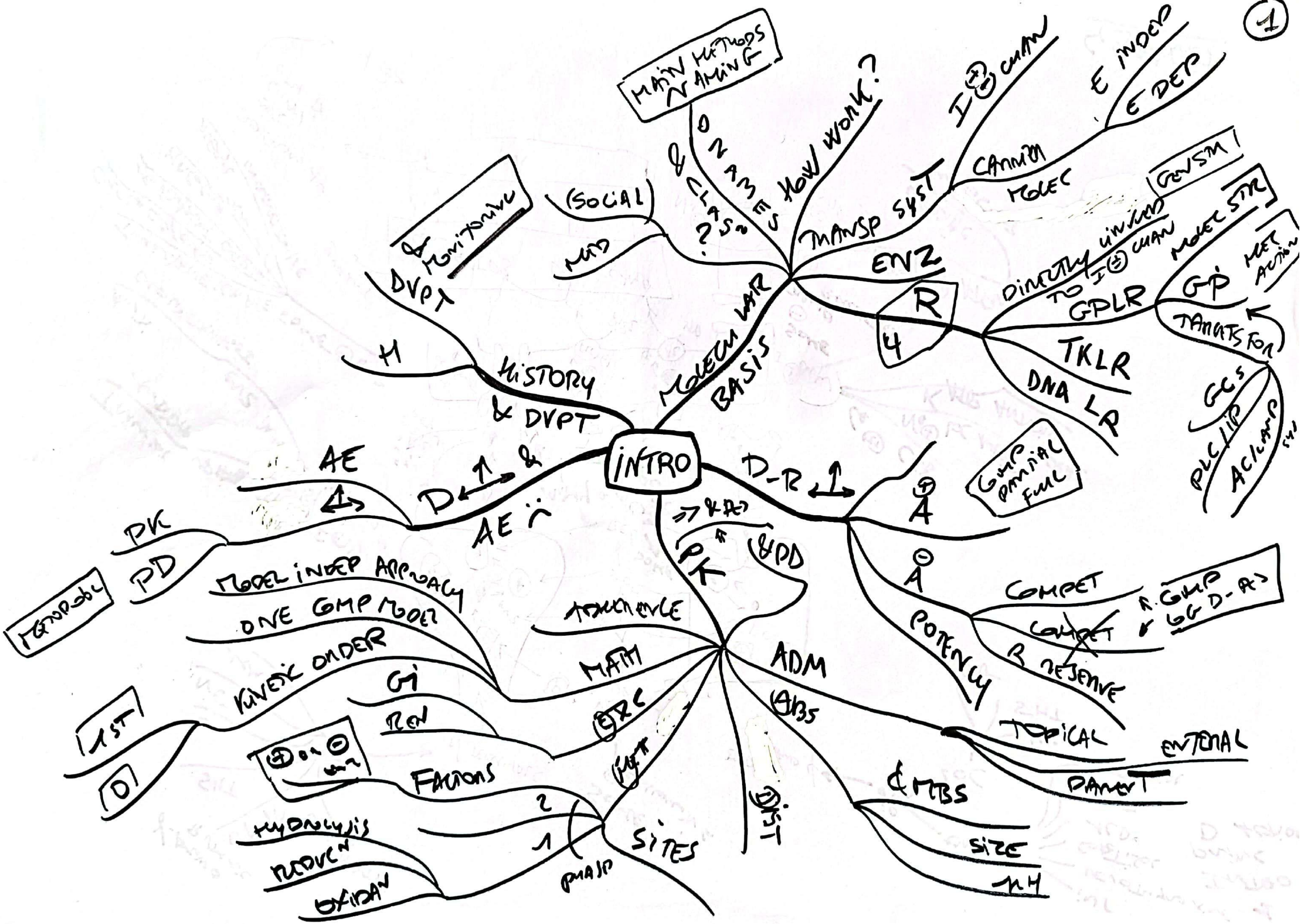
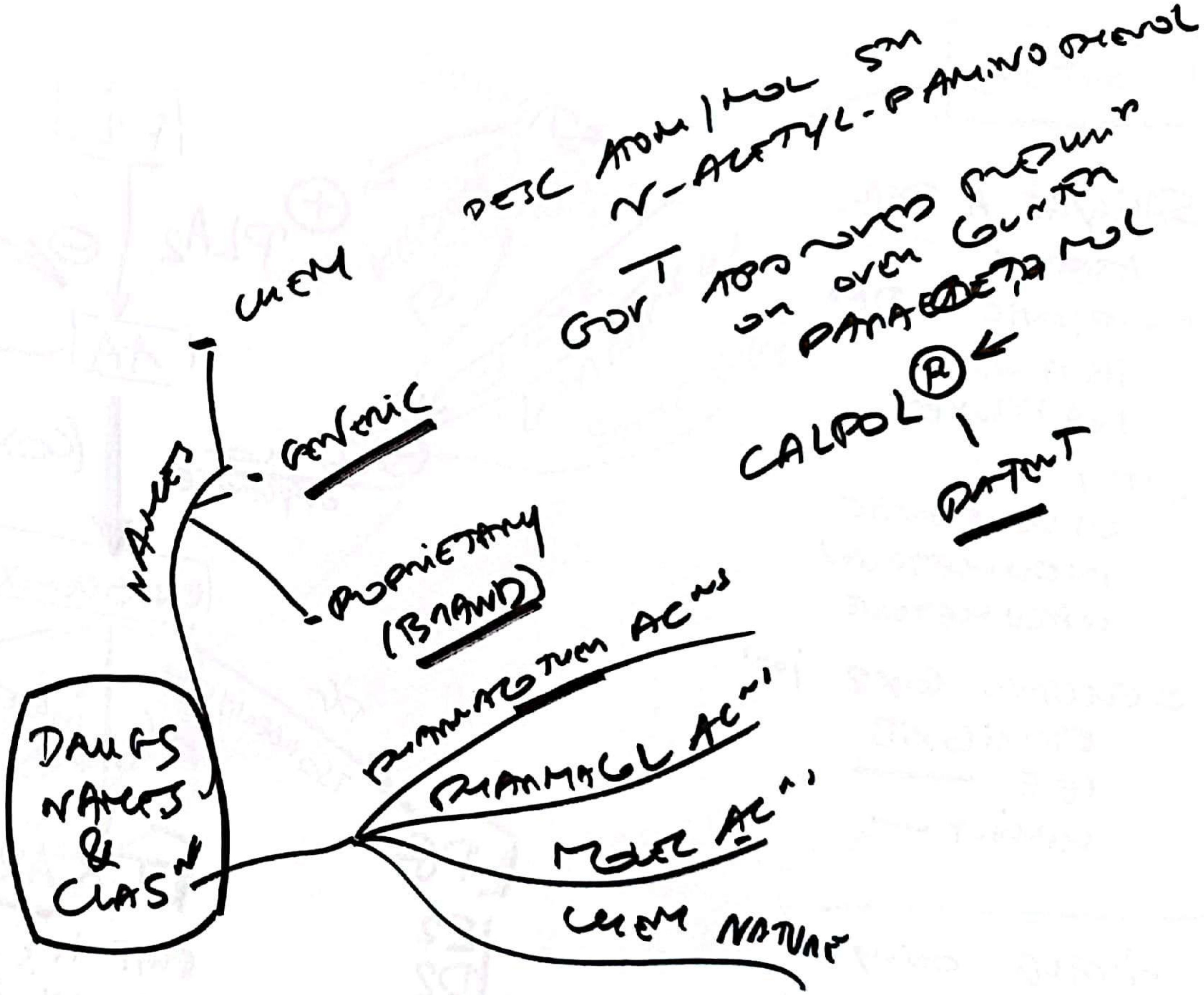
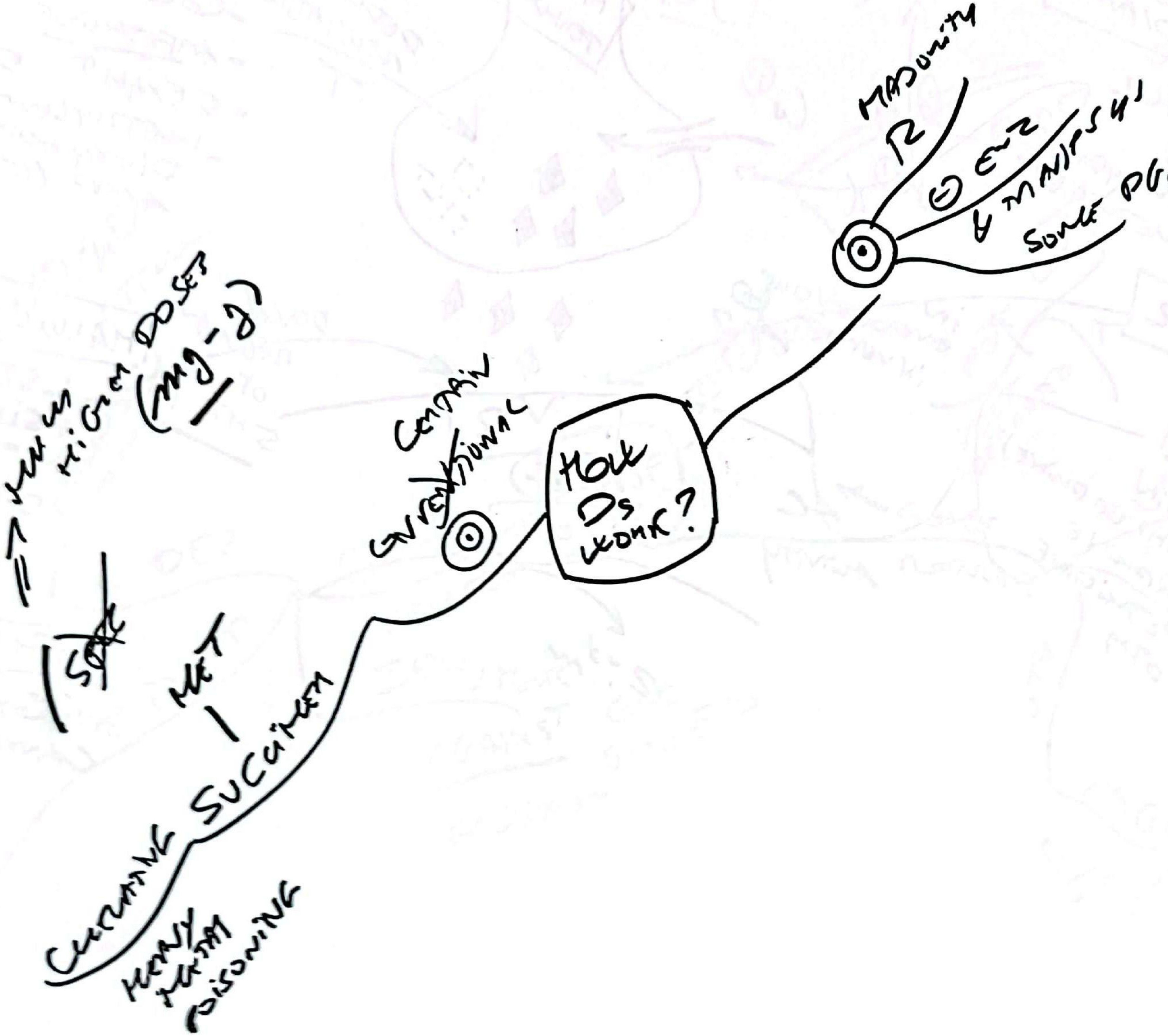
