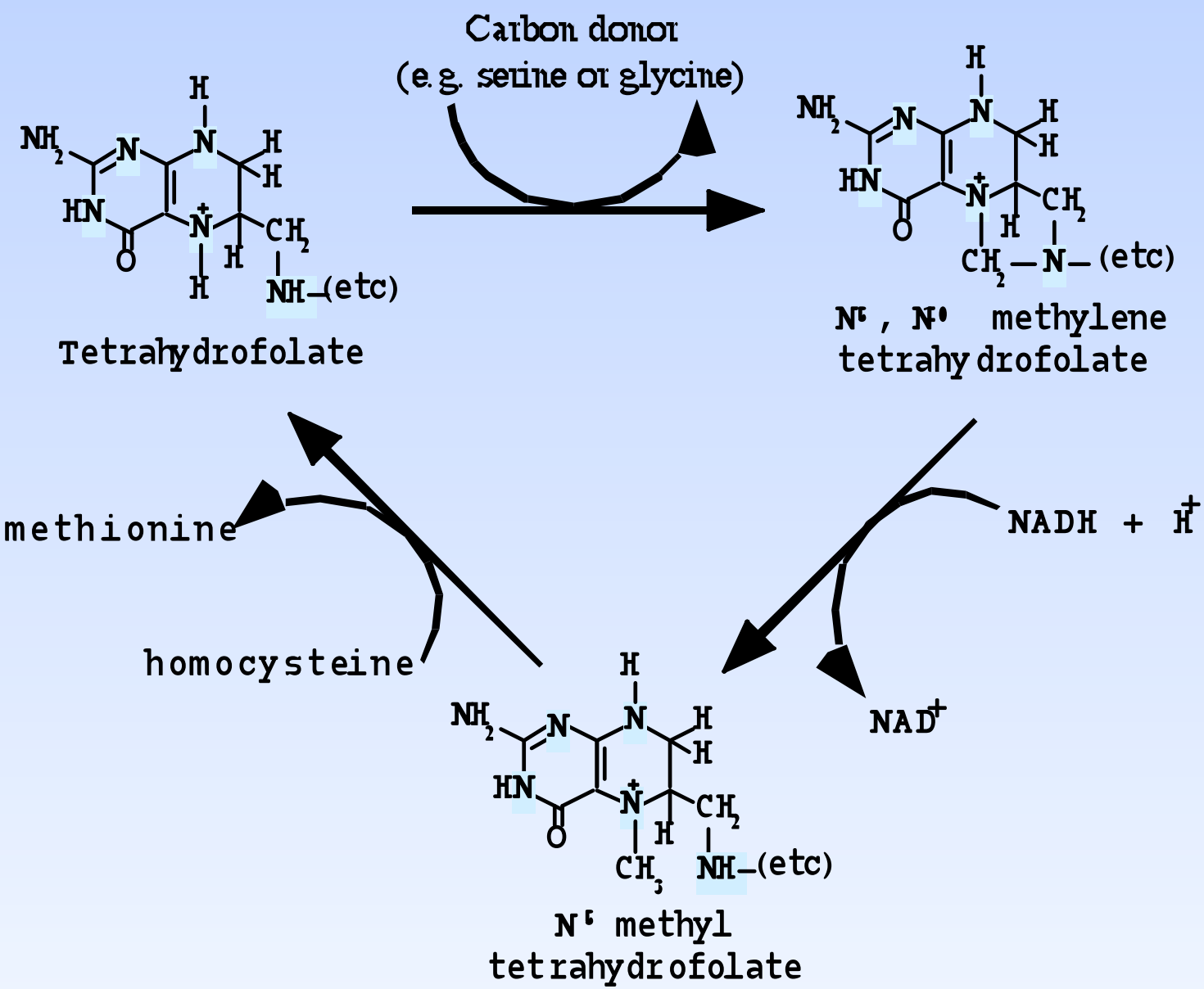


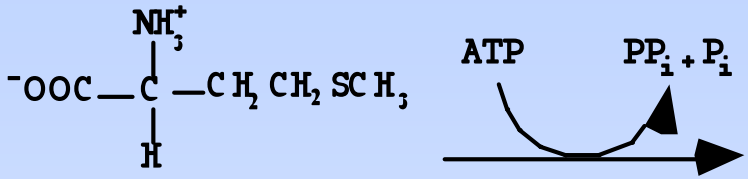
N10 formyl tetrahydrofolate

Methionine Cycle And Biological Methyl Groups

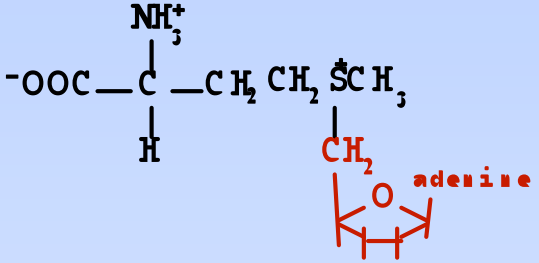



N5 -methyl THF
THF
vitamin B12
