```
In[]:= (* Mathematica code for Model1 of Eshra et al. eLife 2021 *)
       (* Stefan Hallermann and Hartmut Schmidt Aug 2021 *)
```

Import

general

```
(* all Ca in uM, all times in ms, all ampltiudes and Nv in vesicels *)

In[]:= CmToVesConversionFactor = (1/90.12) * (1/70*^-18);(* explained in methods *)

In[]:= rrp = 10;(* pool of release-ready vesicles per connection *)

In[]:= dir = NotebookDirectory[];
       SetDirectory[dir];
       dataFolder = "../data to fit/";
```

tau1 Cm 5kHz

```
In[]:= data = Import[dataFolder <> "all_t1_v02_C5.txt", "Table"];
```

```
In[•]:= dataT1C5Ca = 0.001 * data[[All, 1]];
dataT1C5RelRate = 1000. * data[[All, 2]];
dataT1C5Delay = data[[All, 3]];
dataT1C5ChiRatio = data[[All, 4]];
dataT1C5Amplitude = CmToVesConversionFactor data[[All, 5]];

dataT1C5Nv = Table[0, {7}];
tmp1 = 1;
tmp2 = 6;
dataT1C5Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C5Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C5Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C5Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C5Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C5Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C5Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
```

tau1 Cm 10kHz

```
In[•]:= data = Import[dataFolder <> "all_t1_v02_C10.txt", "Table"];
```

In[ ]:=
```
dataT1C10Ca = 0.001 * data[[All, 1]];
dataT1C10RelRate = 1000. * data[[All, 2]];
dataT1C10Delay = data[[All, 3]];
dataT1C10ChiRatio = data[[All, 4]];
dataT1C10Amplitude = CmToVesConversionFactor data[[All, 5]];

dataT1C10Nv = Table[0, {7}];
tmp1 = 1;
tmp2 = 6;
dataT1C10Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C10Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C10Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C10Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C10Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C10Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
tmp1 += 1;
tmp2 += 1;
dataT1C10Nv[[tmp1]] = CmToVesConversionFactor data[[All, tmp2]];
```

tau1 Deconv

In[ ]:=
```
data = Import[dataFolder <> "all_t1_v02_D.txt", "Table"];
```

```
In[•]:= dataT1DCa = 0.001 * data[[All, 1]];
dataT1DRelRate = 1000. * data[[All, 2]];
dataT1DDelay = data[[All, 3]];
dataT1DChiRatio = data[[All, 4]];
dataT1DAmplitude = data[[All, 5]];

dataT1DNv = Table[0, {7}];
tmp1 = 1; tmp2 = 6; dataT1DNv[[tmp1]] = data[[All, tmp2]];
tmp1 += 1; tmp2 += 1; dataT1DNv[[tmp1]] = data[[All, tmp2]];
tmp1 += 1; tmp2 += 1; dataT1DNv[[tmp1]] = data[[All, tmp2]];
tmp1 += 1; tmp2 += 1; dataT1DNv[[tmp1]] = data[[All, tmp2]];
tmp1 += 1; tmp2 += 1; dataT1DNv[[tmp1]] = data[[All, tmp2]];
tmp1 += 1; tmp2 += 1; dataT1DNv[[tmp1]] = data[[All, tmp2]];
tmp1 += 1; tmp2 += 1; dataT1DNv[[tmp1]] = data[[All, tmp2]];
```

tau2 Cm 5kHz

```
In[•]:= data = Import[dataFolder <> "all_t2_v02_C5.txt", "Table"];
```

```
In[•]:= dataT2C5Ca = 0.001 * data[[All, 1]];
dataT2C5RelRate = 1000. * data[[All, 2]];
dataT2C5Amplitude2 = CmToVesConversionFactor data[[All, 3]];
dataT2C5Amplitude1 = CmToVesConversionFactor data[[All, 4]];
```

tau2 Cm 10kHz

```
In[•]:= data = Import[dataFolder <> "all_t2_v02_C10.txt", "Table"];
```

```
In[•]:= dataT2C10Ca = 0.001 * data[[All, 1]];
dataT2C10RelRate = 1000. * data[[All, 2]];
dataT2C10Amplitude2 = CmToVesConversionFactor data[[All, 3]];
dataT2C10Amplitude1 = CmToVesConversionFactor data[[All, 4]];
```

tau2 Deconv

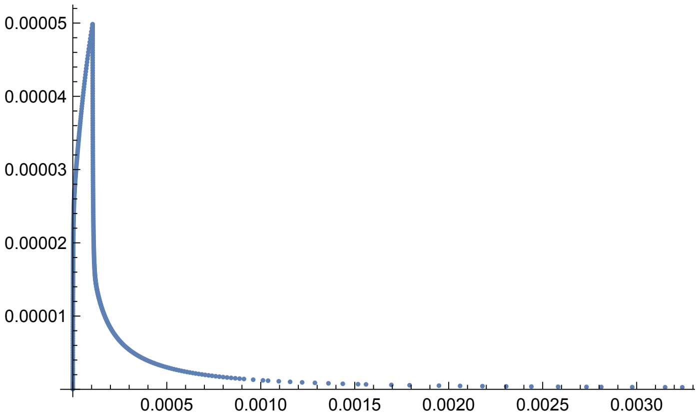
```
In[•]:= data = Import[dataFolder <> "all_t2_v02_D.txt", "Table"];
```

```
In[•]:= dataT2DCa = 0.001 * data[[All, 1]];
dataT2DRelRate = 1000. * data[[All, 2]];
dataT2DAmplitude2 = data[[All, 3]];
dataT2DAmplitude1 = data[[All, 4]];
```

local Ca

In[•]:=
```
data = Import[dataFolder <> "local Ca at 20 nm in uM and ms.txt", "Table"];
dataLocalCa = 1*^-6 data[[All, 1]];
dataLocalCaTime = 1*^-3 data[[All, 2]];
ListPlot[Transpose[{dataLocalCaTime, dataLocalCa}], PlotRange → All]
```