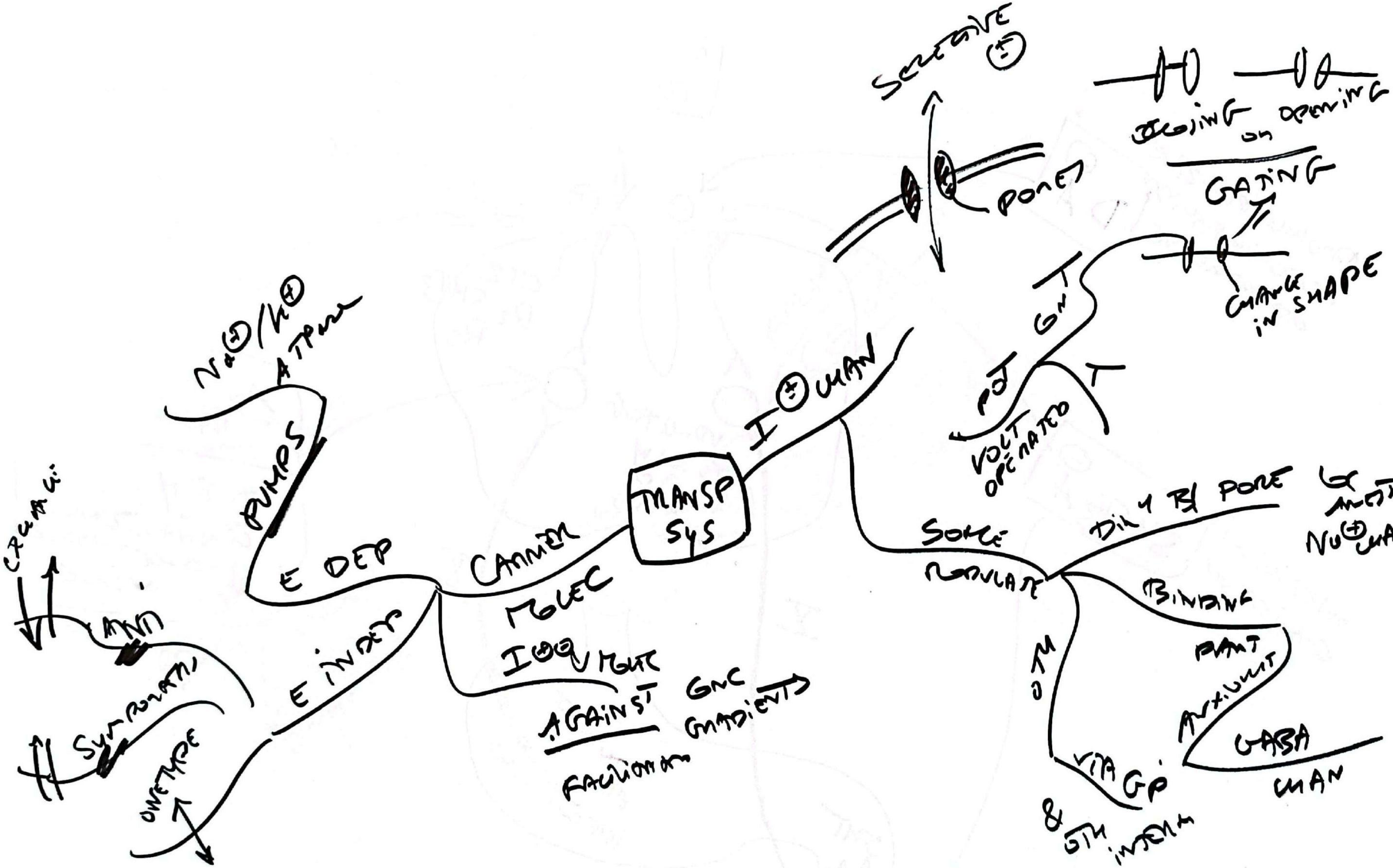
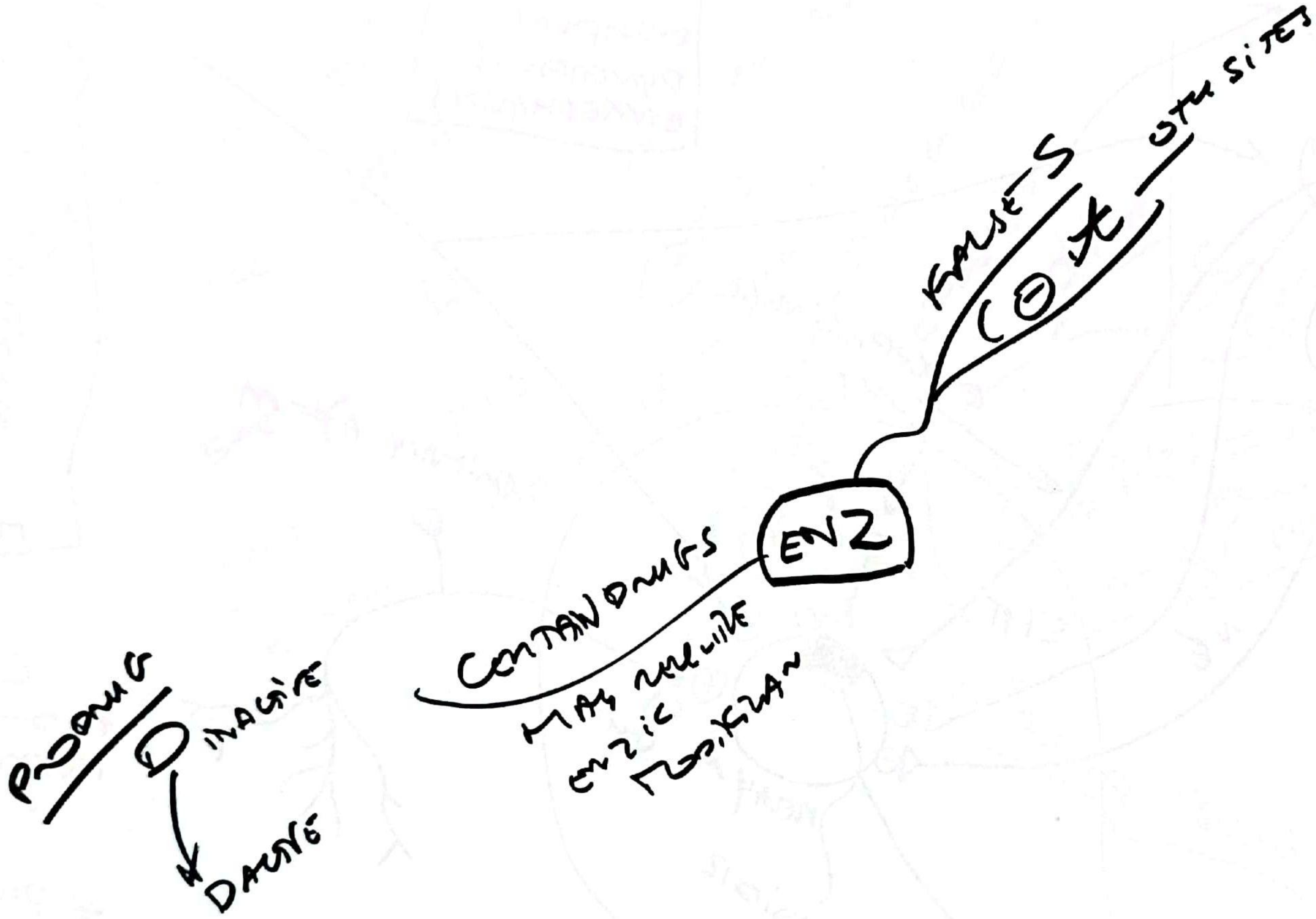