homocysteine
methionine

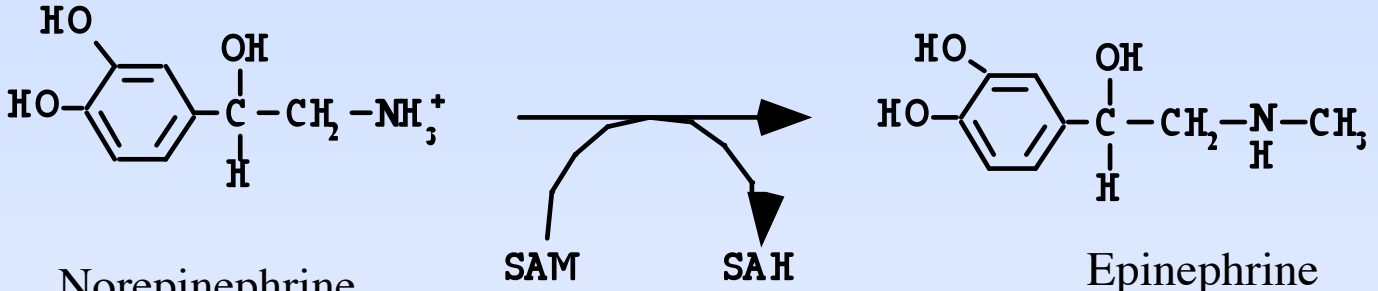

Carbon donor
(e.g. serine or glycine)
Tetrahydrofolate
N5, N10 methylene
tetrahydrofolate
NADH + H+
NAD+
homocysteine
methionine
N5 methyl
tetrahydrofolate