Out[•]=



General parameters and definitions

general stuff

In[•]:=
```
(* for calulations: time in s, Ca in M *)
numberOfFitParamToBeSaved = 16;
(*
1 max release

 Mono
2 chi2Mono
3 delayMono
4 ampMono
5 1/tau1Mono

 Bi
6 chi2Mono/chi2Bi
7 delay
8 amp
9 amp1 (=amp*relative amp1)
10 1/tau1
11 1/tau2

 merge
12 delay
13 amp
14 amp1
15 1/tau1
16 1/tau2
*)
cursorStart = -0.002;(*s*)
cursorEnd = 0.01;(*s*)
cursorEndLong = 0.061;(*s*)
timeOfNv = {0.0001, 0.0002, 0.001, 0.005, 0.01, 0.1, 0.4};
SeedRandom[1];
myMaxIterations = 100;
```

In[•]:=
```
timeStart = AbsoluteTime[]
```

Out[•]= $3.839313629403805 \times 10^9$

noiseRepeats

In[∘]:=
```
noiseRepeats = 3;
(* should be increased to 50 for a full dataset *)
myQuantile1 = 0.25;
myQuantile2 = 0.75;
```

export parameters

In[∘]:=
```
dtOfPlotsForExport = 20*^-5;
exportYes = 1;
```

sampling and myNoise

In[∘]:=
```
samplingOfDataInKHzC5 = 5;
myNoiseC5 = 0.1;(*cannot be 0*)
signalToNoiseRatioC5 = 1.;(*minimum s-to-n-ratio to attempt fitting*)
dtOfDataC5 = (1/(1000 * samplingOfDataInKHzC5));

samplingOfDataInKHzC10 = 10;
myNoiseC10 = 0.1;(*cannot be 0*)
signalToNoiseRatioC10 = 1.;(*minimum s-to-n-ratio to attempt fitting*)
dtOfDataC10 = (1/(1000 * samplingOfDataInKHzC10));

samplingOfDataInKHzD = 10;
myNoiseD = 0.02;(*cannot be 0*)
signalToNoiseRatioD = 1.;(*minimum s-to-n-ratio to attempt fitting*)
dtOfDataD = (1/(1000 * samplingOfDataInKHzD));

samplingOfDataInKHzLong = 1;
myNoiseLong = 0.1;(*cannot be 0*)
dtOfDataLong = (1/(1000 * samplingOfDataInKHzLong));
```

number of simulations per DMN

```
In[]:= aNumberDMN05 = 2;
aNumberDMN2 = 2;
aNumberDMN10 = 2;

(* for full dataset: *)
(*
aNumberDMN05=2*20;
aNumberDMN2=2*17;
aNumberDMN10=2*10;
*)
```

Exp fit function

```
In[]:= myFitMono[t_] :=
  If[t <= delayMono, 0, ampMono (1 - Exp[-(t - delayMono) / tau1Mono])];

myFitBi[t_] := If[t <= delay, 0,
   amp (1 - amp1 Exp[-(t - delay) / tau1] - (1 - amp1) Exp[-(t - delay) / tau2])];

(*guess for 10 uM; will be changed according to a power of 1 law*)(*in s*)
ampGuess = 2.;(*each pool has size 1.0*)
tau1Guess = 0.001;(*in s*)
delayGuess = 0.0005;(*in s*)
amp1Guess = 0.5;
```

Calculate Ca transients

Concentrations in mol/l;
DMn uncaging according to Faas et al., 2005, 2007
First, the resting conditions are numerically calculated. Subsequently, the resulting values are used as initial conditions for the main simulations of the flash-evoked Ca2+ transitions . All calculations are repeated in a loop with increasing uncaging efficacy for three different DMN concentrations. The resulting free Ca2+ concentration is later used to drive the release schemes.

General definitions for all DMN conc.

```
In[]:= CaListReal = CaListDye = {};
```

0.5 mM DMN

general parameters

In[•]:=
```
TimeWindow = 0.006; (*End of simulation*)
tflash = 0.0;  (*Time of flash*)
PlStart = 0.; (*Plot start*)

af = 0.67; (*fast uncaging fraction; Faas et al*)

(*Select dye*)
OGB1 = 0;
OGB5N = 0;
OGB6F = 0;
Fluo5F = 1;

CaRest = 227. * 10 ^ -9; (*Free pre-flash rersting Ca;
equilibrates with all buffers and DM*)
MgT = 0.5 * 10 ^ -3; (*total Mg in pipette*)
γ = 0.; (*Pump rate*)

(*Concentrations of dye, buffers, DM*)
OGtotal  = 50. * 10^-6 ;
ATPtotal  = 5. * 10^-3 ;
MBtotal  = 480. * 10^-6 ;(*(*Delvendahl, PNAS, 2015*)*)

DMT  = 0.5 * 10^-3;  (*total concentration of DMn *)
(*uncaging efficiency*)
aStartDMN05 = 0.08;
aEndDMN05 = 0.5;
```