INTRO
HISTORY & DVPT
DVPT
& MONITORING
H
MOLECULAR BASIS
(SOCIAL
MED
& CLASS ?
NAMES
MAIN METHODS NAMING
HOW WORK?
TRANSP SYST
CANNAL
MOLEC
I ⊕⊖ CHAN
E INDEP
E DEP
ENZ
R
4
DIRECTLY LINKED TO I ⊕⊖ CHAN
GENSM
GPLR
MOLEC STR
G P
MET ACTION
TARGETS FOR
GCS
PLC/IP
AC/cAMP
TKLR
DNA LR
D-R
Ā ⊕
Ā ⊖
GMP PARTIAL FULL
POTENCY
COMPET
COMPET
R GMP & GG D-AS
R RESERVE
D
AE
AE ..
PK
PD
PK
& PD
MODEL INDEP APPROACH
ONE CMP MODEL
KINETIC ORDER
1ST
0
ADMINISTR
MATH
ADM
ABS
TOPICAL
ENTERAL
PARENT
& MBS
SIZE
pH
DIST
EXC
Gi
REN
FACTORS
⊕ or ⊖
SITES
2
1
PHASE
HYDROLYSIS
REDUCN
OXIDAN

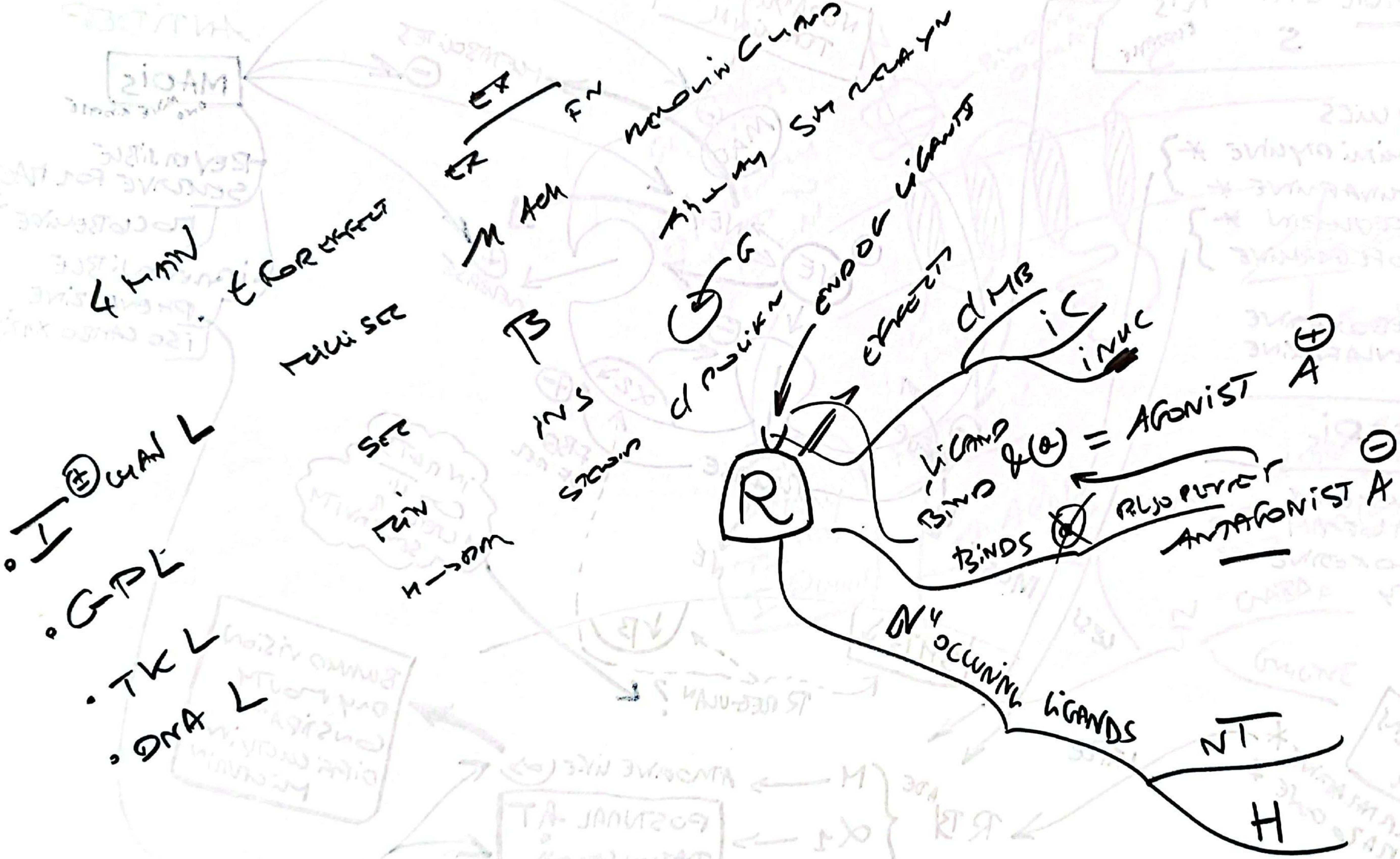

PHARMACOLOGY
?
MEDICINAL
SOCIAL
ILLEGAL
LEGAL

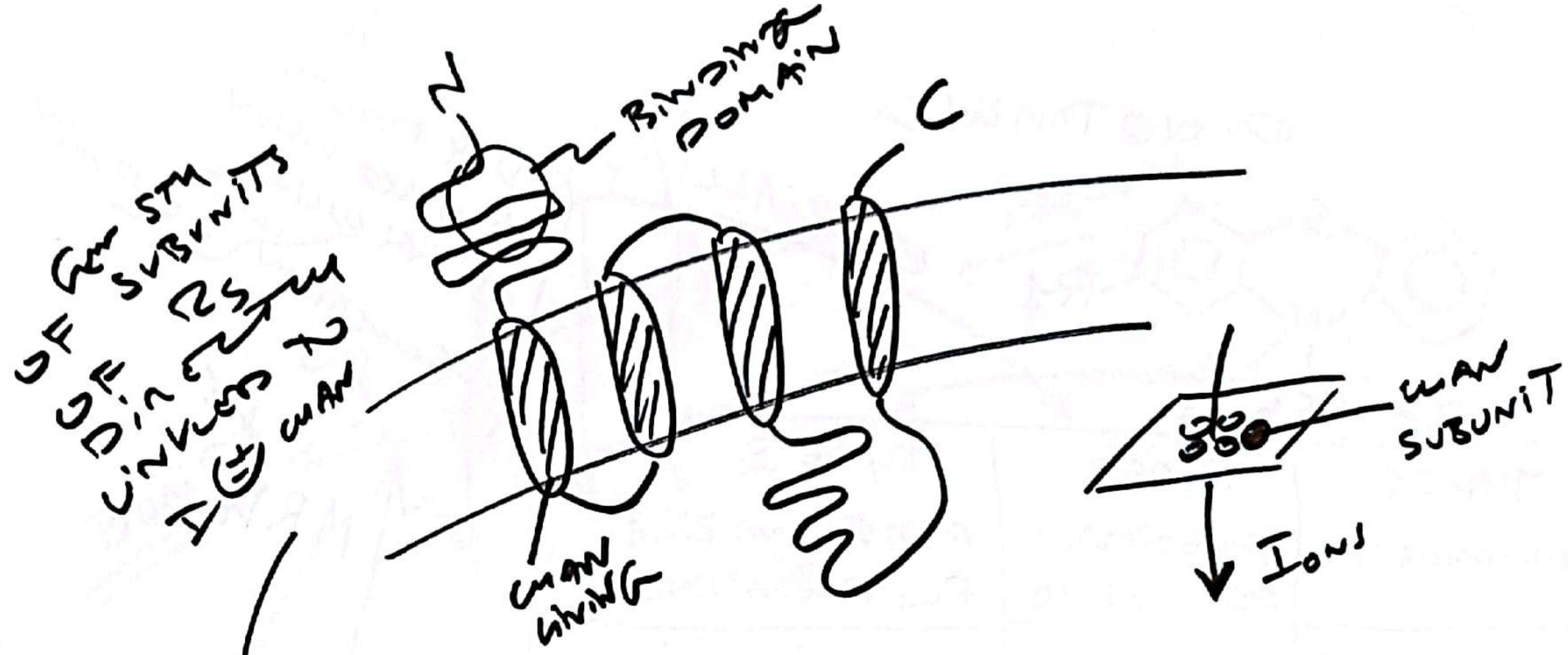

DRUGS NAMES & CLASSN
NAMES
CHEM
DESC ATOM/MOL STR
N-ACETYL-P-AMINO PHENOL
GENERIC
GOVT APPROVED MEDIUM ON OVER COUNTER
PARACETAMOL
CALPOL®
PATENT
PROPRIETARY (BRAND)
PHARMACOL ACN
MOLEC ACN
CHEM NATURE


HOW DS WORK?
CONVENTIONAL
MAJORITY
SOME PGs
SUCCIMER
MET
CHELATING
HEAVY METAL POISONING
HIGHER DOSES
(mg-g)


TRANSP SYS
CARRIER
MOLEC
E DEP
PUMPS
ATPase
E INDEP
ANTI
ONE TYPE
AGAINST
GRADIENTS
CHAN
SELECTIVE
PORES
GATING
CHANGE IN SHAPE
VOLT OPERATED
BINDING
GABA
CHAN


ENZ
OTH SITES
INACTIVE


4 MAIN
• I ⊕ CHAN L
• GPL
• TKL
• DNA L
E FOR EFFECT
EX
EX
FN
M ACH
B
INS
SEC
H—DOM
STEROID
G
ENDOG LIGANDS
EFFECTS
CMB
IC
INUC
R
LIGAND BINDS & (a) = AGONIST A ⊕
BINDS
ANTAGONIST A ⊖
N OCCURING LIGANDS
NT
H



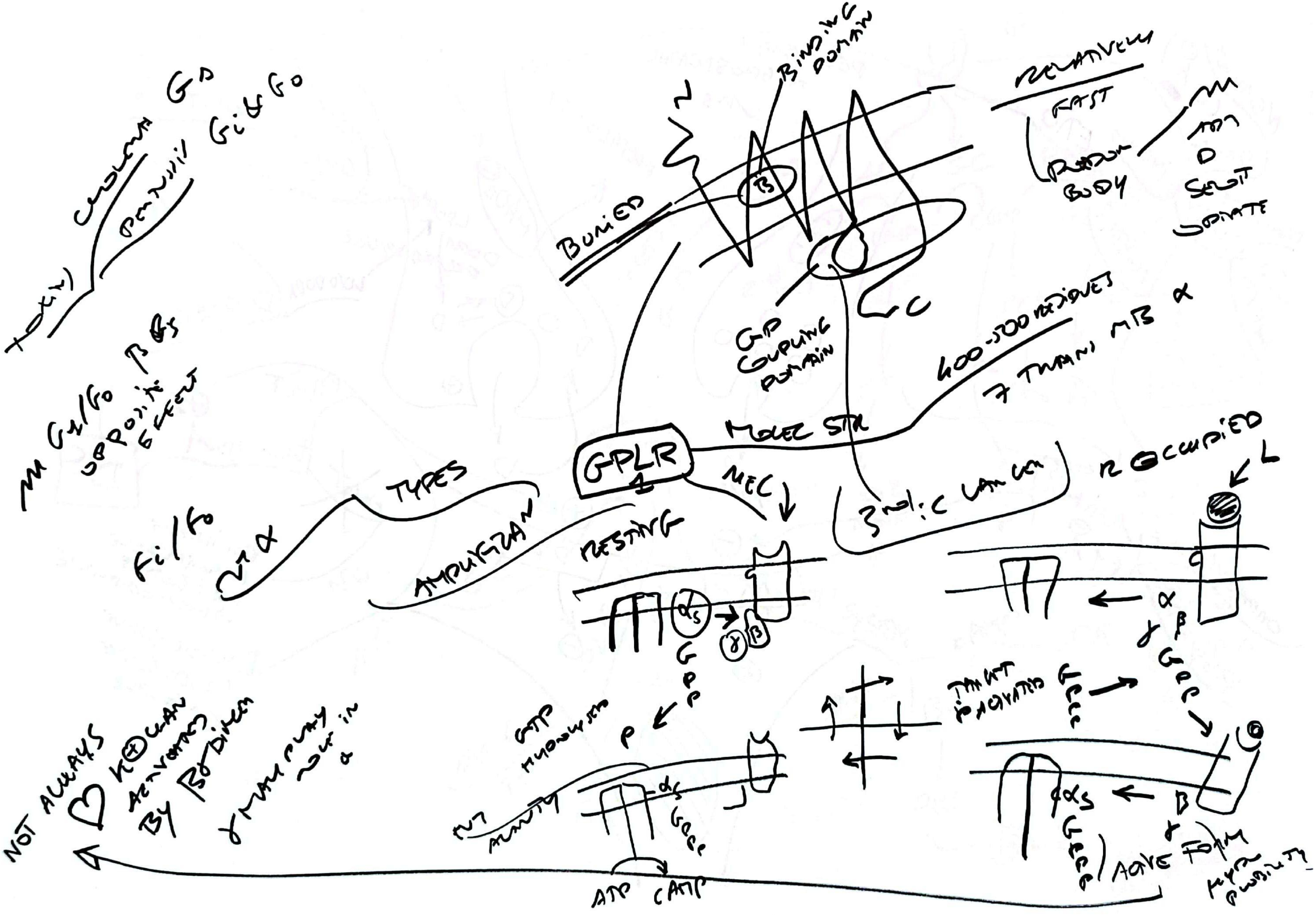
R DIRECTLY LINKED TO I ⊕ CHAN

FAST SYN

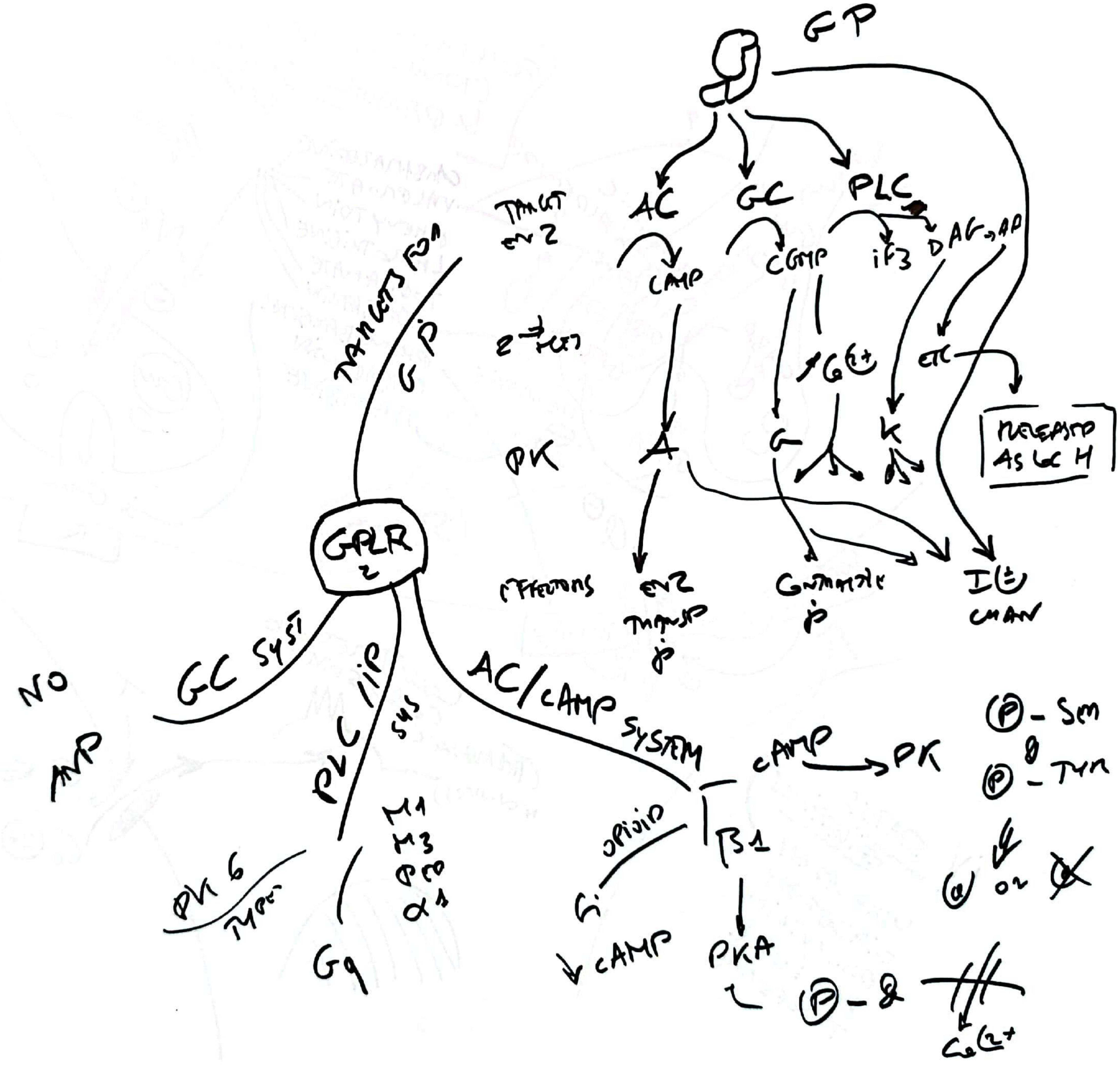
nAChRs — ACh — BOTH α SUBUNITS IN ORDER TO (a) R