Methionine



S-Adenosyl methionine



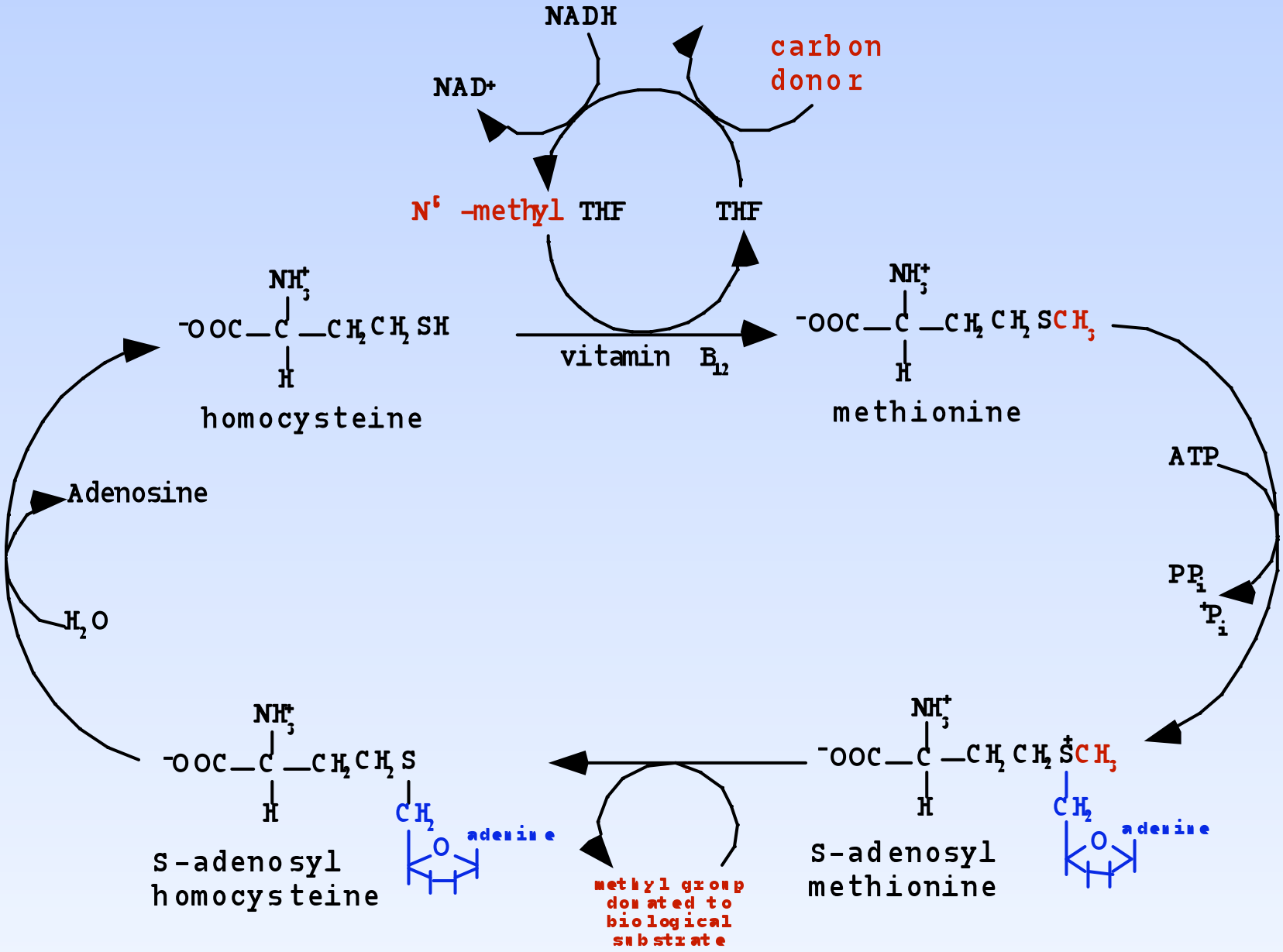
Norepinephrine

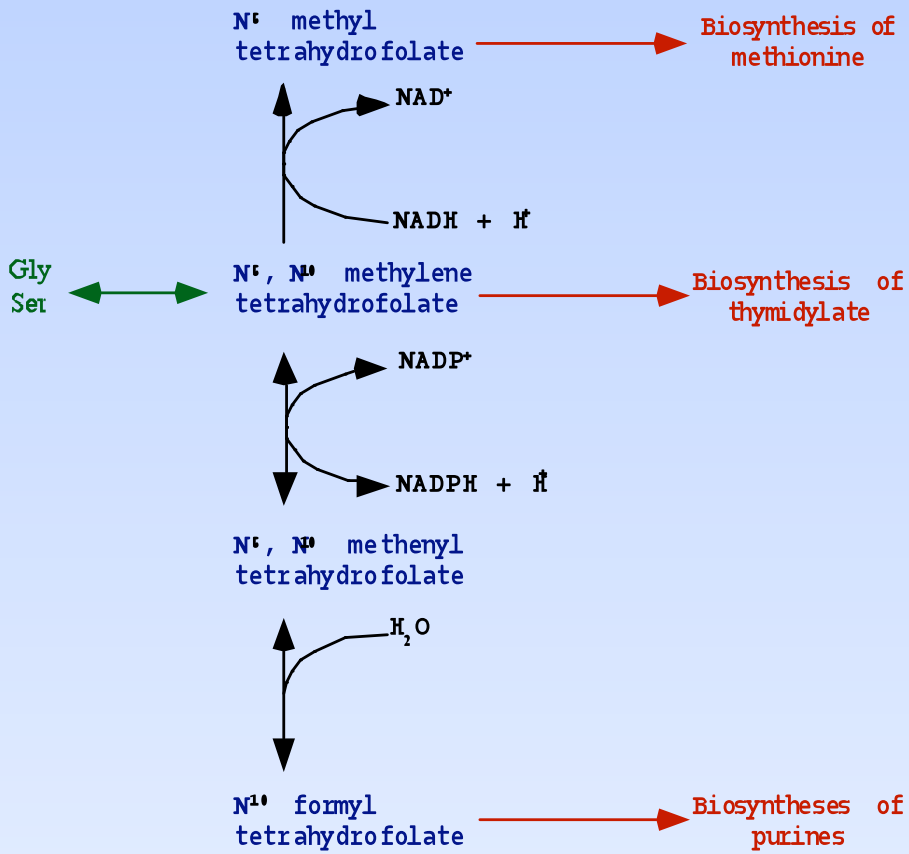
Epinephrine

Other methyl acceptors:

DNA ("CpG Islands")

RNA


NADH
carbon donor
NAD+
N5 -methyl THF
THF
homocysteine
vitamin B12
methionine
ATP
PPi
+Pi
Adenosine
H2O
S-adenosyl homocysteine
adenine
methyl group donated to biological substrate
S-adenosyl methionine
adenine



Folate Deficiencies: Symptom: megaloblastic anemia

Dietary deficiency:

Common especially in developing countries, lower socioeconomic classes

Folate deficiency secondary to bowel irritation:

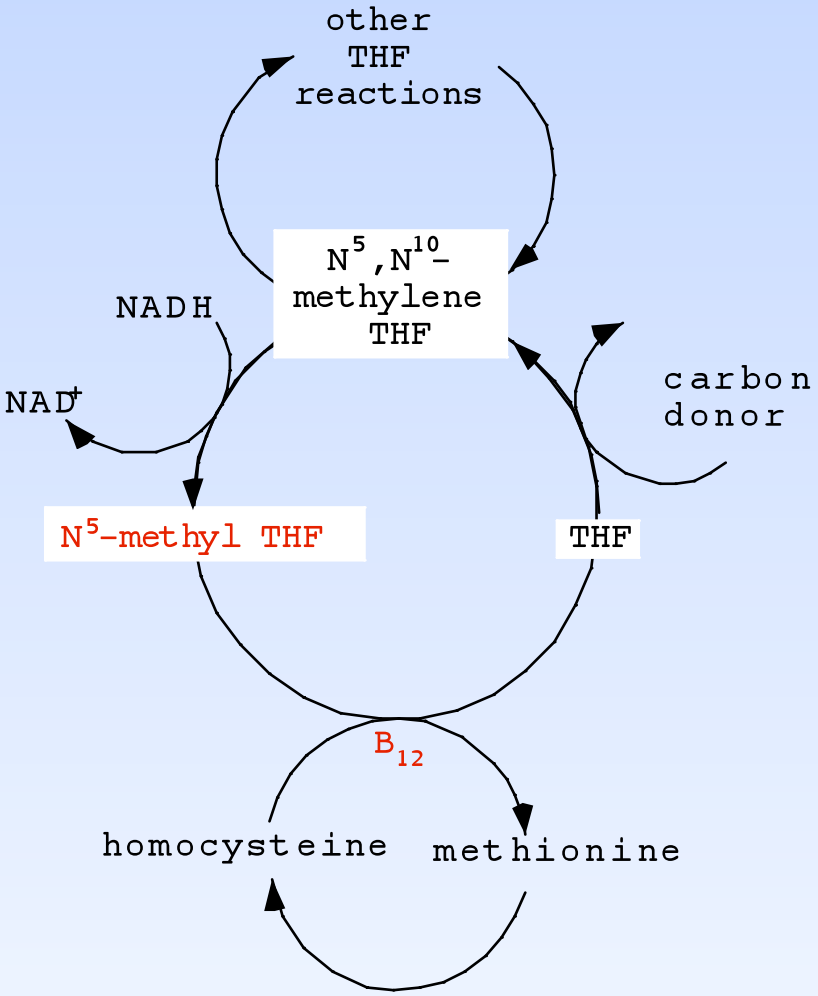
- Conjugase is essential for adequate absorption of dietary folates

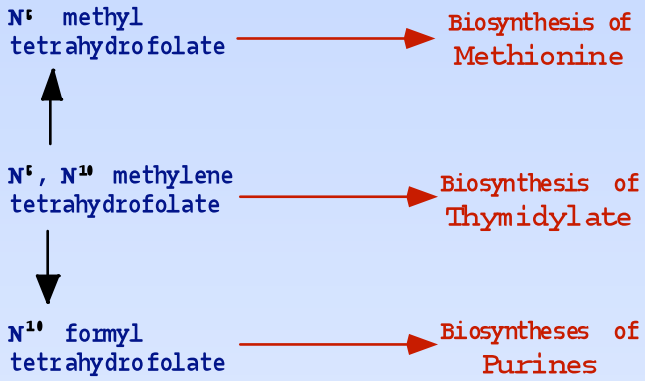
- Conjugase production may be compromised by bowel irritation:

  '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.