definitions and loop

In[•]:=
```
(*Dye*)
If[OGB1 == 1,
 kOnOG  = 4.3 * 10^8;
kOffOG  = 103.;]

If[OGB5N == 1,
 kOnOG  = 2.5 * 10^8;
kOffOG  = 6000.;]

If[OGB6F == 1,
```

```
 kOnOG  = 3. * 10^8;
kOffOG = 900.;]

If[Fluo5F == 1,
 kOnOG  = 3. * 10^8;
kOffOG = 249.;] (*Delvendahl PNAS; before: 432*)

KdOG = kOffOG / kOnOG;
kappaOG = OGtotal / KdOG;

(*ATP*)
kOnATP  = 5. * 10^8;
kOffATP = 100 000.;
kOnMgATP  = 1. * 10^7; (*Bollmann Dissertation S. 59; *)
kOffMgATP = 1000.;

KdATP = kOffATP / kOnATP;
kappaATP = ATPtotal / KdATP;
KdMgATP = kOffMgATP / kOnMgATP;

(*DM*)
If[MgT == 0.,
 kOnDM = 1.98 * 10^7; (*Faas Plos Biol, 2007*)
kOffDM = 0.14;
 ,
 kOnDM = 2.9 * 10^7; (*Faas Biophys J, 2005*)
kOffDM = 0.19;
]

(*Mg binding constants for DMn, DMf, DMs*)
kOnMg = 1.3 * 10^5; (*all values for Mg are from Faas et al., 2005*)
kOffMg = 0.2;

(*Ca binding constants for PP*)
kOnPP2 = kOnPP1 = kOnDM;
kOffPP2 = 3.6 * 10 ^ 3;
If[MgT == 0.,
 kOffPP1 = 7. * 10 ^ 4;,
 kOffPP1 = 6.9 * 10 ^ 4; ]

(*Mg binding constants for PP1,PP2*)
kOffMgPP = 3. * 10 ^ 2; (*for PP1,PP2*)
konMgPP = kOnMg; (*koMgPP not used in below diff. eq., only kOnMg*)

(*Equilibrium constants (not complete)*)
KdDM = kOffDM / kOnDM;
```

```
KdPP1 = kOffPP1 / kOnPP1;
KdMg  =  kOffMg / kOnMg;
kappaDM = DMT / KdDM;

 (*Endogenous buffer*)
kOnMB  = 5 * 10^8; (*Delvendahl, PNAS, 2015*)
kOffMB  = 16 000;
KdMB  =  kOffMB / kOnMB;

TRest = 1000.;


(*---------------------------------  Loop  ----------
 ---------------------------------------*)
(*---------------------------------  Loop  ----------
 ---------------------------------------*)
(*---------------------------------  Loop  ----------
 ---------------------------------------*)


For[aCount = 1, aCount ≤ aNumberDMN05, aCount += 1,
  a = 10 ^ (Log10[aStartDMN05] +
      (aCount - 1) * (Log10[aEndDMN05] - Log10[aStartDMN05]) / (aNumberDMN05 - 1));

  (*------------------------- Resting
    Equations -----------------------------------------*)

  (*Dye*)
  OGRest := {

    OG[0] == OGtotal,
    CaOG[0] == 0,

    OG '[tt] == - kOnOG * CaRest * OG[tt] + kOffOG * CaOG[tt],
    CaOG '[tt] == kOnOG * CaRest * OG[tt] - kOffOG * CaOG[tt]
   }
  ;

  (*ATP*)
  ATPRest := {

    ATP[0] == ATPtotal,
    CaATP[0] == 0,
    MgATP[0] == 0,

    ATP '[tt] == - kOnATP * CaRest * ATP[tt] + kOffATP * CaATP[tt] -
      kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt],
```

```
   CaATP'[tt] == kOnATP * CaRest * ATP[tt] - kOffATP * CaATP[tt],
   MgATP'[tt] == kOnMgATP * Mg[tt] * ATP[tt] - kOffMgATP * MgATP[tt]

  }

;

(*DM nitrophene*)
DMnRest := {

   DMn[0] == (1 - a) * DMT,
   CaDMn[0] == 0.,
   MgDMn[0] == 0.,

   DMn'[tt] == -kOnDM * CaRest * DMn[tt] +
     kOffDM * CaDMn[tt] - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt],
   CaDMn'[tt] == kOnDM * CaRest * DMn[tt] - kOffDM * CaDMn[tt],
   MgDMn'[tt] == kOnMg * Mg[tt] * DMn[tt] - kOffMg * MgDMn[tt]
  }

;
DMfRest := {

   DMf[0] == a * af * DMT,
   CaDMf[0] == 0.,
   MgDMf[0] == 0.,

   DMf'[tt] == -kOnDM * CaRest * DMf[tt] +
     kOffDM * CaDMf[tt] - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt],
   CaDMf'[tt] == kOnDM * CaRest * DMf[tt] - kOffDM * CaDMf[tt],
   MgDMf'[tt] == kOnMg * Mg[tt] * DMf[tt] - kOffMg * MgDMf[tt]
  }

;
DMsRest := {

   DMs[0] == a * (1 - af) * DMT,
   CaDMs[0] == 0.,
   MgDMs[0] == 0.,

   DMs'[tt] == -kOnDM * CaRest * DMs[tt] +
     kOffDM * CaDMs[tt] - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt],
   CaDMs'[tt] == kOnDM * CaRest * DMs[tt] - kOffDM * CaDMs[tt],