~ GABA A

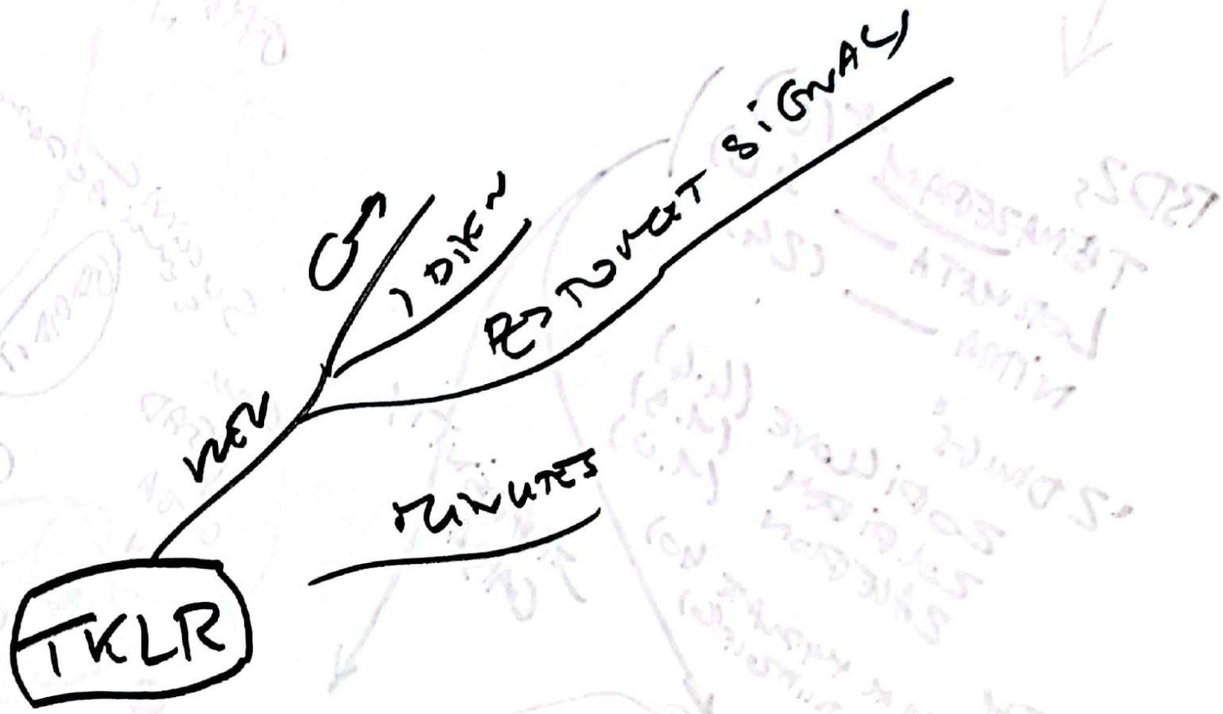
GLYCINE

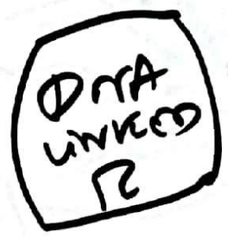


GPLR
TYPES
RESTING
MOLEC STR
7 TRANS MB α
BURIED
BINDING DOMAIN
N
C
RELATIVELY
FAST
OCCUPIED
L
GDP
GTP
ACTIVE FORM
ATP
CAMP
NOT ALWAYS
BY βγ DIMER

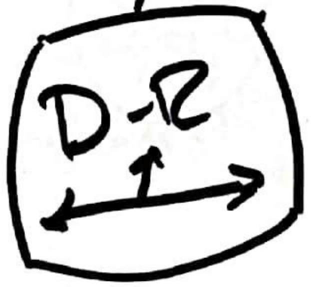


GP
AC
GC
PLC
TARGET ENZ
CAMP
CGMP
IP3
DAG
TARGETS FOR GP
PK
A
G
K
RELEASED AS CC H
EFFECTORS
ENZ TRANSP
I CHAN
GPCR
GC SYST
NO
PLC/IP SYS
AC/cAMP SYSTEM
cAMP
PK
M1
M3
α1
Gq
OPIOID
β1
PKA
↓cAMP
Ca2+


TKLR


DATA
LINKED
?

higher affinity ← K_d lower
in nanomolar range



$$D + R \underset{K_{-1}}{\overset{K_{+1}}{\rightleftharpoons}} DR$$

Forward rate = $K_{+1} [D][R]$

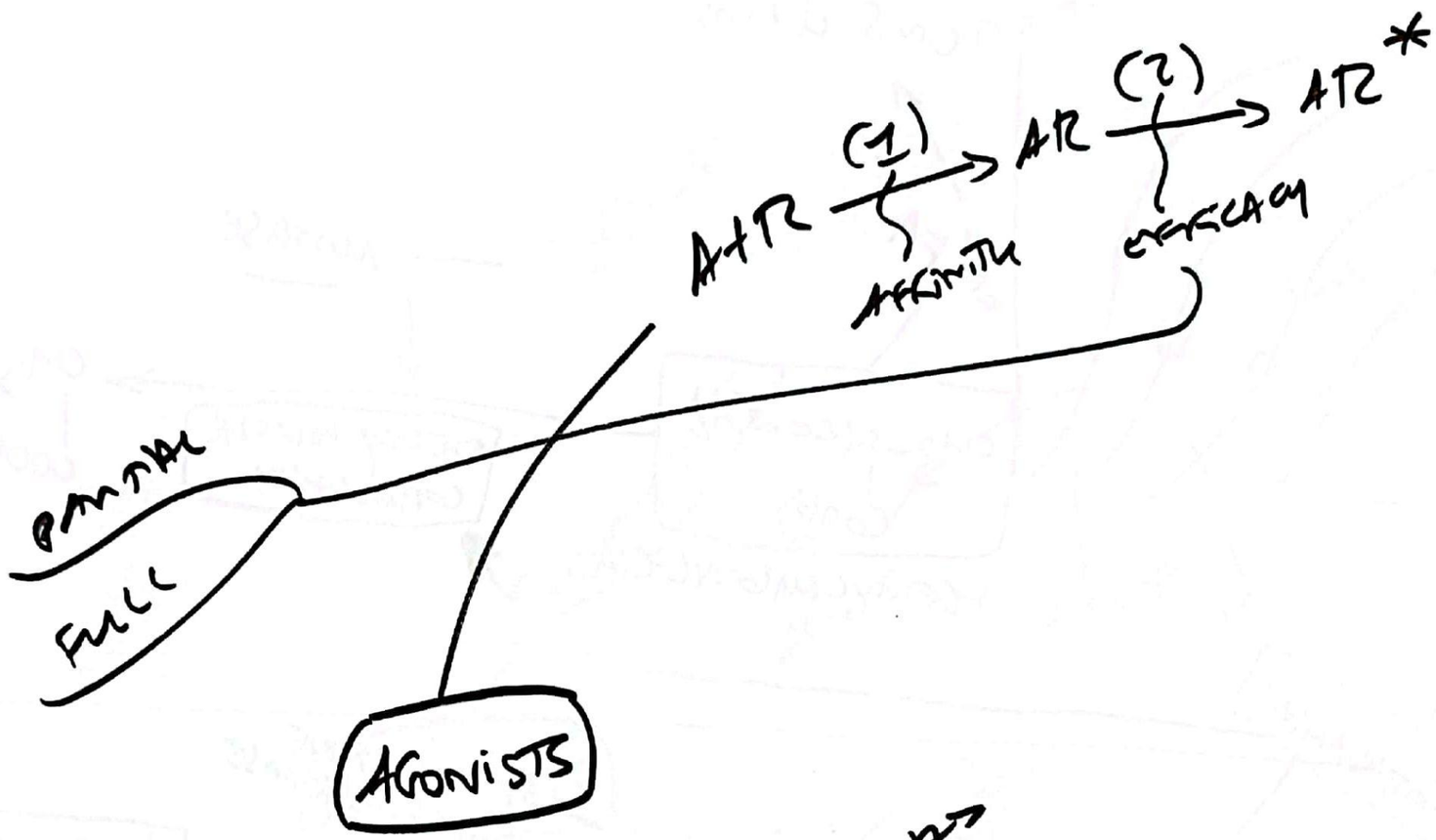
Backward rate = $K_{-1} [DR]$

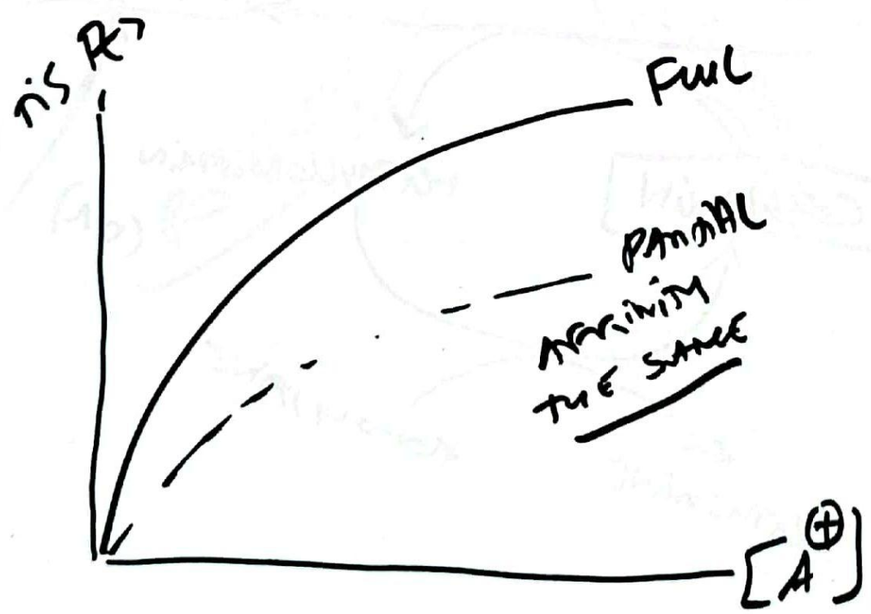
$K_d = K_{-1} / K_{+1}$

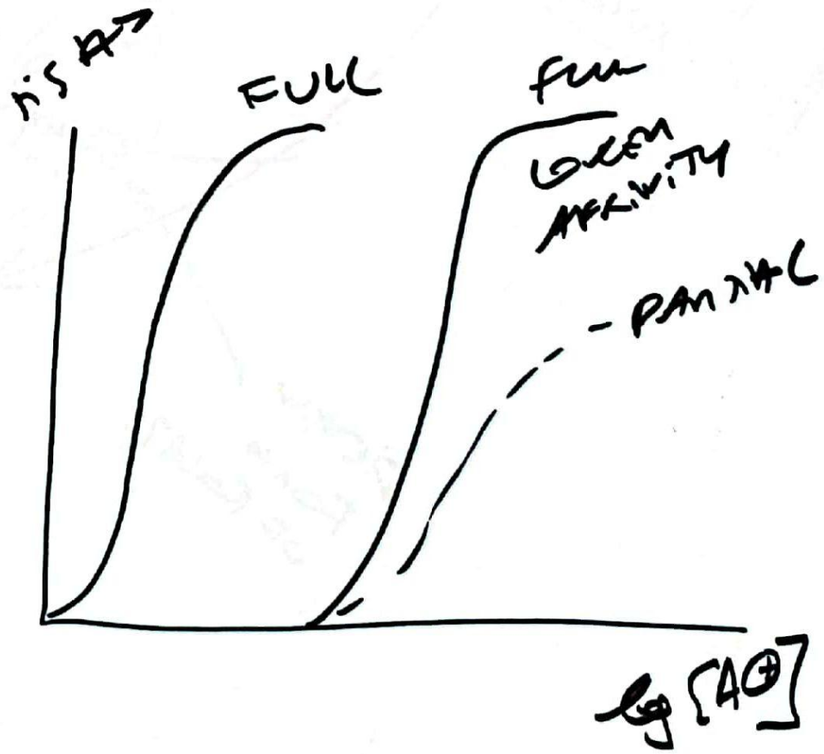
K_d dissociation constant
conc D that produces 50% max at ⇌