   MgDMs'[tt] == kOnMg * Mg[tt] * DMs[tt] - kOffMg * MgDMs[tt]
  }
;
```

```
(*Endogeneous buffer*)
MBRest := {

   MB[0] == MBtotal,
   CaMB[0] == 0,

   MB'[tt] == -kOnMB * CaRest * MB[tt] + kOffMB * CaMB[tt],
   CaMB'[tt] == kOnMB * CaRest * MB[tt] - kOffMB * CaMB[tt]
  }

;

(*Free Mg*)
MgfRest := {
   Mg[0] == MgT,

   Mg'[tt] ==
    -kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt]
     - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt]
     - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt]
     - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt]
  }

;
EqRest := {ATPRest, MgfRest, OGRest, DMnRest, DMfRest, DMsRest, MBRest};
VarsRest := {ATP, Mg, CaATP, MgATP, CaOG, OG, DMn,
   CaDMn, MgDMn, DMf, CaDMf, MgDMf, DMs, CaDMs, MgDMs, MB, CaMB}
;
solr := NDSolve[EqRest, VarsRest, {tt, 0, TRest}]
;

Ca0 = CaRest;
Mg0 = Extract[Mg[TRest] /. solr, 1];
ATP0 = Extract[ATP[TRest] /. solr, 1];
CaATP0 = Extract[CaATP[TRest] /. solr, 1];
MgATP0 = Extract[MgATP[TRest] /. solr, 1];
OG0 = Extract[OG[TRest] /. solr, 1];
CaOG0 = Extract[CaOG[TRest] /. solr, 1];
DMn0 = Extract[DMn[TRest] /. solr, 1];
CaDMn0 = Extract[CaDMn[TRest] /. solr, 1];
MgDMn0 = Extract[MgDMn[TRest] /. solr, 1];
DMf0 = Extract[DMf[TRest] /. solr, 1];
CaDMf0 = Extract[CaDMf[TRest] /. solr, 1];
MgDMf0 = Extract[MgDMf[TRest] /. solr, 1];
DMs0 = Extract[DMs[TRest] /. solr, 1];
CaDMs0 = Extract[CaDMs[TRest] /. solr, 1];
MgDMs0 = Extract[MgDMs[TRest] /. solr, 1];
```

```
MB0 = Extract[MB[TRest] /. solr, 1];
CaMB0 = Extract[CaMB[TRest] /. solr, 1];


ClearAll[EqRest, VarsRest];


(*------------------------- Flash
  Equations -------------------------------------------*)

(*Dye*)
BufferOG := {

  OG[0] == OG0,
  CaOG[0] == CaOG0,

  OG'[tt] == -kOnOG * Ca[tt] * OG[tt] + kOffOG * CaOG[tt],
  CaOG'[tt] == kOnOG * Ca[tt] * OG[tt] - kOffOG * CaOG[tt]}
;

(*ATP*)
BufferATP := {

  ATP[0] == ATP0,
  CaATP[0] == CaATP0,
  MgATP[0] == MgATP0,

  ATP'[tt] == -kOnATP * Ca[tt] * ATP[tt] + kOffATP * CaATP[tt] -
    kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt],
  CaATP'[tt] == kOnATP * Ca[tt] * ATP[tt] - kOffATP * CaATP[tt],
  MgATP'[tt] == kOnMgATP * Mg[tt] * ATP[tt] - kOffMgATP * MgATP[tt]
 }
;

(*fast (tauf) and slow (taus) time constants for uncageing;
Faas et al., 2005,2007*)
If[MgT == 0.,
  tauf = 15.2 * 10^-6; (*Faas, 2007*)
  taus = 1.9 * 10^-3;
  ,
  tauf = 15. * 10^-6; (*Faas,2005*)
  taus = 2. * 10^-3; ]

;

(*The differential equations*)
(*non uncaging fraction of DMn*)
```

```
BufferDMn := {

  DMn[0] == DMn0,
  CaDMn[0] == CaDMn0,
  MgDMn[0] == MgDMn0,

  DMn'[tt] == -kOnDM * Ca[tt] * DMn[tt] +
    kOffDM * CaDMn[tt] - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt],
  CaDMn'[tt] == kOnDM * Ca[tt] * DMn[tt] - kOffDM * CaDMn[tt],
  MgDMn'[tt] == kOnMg * Mg[tt] * DMn[tt] - kOffMg * MgDMn[tt]
 }
;

(*fast uncaging fraction of DMn*)
BufferDMf := {

  DMf[0] == DMf0,
  CaDMf[0] == CaDMf0,
  MgDMf[0] == MgDMf0,

  DMf'[tt] == -kOnDM * Ca[tt] * DMf[tt] + kOffDM * CaDMf[tt] - kOnMg * Mg[tt] *
     DMf[tt] + kOffMg * MgDMf[tt] - 1/tauf * DMf[tt] * UnitStep[tt - tflash],
  CaDMf'[tt] == kOnDM * Ca[tt] * DMf[tt] - kOffDM * CaDMf[tt] -
    1/tauf * CaDMf[tt] * UnitStep[tt - tflash],
  MgDMf'[tt] == kOnMg * Mg[tt] * DMf[tt] - kOffMg * MgDMf[tt] -
    1/tauf * MgDMf[tt] * UnitStep[tt - tflash]
 }

;
(*slow uncaging fraction of DMn*)
BufferDMs := {

  DMs[0] == DMs0,
  CaDMs[0] == CaDMs0,
  MgDMs[0] == MgDMs0,

  DMs'[tt] == -kOnDM * Ca[tt] * DMs[tt] + kOffDM * CaDMs[tt] - kOnMg * Mg[tt] *
     DMs[tt] + kOffMg * MgDMs[tt] - 1 / taus * DMs[tt] * UnitStep[tt - tflash],
  CaDMs'[tt] == kOnDM * Ca[tt] * DMs[tt] - kOffDM * CaDMs[tt] -
    1 / taus * CaDMs[tt] * UnitStep[tt - tflash],
  MgDMs'[tt] == kOnMg * Mg[tt] * DMs[tt] - kOffMg * MgDMs[tt] -
    1 / taus * MgDMs[tt] * UnitStep[tt - tflash]
 }
;

(*Photoproducts*)
(*PP2: comes from DMf,DMs and MgDMf,MgDMs; but also binds Ca*)
```

```
BufferPP2 := {

  PP2[0] == 0,
  CaPP2[0] == 0,
  MgPP2[0] == 0,

  PP2'[tt] == -kOnPP2 * Ca[tt] * PP2[tt] + kOffPP2 * CaPP2[tt] -
    kOnMg * Mg[tt] * PP2[tt] + kOffMgPP * MgPP2[tt] + 2 * (1 / tauf * DMf[tt] *
        UnitStep[tt - tflash] + 1 / taus * DMs[tt] * UnitStep[tt - tflash])
    + 1 / tauf * MgDMf[tt] * UnitStep[tt - tflash] +
    1 / taus * MgDMs[tt] * UnitStep[tt - tflash],

  CaPP2'[tt] == kOnPP2 * Ca[tt] * PP2[tt] - kOffPP2 * CaPP2[tt],

  MgPP2'[tt] == kOnMg * Mg[tt] * PP2[tt] - kOffMgPP * MgPP2[tt] + 1 / tauf *
     MgDMf[tt] * UnitStep[tt - tflash] + 1 / taus * MgDMs[tt] * UnitStep[tt - tflash]
 }
;

(*PP1: Comes from CaDMf,CaDMs and binds Ca and Mg*)
BufferPP1 := {

  PP1[0] == 0,
  CaPP1[0] == 0,
  MgPP1[0] == 0,

  PP1'[tt] == -kOnPP1 * Ca[tt] * PP1[tt] +
    kOffPP1 * CaPP1[tt] - kOnMg * Mg[tt] * PP1[tt] + kOffMgPP * MgPP1[tt]
    + 1 / tauf * CaDMf[tt] * UnitStep[tt - tflash] +
    1 / taus * CaDMs[tt] * UnitStep[tt - tflash],

  CaPP1'[tt] == kOnPP1 * Ca[tt] * PP1[tt] -
    kOffPP1 * CaPP1[tt] + 1 / tauf * CaDMf[tt] * UnitStep[tt - tflash] +
    1 / taus * CaDMs[tt] * UnitStep[tt - tflash],

  MgPP1'[tt] == kOnMg * Mg[tt] * PP1[tt] - kOffMgPP * MgPP1[tt]

 }
;

(*Endogeneous Buffer*)
BufferMB := {

  MB[0] == MB0,
  CaMB[0] == CaMB0,

  MB'[tt] == -kOnMB * Ca[tt] * MB[tt] + kOffMB * CaMB[tt],
```

```
    CaMB'[tt] == kOnMB * Ca[tt] * MB[tt] - kOffMB * CaMB[tt]}

  ;

(*Clear[Eqns,Vars,sol]*)

  (*Free Ca*)
  FreeCa := {
    Ca[0] == Ca0,

    Ca'[tt] == -γ * (Ca[tt] - CaRest)
      (*DMn*)
      - kOnPP1 * Ca[tt] * PP1[tt] + kOffPP1 * CaPP1[tt]
      - kOnPP2 * Ca[tt] * PP2[tt] + kOffPP2 * CaPP2[tt]
      - kOnDM * Ca[tt] * DMn[tt] + kOffDM * CaDMn[tt]
      - kOnDM * Ca[tt] * DMf[tt] + kOffDM * CaDMf[tt]
      - kOnDM * Ca[tt] * DMs[tt] + kOffDM * CaDMs[tt]
      (*buffers*)
      - kOnATP * Ca[tt] * ATP[tt] + kOffATP * CaATP[tt]
      - kOnMB * Ca[tt] * MB[tt] + kOffMB * CaMB[tt]
      (*dye*)
      - kOnOG * Ca[tt] * OG[tt] + kOffOG * CaOG[tt]
    }
  ;

  (*Free Mg*)
  FreeMg := {
    Mg[0] == Mg0,

    Mg'[tt] ==
     -kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt]
      - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt]
      - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt]
      - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt]
      - kOnMg * Mg[tt] * PP2[tt] + kOffMgPP * MgPP2[tt]
      - kOnMg * Mg[tt] * PP1[tt] + kOffMgPP * MgPP1[tt]
   }

  ;

  Eqns := {BufferDMn, BufferDMf, BufferDMs, BufferATP,
    BufferPP1, BufferPP2, FreeCa, FreeMg, BufferMB, BufferOG}
  ;
  Vars := {ATP, CaATP, MgATP, Ca, Mg, CaDMn, DMn, CaDMf, DMf, CaDMs,
    DMs, CaPP1, PP1, CaPP2, PP2, MgPP2, MgPP1, MB, CaMB, OG, CaOG}
  ;
  sol := NDSolve[Eqns, Vars, {tt, 0., TimeWindow}
```

```
    (*,Method→{"EquationSimplification"->"Solve"}*)]
  ;
  CafP = Extract[Ca[TimeWindow] /. sol, 1];
  CafOG = KdOG * CaOG[tt] / OG[tt];

  AppendTo[CaListReal, Evaluate[{Ca[tt]} /. sol]];
  AppendTo[CaListDye, Evaluate[{CafOG} /. sol]];

 ];
```