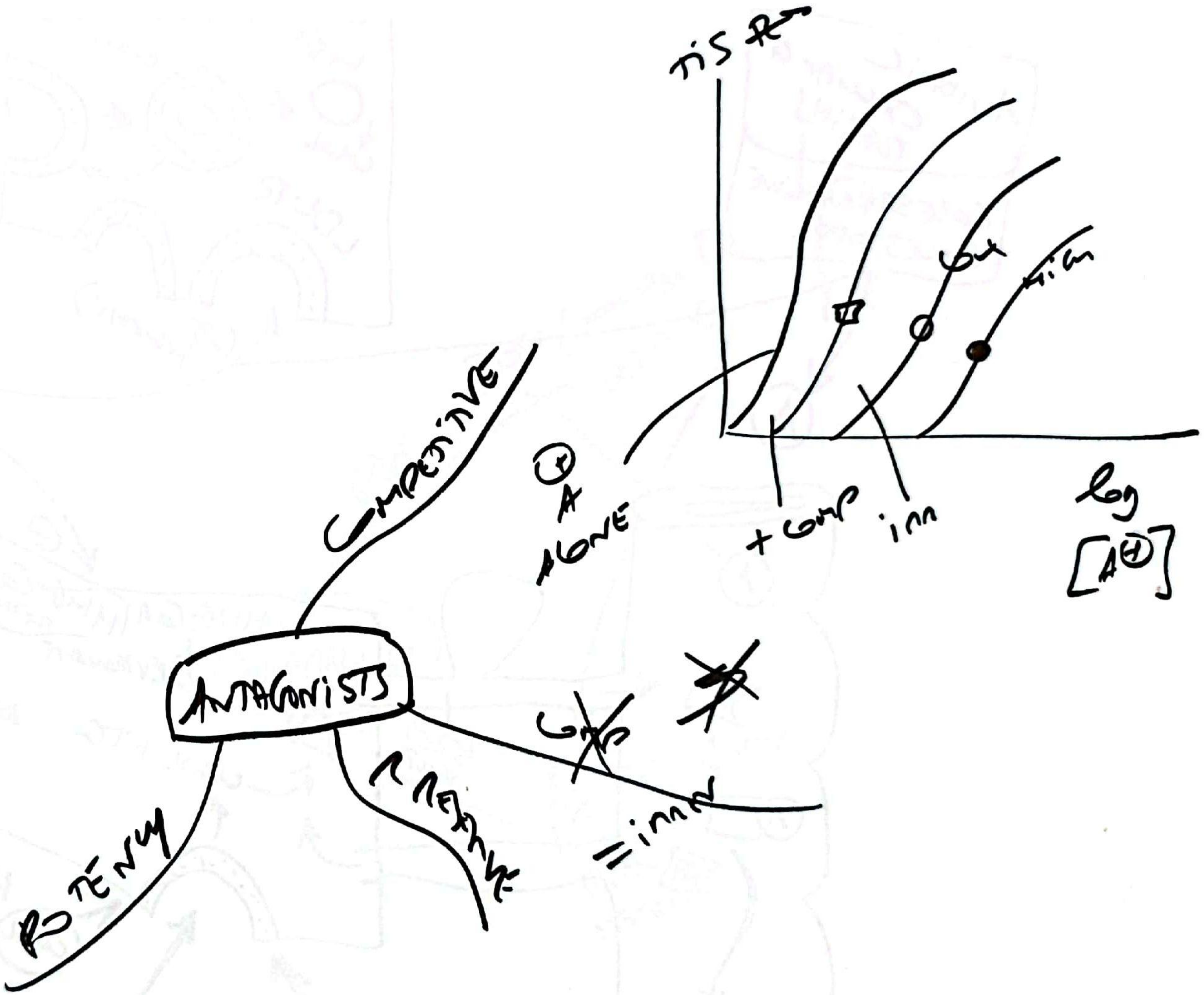
∅ R reserve

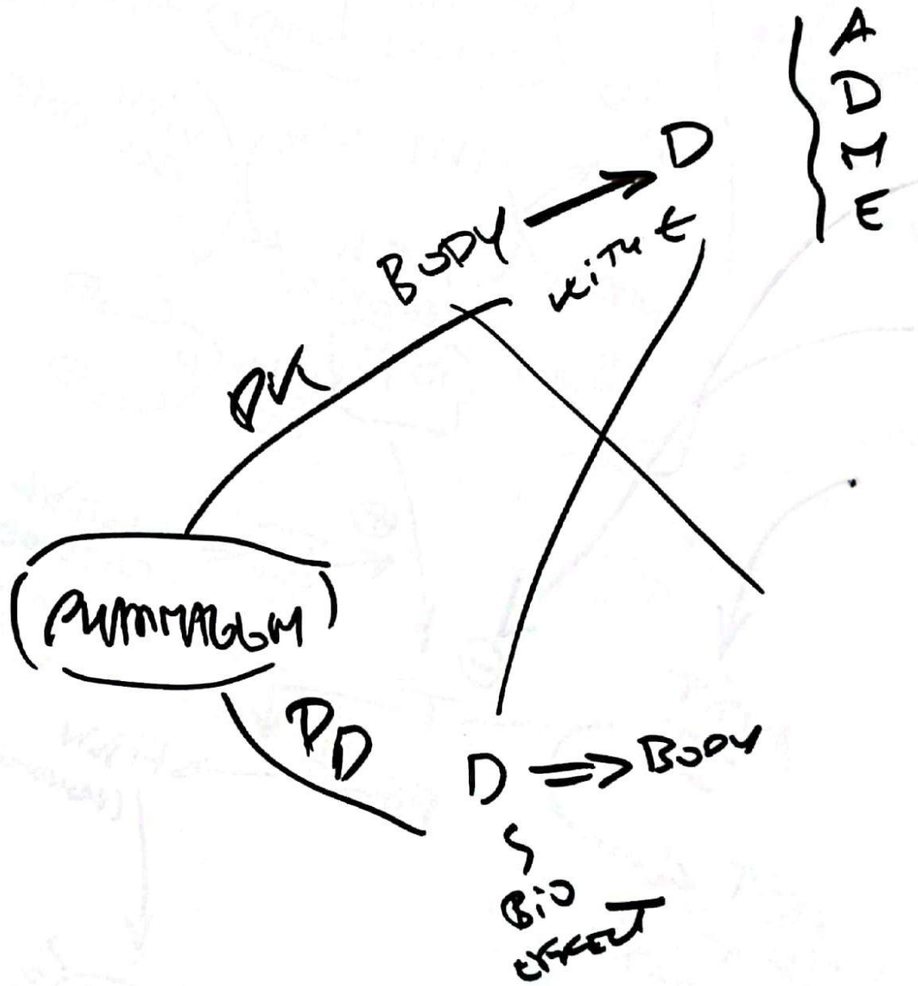
$K_a = 1/K_d$

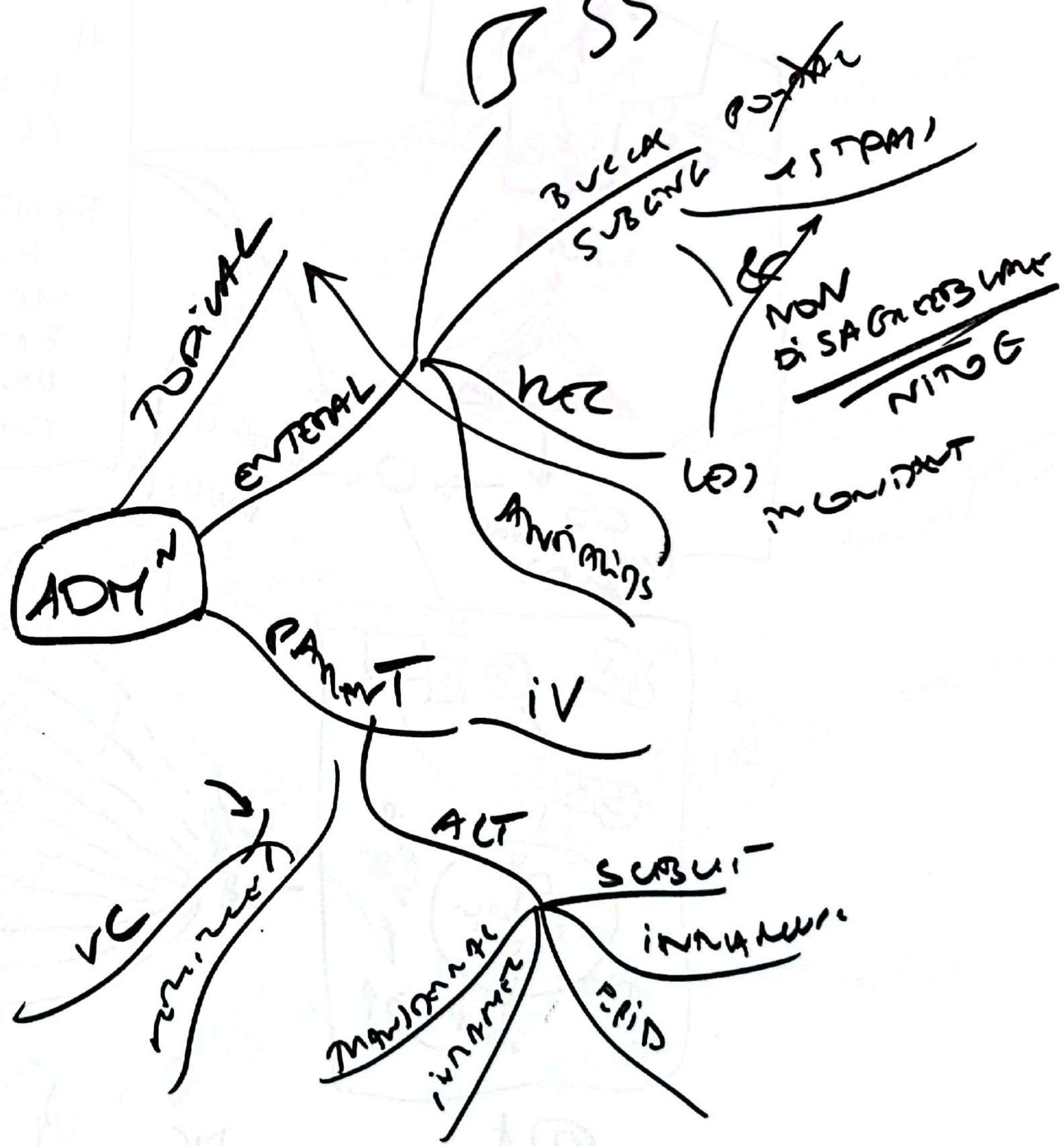

A+R
(1)
AR
(2)
AR*
AFFINITY
EFFICACY
PARTIAL
FULL
AGONISTS

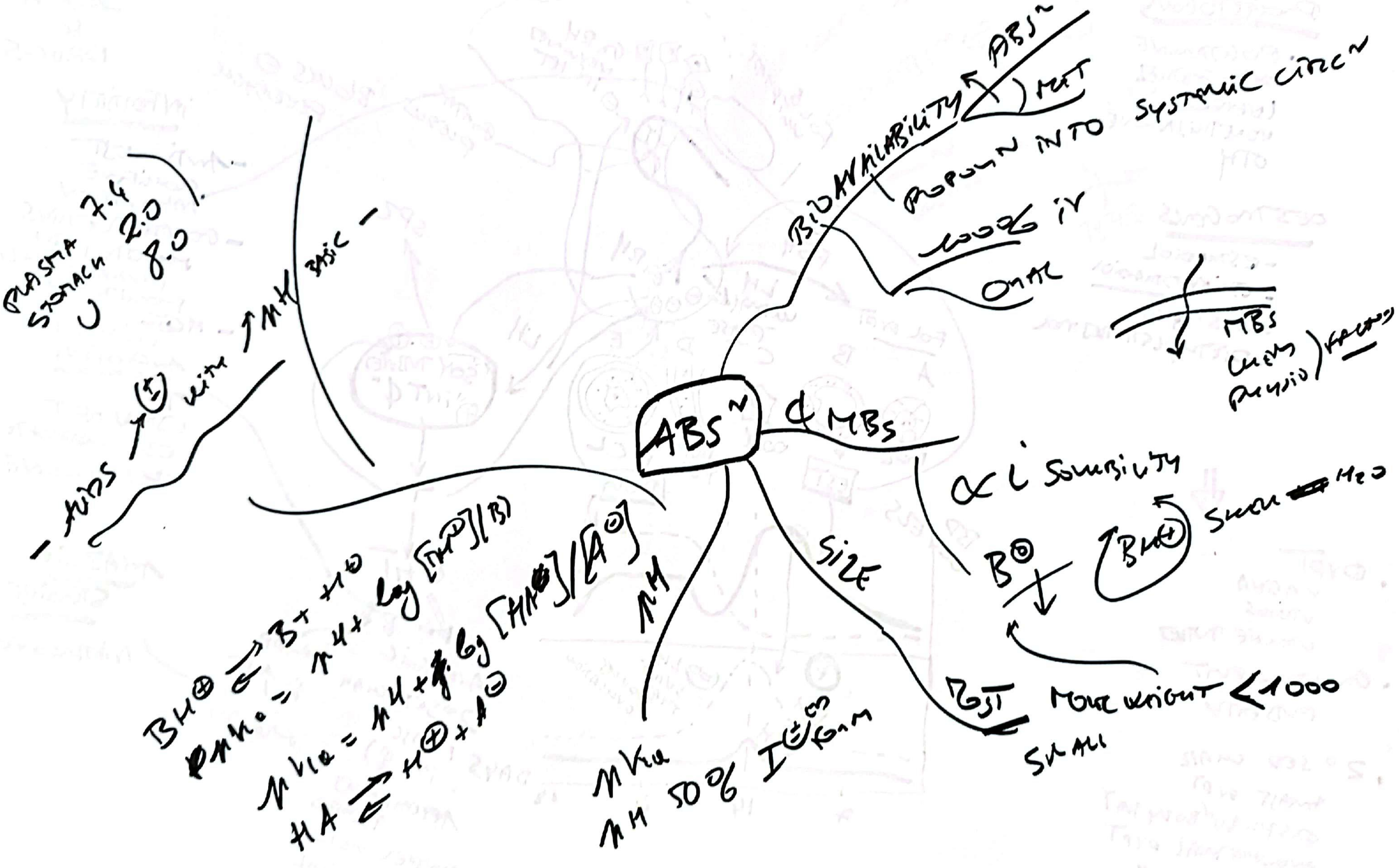

% R→
FULL
PARTIAL
AFFINITY
THE SAME
[A⊕]