2 mM DMN

general parameters

```
In[•]:= TimeWindow = 0.006; (*End of simulation*)
tflash = 0.0;  (*Time of flash*)
PlStart = 0.; (*Plot start*)

af = 0.67; (*fast uncaging fraction; Faas et al*)

(*Select dye*)
OGB1 = 0;
OGB5N = 1;
OGB6F = 0;
Fluo5F = 0;

CaRest = 227. * 10^-9; (*Free pre-flash rersting Ca;
equilibrates with all buffers and DM*)
MgT = 0.5 * 10^-3; (*total Mg in pipette*)
γ = 0.; (*Pump rate*)

(*Concentrations of dye, buffers, DM*)
OGtotal  = 200. * 10^-6 ;
ATPtotal  = 5. * 10^-3 ;
MBtotal  = 480. * 10^-6 ;(*(*Delvendahl, PNAS, 2015*)*)

DMT  = 2. * 10^-3;  (*total concentration of DMn *)
(*uncaging efficiency*)
aStartDMN2 = 0.15;
aEndDMN2 = 0.55;
```

definitions and loop

```
In[•]:= (*Dye*)
If[OGB1 == 1,
```

```
 kOnOG  = 4.3 * 10^8;
kOffOG = 103.;]

If[OGB5N == 1,
 kOnOG  = 2.5 * 10^8;
kOffOG = 6000.;]

If[OGB6F == 1,
 kOnOG  = 3. * 10^8;
kOffOG = 900.;]

If[Fluo5F == 1,
 kOnOG  = 3. * 10^8;
kOffOG = 249.;] (*Delvendahl PNAS; before: 432*)

KdOG = kOffOG / kOnOG;
kappaOG = OGtotal / KdOG;

(*ATP*)
kOnATP  = 5. * 10^8;
kOffATP = 100 000.;
kOnMgATP  = 1. * 10^7; (*Bollmann Dissertation S. 59; *)
kOffMgATP = 1000.;

KdATP = kOffATP / kOnATP;
kappaATP = ATPtotal / KdATP;
KdMgATP = kOffMgATP / kOnMgATP;

(*DM*)
If[MgT == 0.,
 kOnDM = 1.98 * 10^7; (*Faas Plos Biol, 2007*)
kOffDM = 0.14;
 ,
 kOnDM = 2.9 * 10^7; (*Faas Biophys J, 2005*)
kOffDM = 0.19;
]

(*Mg binding constants for DMn, DMf, DMs*)
kOnMg = 1.3 * 10^5; (*all values for Mg are from Faas et al., 2005*)
kOffMg = 0.2;

(*Ca binding constants for PP*)
kOnPP2 = kOnPP1 = kOnDM;
kOffPP2 = 3.6 * 10^3;
If[MgT == 0.,
 kOffPP1 = 7. * 10^4;,
```

```
 kOffPP1 = 6.9 * 10^4; ]

(*Mg binding constants for PP1,PP2*)
kOffMgPP = 3. * 10^2; (*for PP1,PP2*)
konMgPP = kOnMg; (*koMgPP not used in below diff. eq., only kOnMg*)

(*Equilibrium constants (not complete)*)
KdDM = kOffDM / kOnDM;
KdPP1 = kOffPP1 / kOnPP1;
KdMg = kOffMg / kOnMg;
kappaDM = DMT / KdDM;

 (*Endogenous buffer*)
kOnMB = 5 * 10^8;(*Delvendahl, PNAS, 2015*)
kOffMB = 16000;
KdMB = kOffMB / kOnMB;

TRest = 1000.;


(*----------------------------------  Loop  ----------
 ----------------------------------------*)
(*----------------------------------  Loop  ----------
 ----------------------------------------*)
(*----------------------------------  Loop  ----------
 ----------------------------------------*)

For[aCount = 1, aCount ≤ aNumberDMN2, aCount += 1,
  a = 10^(Log10[aStartDMN2] +
      (aCount - 1) * (Log10[aEndDMN2] - Log10[aStartDMN2]) / (aNumberDMN2 - 1));

  (*------------------------- Resting
    Equations ------------------------------------------*)

  (*Dye*)
  OGRest := {

    OG[0] == OGtotal,
    CaOG[0] == 0,

    OG'[tt] == -kOnOG * CaRest * OG[tt] + kOffOG * CaOG[tt],
    CaOG'[tt] == kOnOG * CaRest * OG[tt] - kOffOG * CaOG[tt]
   }
  ;

  (*ATP*)
  ATPRest := {
```

```
  ATP[0] == ATPtotal,
  CaATP[0] == 0,
  MgATP[0] == 0,

  ATP'[tt] == -kOnATP * CaRest * ATP[tt] + kOffATP * CaATP[tt] -
    kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt],
  CaATP'[tt] == kOnATP * CaRest * ATP[tt] - kOffATP * CaATP[tt],
  MgATP'[tt] == kOnMgATP * Mg[tt] * ATP[tt] - kOffMgATP * MgATP[tt]

 }

;

(*DM nitrophene*)
DMnRest := {

  DMn[0] == (1 - a) * DMT,
  CaDMn[0] == 0.,
  MgDMn[0] == 0.,

  DMn'[tt] == -kOnDM * CaRest * DMn[tt] +
    kOffDM * CaDMn[tt] - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt],
  CaDMn'[tt] == kOnDM * CaRest * DMn[tt] - kOffDM * CaDMn[tt],
  MgDMn'[tt] == kOnMg * Mg[tt] * DMn[tt] - kOffMg * MgDMn[tt]
 }

;
DMfRest := {

  DMf[0] == a * af * DMT,
  CaDMf[0] == 0.,
  MgDMf[0] == 0.,

  DMf'[tt] == -kOnDM * CaRest * DMf[tt] +
    kOffDM * CaDMf[tt] - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt],
  CaDMf'[tt] == kOnDM * CaRest * DMf[tt] - kOffDM * CaDMf[tt],
  MgDMf'[tt] == kOnMg * Mg[tt] * DMf[tt] - kOffMg * MgDMf[tt]
 }

;
DMsRest := {

  DMs[0] == a * (1 - af) * DMT,
  CaDMs[0] == 0.,
  MgDMs[0] == 0.,
```

```
  DMs'[tt] == -kOnDM * CaRest * DMs[tt] +
     kOffDM * CaDMs[tt] - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt],
  CaDMs'[tt] == kOnDM * CaRest * DMs[tt] - kOffDM * CaDMs[tt],
  MgDMs'[tt] == kOnMg * Mg[tt] * DMs[tt] - kOffMg * MgDMs[tt]
 }
;

(*Endogeneous buffer*)
MBRest := {

  MB[0] == MBtotal,
  CaMB[0] == 0,

  MB'[tt] == -kOnMB * CaRest * MB[tt] + kOffMB * CaMB[tt],
  CaMB'[tt] == kOnMB * CaRest * MB[tt] - kOffMB * CaMB[tt]
 }

;

(*Free Mg*)
MgfRest := {
  Mg[0] == MgT,

  Mg'[tt] ==
   -kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt]
    - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt]
    - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt]
    - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt]
 }

;
EqRest := {ATPRest, MgfRest, OGRest, DMnRest, DMfRest, DMsRest, MBRest};
VarsRest := {ATP, Mg, CaATP, MgATP, CaOG, OG, DMn,
  CaDMn, MgDMn, DMf, CaDMf, MgDMf, DMs, CaDMs, MgDMs, MB, CaMB}
;
solr := NDSolve[EqRest, VarsRest, {tt, 0, TRest}]
;

Ca0 = CaRest;
Mg0 = Extract[Mg[TRest] /. solr, 1];
ATP0 = Extract[ATP[TRest] /. solr, 1];
CaATP0 = Extract[CaATP[TRest] /. solr, 1];
MgATP0 = Extract[MgATP[TRest] /. solr, 1];
OG0 = Extract[OG[TRest] /. solr, 1];
CaOG0 = Extract[CaOG[TRest] /. solr, 1];
DMn0 = Extract[DMn[TRest] /. solr, 1];
CaDMn0 = Extract[CaDMn[TRest] /. solr, 1];
```

```
  MgDMn0 = Extract[MgDMn[TRest] /. solr, 1];
  DMf0 = Extract[DMf[TRest] /. solr, 1];
  CaDMf0 = Extract[CaDMf[TRest] /. solr, 1];
  MgDMf0 = Extract[MgDMf[TRest] /. solr, 1];
  DMs0 = Extract[DMs[TRest] /. solr, 1];
  CaDMs0 = Extract[CaDMs[TRest] /. solr, 1];
  MgDMs0 = Extract[MgDMs[TRest] /. solr, 1];
  MB0 = Extract[MB[TRest] /. solr, 1];
  CaMB0 = Extract[CaMB[TRest] /. solr, 1];


  ClearAll[EqRest, VarsRest];


  (*------------------------- Flash
    Equations -------------------------------------------*)

  (*Dye*)
  BufferOG := {

    OG[0] == OG0,
    CaOG[0] == CaOG0,

    OG'[tt] == -kOnOG * Ca[tt] * OG[tt] + kOffOG * CaOG[tt],
    CaOG'[tt] == kOnOG * Ca[tt] * OG[tt] - kOffOG * CaOG[tt]}
  ;

  (*ATP*)
BufferATP := {

    ATP[0] == ATP0,
    CaATP[0] == CaATP0,
    MgATP[0] == MgATP0,

    ATP'[tt] == -kOnATP * Ca[tt] * ATP[tt] + kOffATP * CaATP[tt] -
      kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt],
    CaATP'[tt] == kOnATP * Ca[tt] * ATP[tt] - kOffATP * CaATP[tt],
    MgATP'[tt] == kOnMgATP * Mg[tt] * ATP[tt] - kOffMgATP * MgATP[tt]
   }
  ;

  (*fast (tauf) and slow (taus) time constants for uncageing;
  Faas et al., 2005,2007*)
If[MgT == 0.,
   tauf = 15.2 * 10^-6;  (*Faas, 2007*)
   taus = 1.9 * 10^-3;
   ,
```

```
 tauf = 15. * 10 ^ -6;  (*Faas,2005*)
 taus = 2. * 10 ^ -3; ]

;

(*The differential equations*)
(*non uncaging fraction of DMn*)
BufferDMn := {

  DMn[0] == DMn0,
  CaDMn[0] == CaDMn0,
  MgDMn[0] == MgDMn0,

  DMn'[tt] == -kOnDM * Ca[tt] * DMn[tt] +
    kOffDM * CaDMn[tt] - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt],
  CaDMn'[tt] == kOnDM * Ca[tt] * DMn[tt] - kOffDM * CaDMn[tt],