% R→
FULL
FULL
GREATER
AFFINITY
PARTIAL
log [A⊕]


ANTAGONISTS
COMPETITIVE
POTENCY
A
ALONE
+ comp
irr
log


ADME
D
BODY
TIME
PK
PD
D ⇒ BODY
BIO
EFFECT

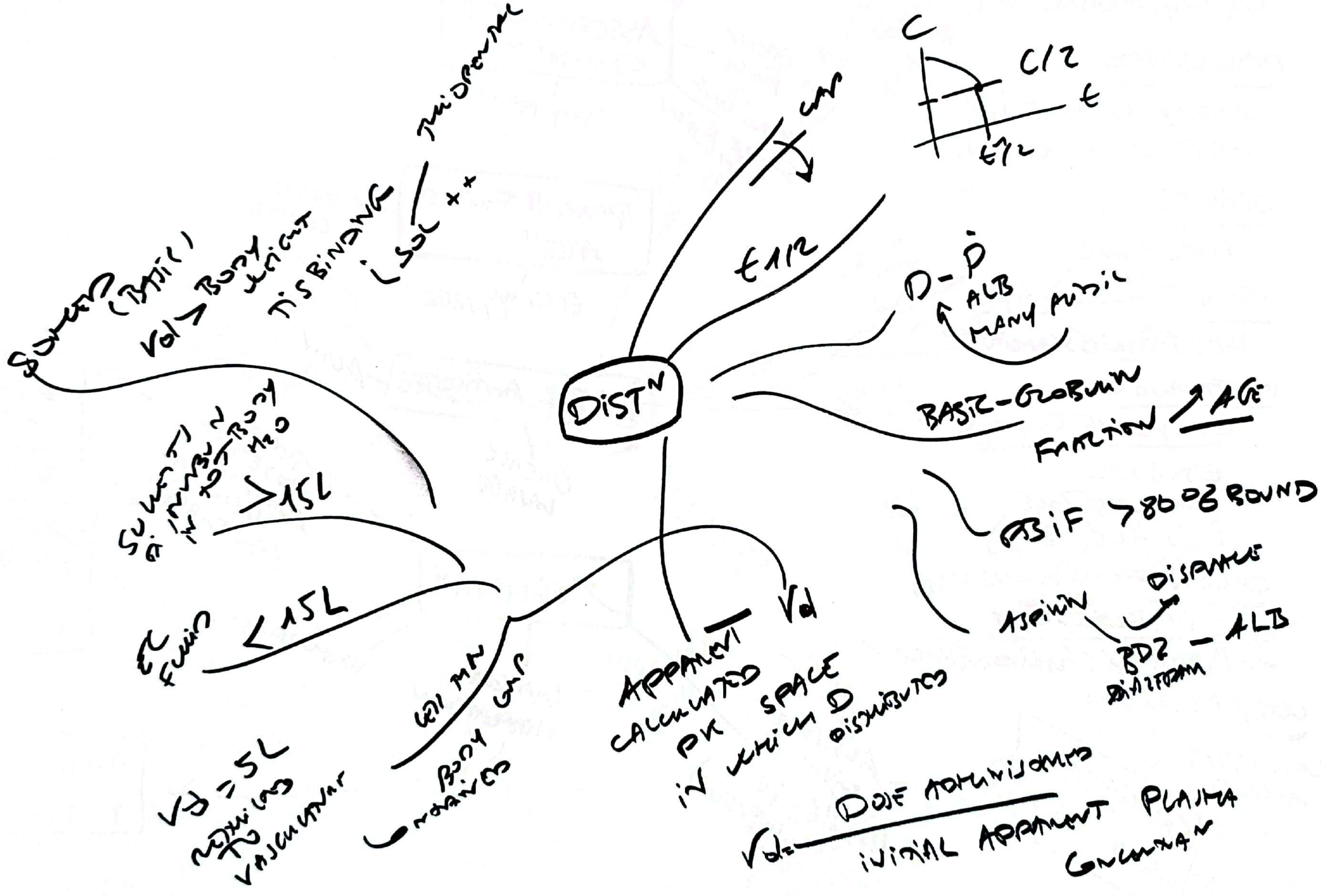

ADMIN
TOPICAL
ENTERAL
SS
REC
iV
ACT


ABSⁿ
BIOAVAILABILITY
ABSⁿ
MET
PROPORTION INTO SYSTEMIC CIRCⁿ
100% IV
ORAL
α MBs
MBs
LIPIDS
PROTEINS
α i SOLUBILITY
B⊖
BH⊕
SMALL
H2O
SIZE
POST
MOLE WEIGHT < 1000
SMALL
pH
pKa
pH 50% I⊕ ION
BH⊕ ⇌ B + H⊕
pKa = pH + log [BH⊕]/[B]
pKa = pH + log [HA]/[A⊖]
HA ⇌ H⊕ + A⊖
ACIDS → ⊕ with ↑pH
BASIC
PLASMA 7.4
STOMACH 2.0
U 8.0

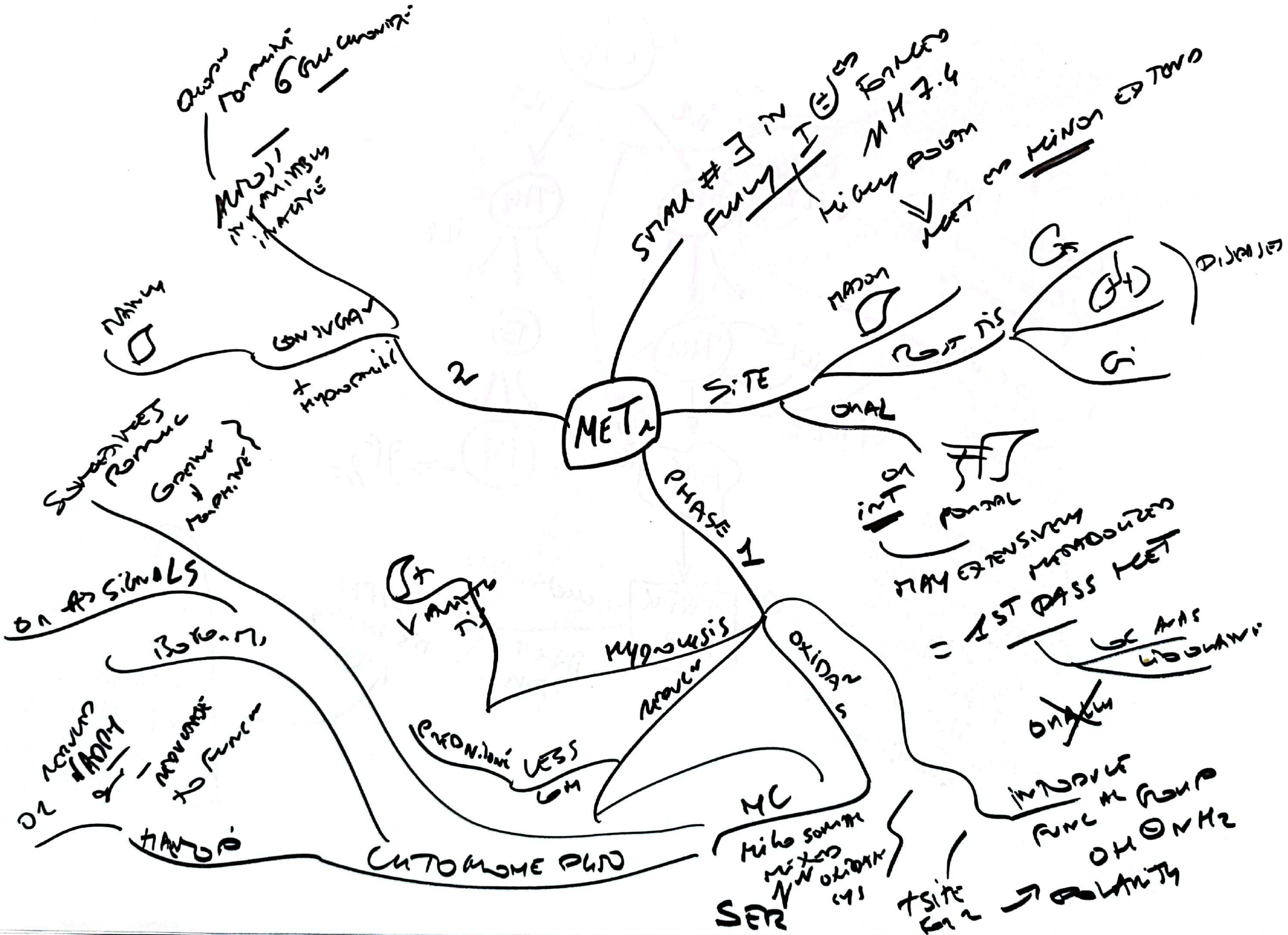
pH

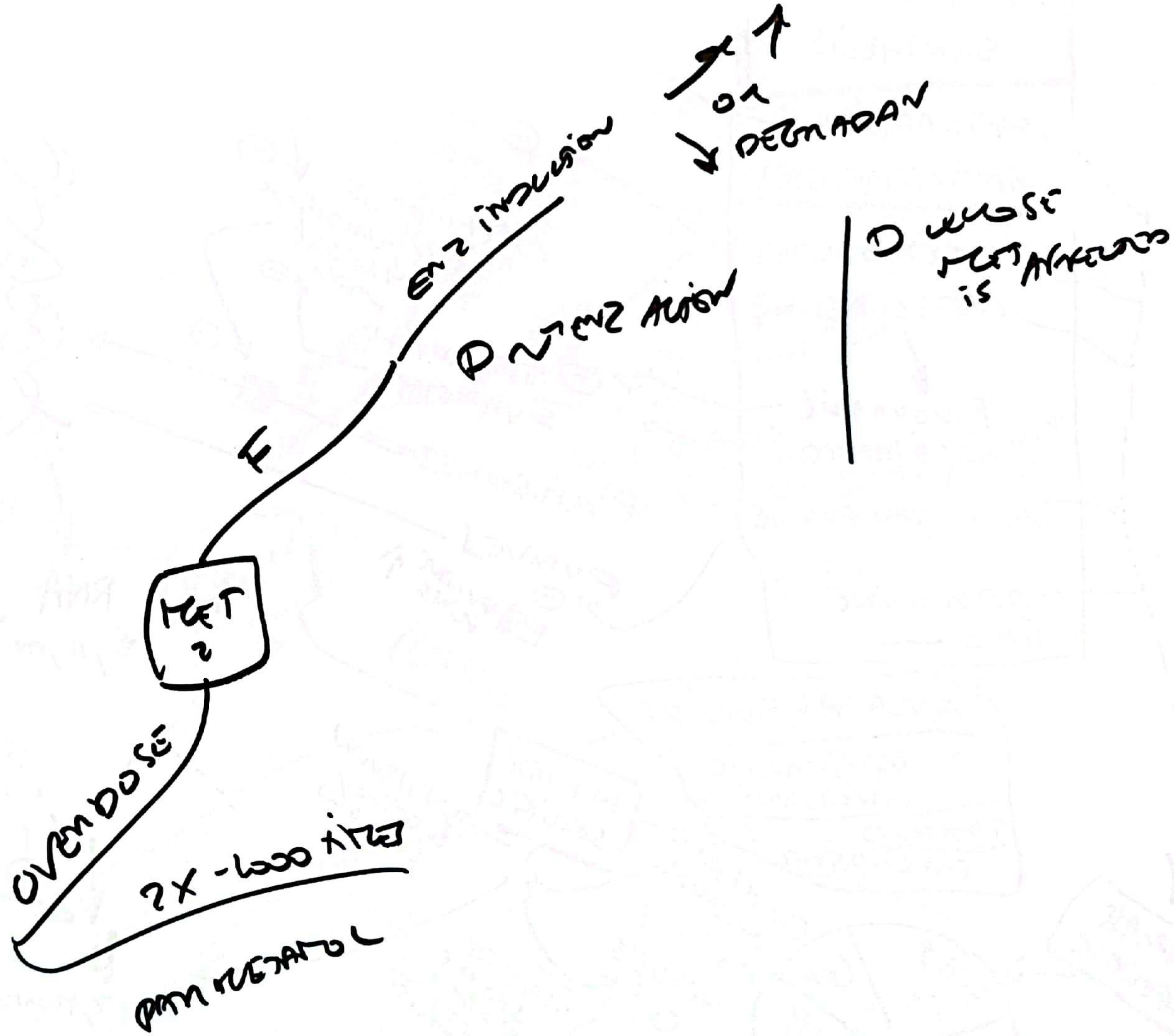
Aspirin weak acid pKa = 3.5
=> ABS^N (+) in STOM
weaker (0)

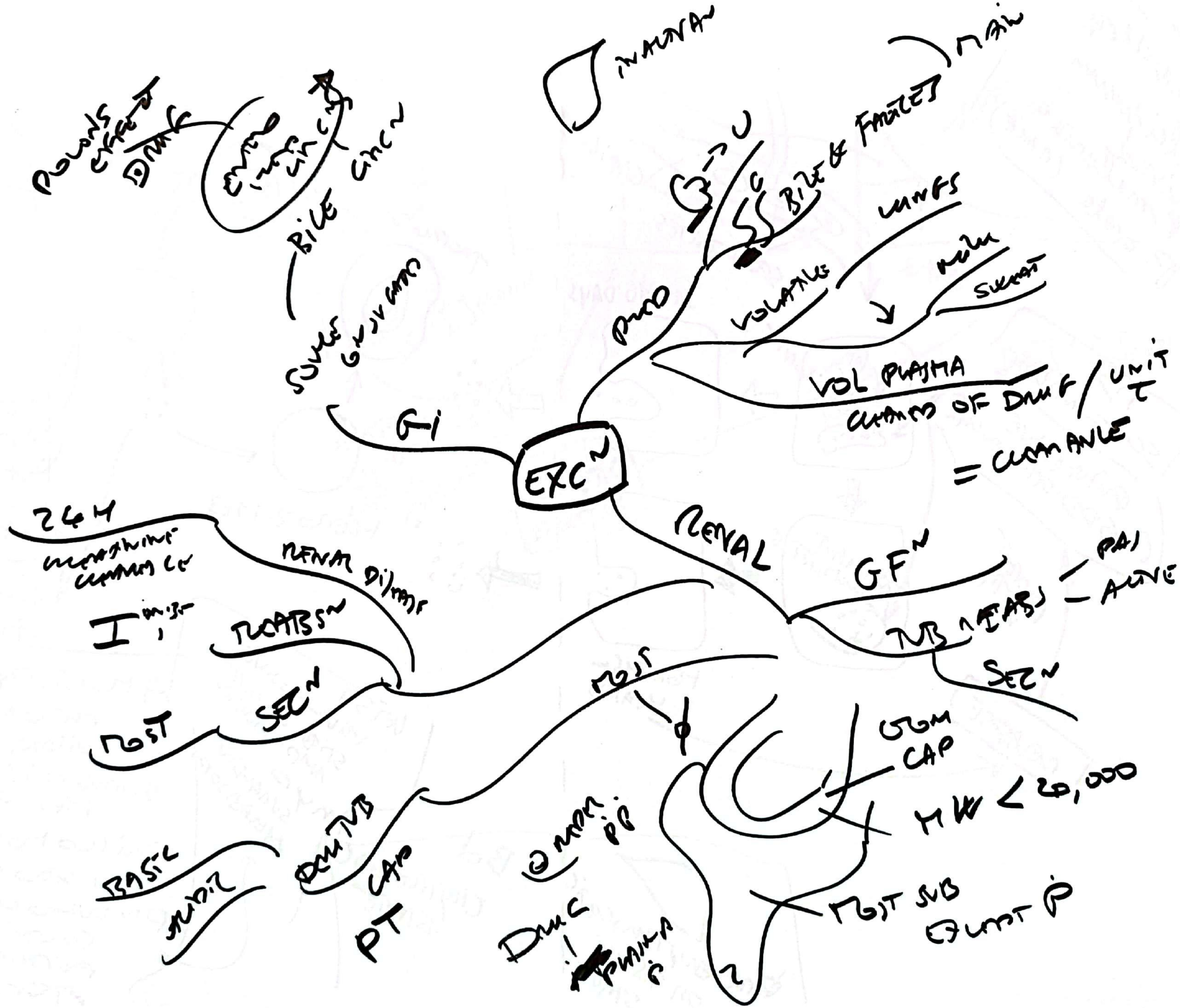
Morphine weak BASE pKa = 8.0
→ BBB

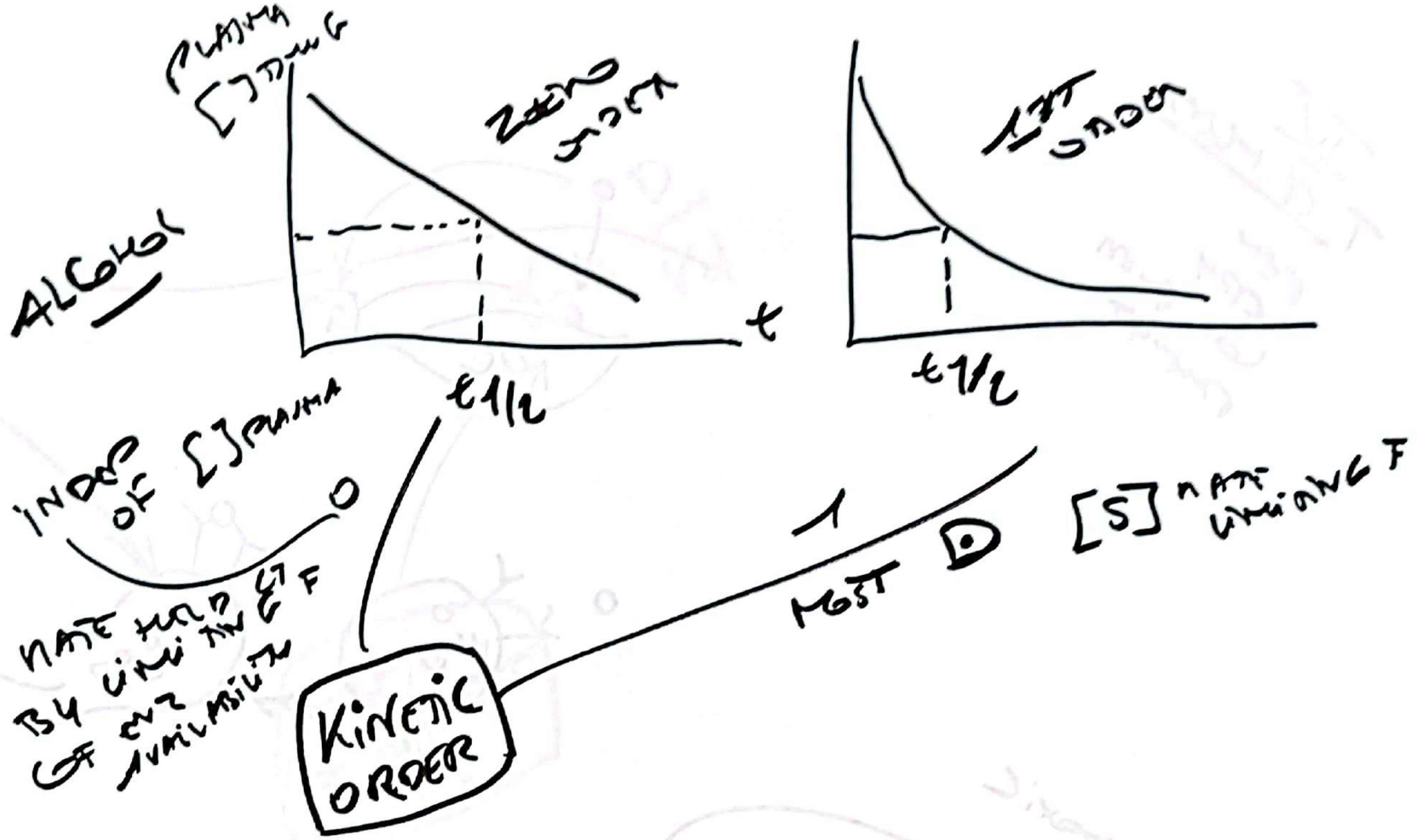


DISTN
C
C/2
t
t1/2
t1/2
D - D
ALB
MANY ACIDIC
BASIC - GLOBULIN
FRACTION ↗ AGE
PB iF > 80% BOUND
ASPIRIN
DISPLACE
BDZ - ALB
DIAZEPAM
APPARENT Vd
CALCULATED FOR SPACE IN WHICH D DISTRIBUTED
Vd = DOSE ADMINISTERED / INITIAL APPARENT PLASMA CONCENTRATION
Vd = 5L
RESTRICTED TO VASCULAR
CELL MEM
BODY CONTAINED
EC FLUID
< 15L
> 15L
Vd > BODY WEIGHT
TISSBINDING
L SOL ++


MET
2
CONJUGAT
+ HYDROPHILIC
MAINLY
MAKES MAINLY INACTIVE
COMMON FORMATION
GLUCURONIDATION
SITE
MAJOR
REST TIS
Gs
(H)
Gi
DISEASE
ORAL
INT OR PORTAL
MAY EXTENSIVELY METABOLIZED
= 1ST PASS MET
SMALL # ∃ IN ⊕ED FORMED
FULLY I MH 7.4
HIGHLY POLAR
⇒ MET ED MINOR EXTENT
PHASE 1
HYDROLYSIS
REDUCTION
OXIDATIONS
INTRODUCE FUNC AL GROUP
OH ⊖ NH2
OH
+ SITE FOR 2
→ POLARITY
MC
MICROSOMAL MIXED FUNCTION OXIDASE SYS
SER
β+ VARIOUS TIS
PREDOMINANT LESS
CYTOCHROME P450
HAEMO
O2
NADPH
MODERATE TO FUNCTION
OR AS SIGNALS
BIOTRANS
SUBSTANCES FORMING
GROWTH & MORPHINE

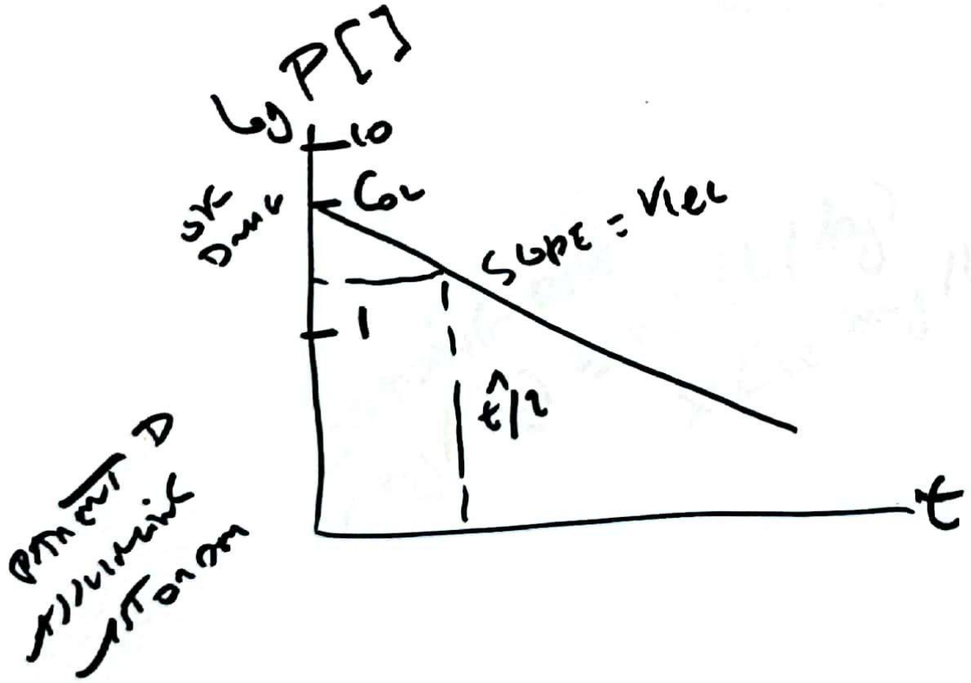

MET 2
F
ENZ INDUCTION
OR
OVERDOSE
PARACETAMOL

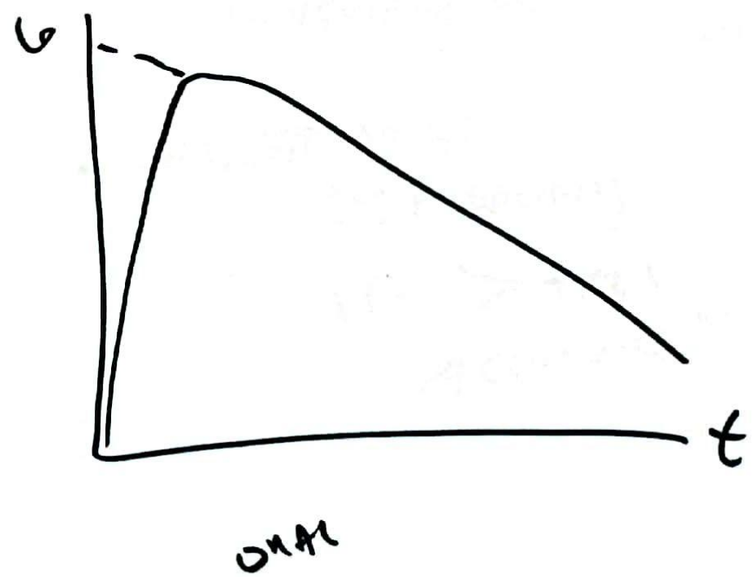

EXCN
GI
BILE
BILE CIRCN
PROLONGS EFFECT
DRUG
PULM
VOLATILE
LUNGS
MILK
SWEAT
BILE & FAECES
MAIN
VOL PLASMA
CLEARED OF DRUG / UNIT T
= CLEARANCE
RENAL
GFN
TUB REABS
PAS
ACTIVE
SECN
MOST
CAP
MW < 20,000
MOST SUB
DRUG
PLASMA
PT
CAP
BASIC
ACIDIC
MOST
SECN
REABSN
RENAL DISEASE
DECREASING CLEARANCE


PLASMA [ ] DRUG
ZERO ORDER
1ST ORDER
ALCOHOL
t
t 1/2
t 1/2
INDEP OF [ ] PLASMA
0
RATE HELD BY LIMITING F
BY LIMITING F OF ENZ AVAILABILITY
KINETIC ORDER
1
MOST D
[S] RATE LIMITING F

$$t_{1/2} = \frac{D}{V_d}$$

ONE COMPARTMENT MODEL





ISOMER

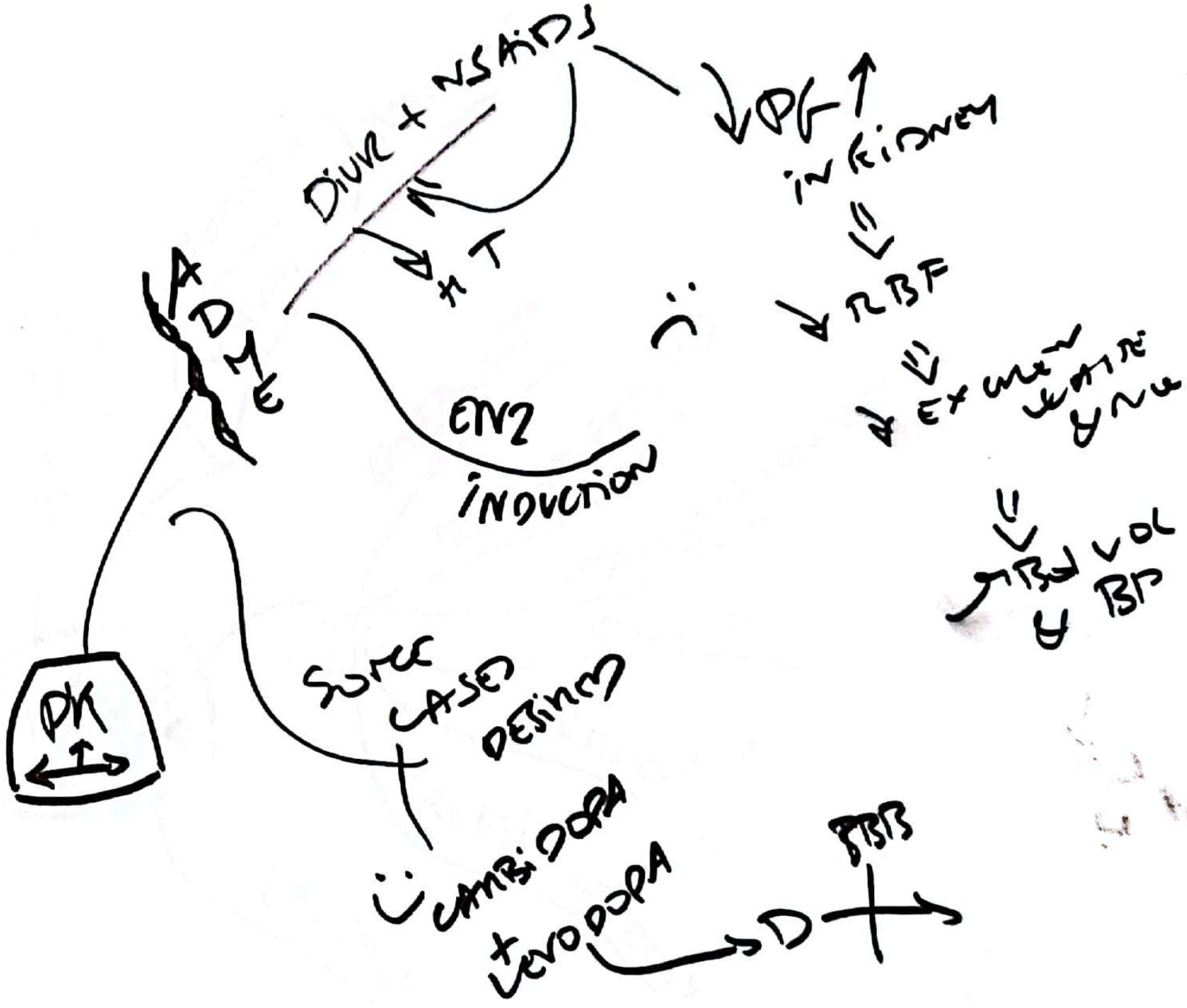
MODEL INDEP APPROACH

ROUTE
EVERY 6 HRS
WHEN ITS TERMINAL DISPOSIT
1/2 LIFE IS 6 HOURS

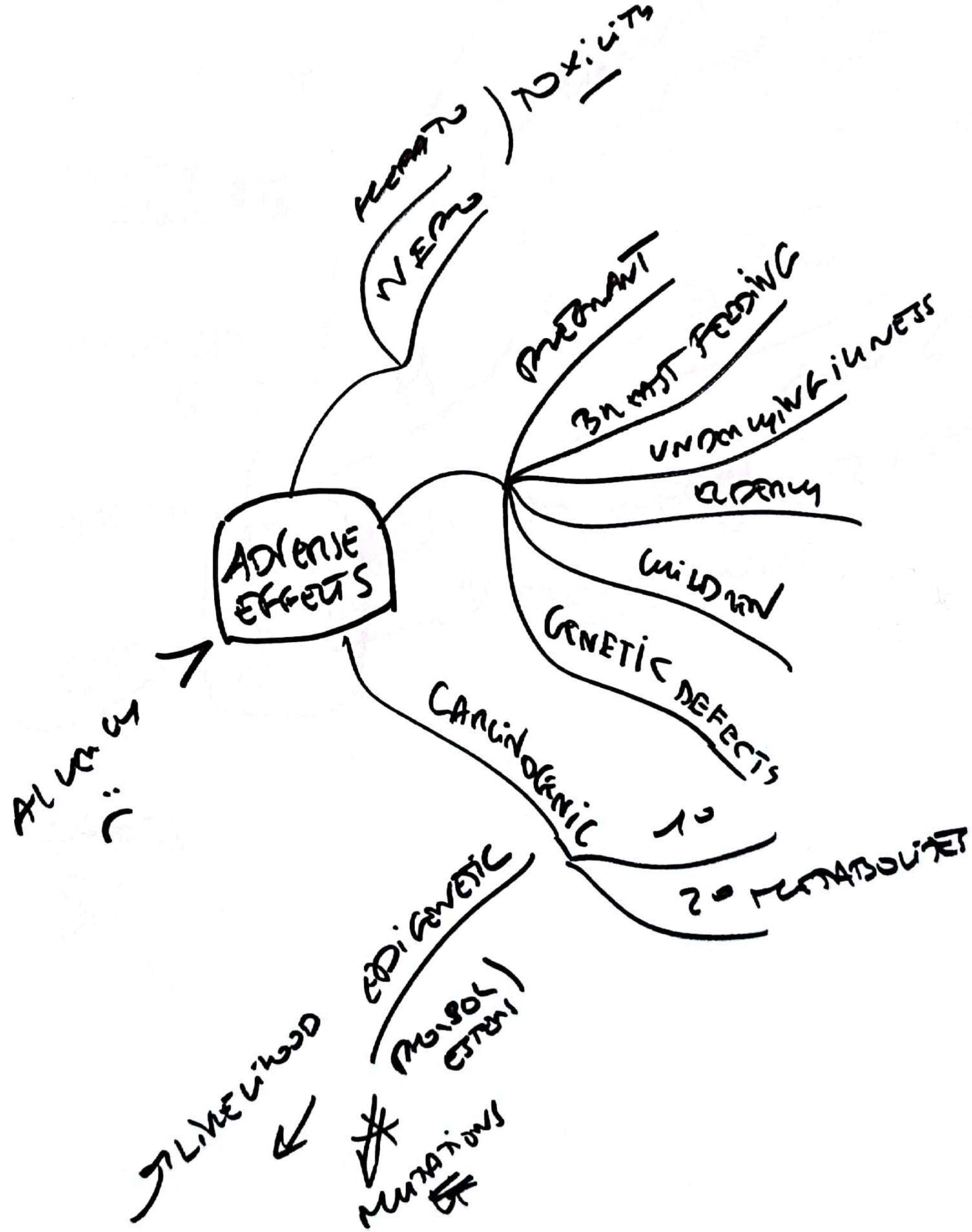
- t TO REACH STEADY STATE IS USUALLY EQUAL TO 4-5 1/2 LIVES

- AMOUNT AT SS ∝ FREQUENCY
  IF > 1/2 l
  ACCUMULATION

LOADING DOSE (mg/kg) = Vd (L/kg) × Css (mg/L)



ADME
DIUR + NSAIDS
HT
PG
IN KIDNEY
RBF
EXCRETION WATER & Na
BLD VOL & BP
ENZ INDUCTION
SOME CASES DESIRED
CARBIDOPA + LEVODOPA
D
BBB
PK



ADVERSE EFFECTS
NEPHRO
TOXICITY
PREGNANT
BREAST FEEDING
UNDERLYING ILLNESS
ELDERLY
CHILDREN
GENETIC DEFECTS
CARCINOGENIC
1°
2° METABOLITES
EPIGENETIC
MUTATIONS
LIKELIHOOD

PRECLINICAL

MAIN AIMS / MEANS OF INVESTIGATION

SUBJECTS

PHARMACOLOGY
TOXICOLOGY

IN VITRO
IN LAB ANIMALS

CLINICAL

(1) CLIN
D EFFECT & BIO AVAIL
EVALUATE SAFETY

HEALTHY &/OR PTS

(2) INITIAL STUDIES
EVALUATE EFFICACY

SMALL PTS

(3) - LARGE RANDOMIZED CONTROLLED TRIALS
- COMPARING NEW & OLD TX'S
- EVALUATE SAFE & EFFIC

LARGE

(4) POST MARKETING SURVEILLANCE
LT SAFETY
& RARE EVENTS
YELLOW CARD SCHEME

PTS
PRESCRIBED D

D HISTORY & DRPT

H
- CURRENT & PREVIOUS
- ADV REACTION & ALLERGIES
- FAM HIS ALLERGY
- RECREATIONAL & GENERAL
- E

DVT

< 10% SUMMATIVE CLINICAL ASSESSMENT

PK PD
: EFFICACY
D-ADR & SAFETY

& MONITORING