  MgDMn'[tt] == kOnMg * Mg[tt] * DMn[tt] - kOffMg * MgDMn[tt]
 }
;

(*fast uncaging fraction of DMn*)
BufferDMf := {

  DMf[0] == DMf0,
  CaDMf[0] == CaDMf0,
  MgDMf[0] == MgDMf0,

  DMf'[tt] == -kOnDM * Ca[tt] * DMf[tt] + kOffDM * CaDMf[tt] - kOnMg * Mg[tt] *
     DMf[tt] + kOffMg * MgDMf[tt] - 1 / tauf * DMf[tt] * UnitStep[tt - tflash],
  CaDMf'[tt] == kOnDM * Ca[tt] * DMf[tt] - kOffDM * CaDMf[tt] -
    1 / tauf * CaDMf[tt] * UnitStep[tt - tflash],
  MgDMf'[tt] == kOnMg * Mg[tt] * DMf[tt] - kOffMg * MgDMf[tt] -
    1 / tauf * MgDMf[tt] * UnitStep[tt - tflash]
 }

;
(*slow uncaging fraction of DMn*)
BufferDMs := {

  DMs[0] == DMs0,
  CaDMs[0] == CaDMs0,
  MgDMs[0] == MgDMs0,

  DMs'[tt] == -kOnDM * Ca[tt] * DMs[tt] + kOffDM * CaDMs[tt] - kOnMg * Mg[tt] *
     DMs[tt] + kOffMg * MgDMs[tt] - 1 / taus * DMs[tt] * UnitStep[tt - tflash],
  CaDMs'[tt] == kOnDM * Ca[tt] * DMs[tt] - kOffDM * CaDMs[tt] -
    1 / taus * CaDMs[tt] * UnitStep[tt - tflash],
```

```
  MgDMs'[tt] == kOnMg * Mg[tt] * DMs[tt] - kOffMg * MgDMs[tt] -
     1 / taus * MgDMs[tt] * UnitStep[tt - tflash]
 }
;

(*Photoproducts*)
(*PP2: comes from DMf,DMs and MgDMf,MgDMs; but also binds Ca*)
BufferPP2 := {

  PP2[0] == 0,
  CaPP2[0] == 0,
  MgPP2[0] == 0,

  PP2'[tt] == -kOnPP2 * Ca[tt] * PP2[tt] + kOffPP2 * CaPP2[tt] -
     kOnMg * Mg[tt] * PP2[tt] + kOffMgPP * MgPP2[tt] + 2 * (1 / tauf * DMf[tt] *
          UnitStep[tt - tflash] + 1 / taus * DMs[tt] * UnitStep[tt - tflash])
     + 1 / tauf * MgDMf[tt] * UnitStep[tt - tflash] +
     1 / taus * MgDMs[tt] * UnitStep[tt - tflash],

  CaPP2'[tt] == kOnPP2 * Ca[tt] * PP2[tt] - kOffPP2 * CaPP2[tt],

  MgPP2'[tt] == kOnMg * Mg[tt] * PP2[tt] - kOffMgPP * MgPP2[tt] + 1 / tauf *
      MgDMf[tt] * UnitStep[tt - tflash] + 1 / taus * MgDMs[tt] * UnitStep[tt - tflash]
 }
;

(*PP1: Comes from CaDMf,CaDMs and binds Ca and Mg*)
BufferPP1 := {

  PP1[0] == 0,
  CaPP1[0] == 0,
  MgPP1[0] == 0,

  PP1'[tt] == -kOnPP1 * Ca[tt] * PP1[tt] +
     kOffPP1 * CaPP1[tt] - kOnMg * Mg[tt] * PP1[tt] + kOffMgPP * MgPP1[tt]
     + 1 / tauf * CaDMf[tt] * UnitStep[tt - tflash] +
     1 / taus * CaDMs[tt] * UnitStep[tt - tflash],

  CaPP1'[tt] == kOnPP1 * Ca[tt] * PP1[tt] -
     kOffPP1 * CaPP1[tt] + 1 / tauf * CaDMf[tt] * UnitStep[tt - tflash] +
     1 / taus * CaDMs[tt] * UnitStep[tt - tflash],

  MgPP1'[tt] == kOnMg * Mg[tt] * PP1[tt] - kOffMgPP * MgPP1[tt]

 }
;
```

```
(*Endogeneous Buffer*)
BufferMB := {

  MB[0] == MB0,
  CaMB[0] == CaMB0,

  MB'[tt] == -kOnMB * Ca[tt] * MB[tt] + kOffMB * CaMB[tt],
  CaMB'[tt] == kOnMB * Ca[tt] * MB[tt] - kOffMB * CaMB[tt]}

;

(*Clear[Eqns,Vars,sol]*)

(*Free Ca*)
FreeCa := {
  Ca[0] == Ca0,

  Ca'[tt] == -γ * (Ca[tt] - CaRest)
    (*DMn*)
    - kOnPP1 * Ca[tt] * PP1[tt] + kOffPP1 * CaPP1[tt]
    - kOnPP2 * Ca[tt] * PP2[tt] + kOffPP2 * CaPP2[tt]
    - kOnDM * Ca[tt] * DMn[tt] + kOffDM * CaDMn[tt]
    - kOnDM * Ca[tt] * DMf[tt] + kOffDM * CaDMf[tt]
    - kOnDM * Ca[tt] * DMs[tt] + kOffDM * CaDMs[tt]
    (*buffers*)
    - kOnATP * Ca[tt] * ATP[tt] + kOffATP * CaATP[tt]
    - kOnMB * Ca[tt] * MB[tt] + kOffMB * CaMB[tt]
    (*dye*)
    - kOnOG * Ca[tt] * OG[tt] + kOffOG * CaOG[tt]
  }
;

(*Free Mg*)
FreeMg := {
  Mg[0] == Mg0,

  Mg'[tt] ==
   -kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt]
    - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt]
    - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt]
    - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt]
    - kOnMg * Mg[tt] * PP2[tt] + kOffMgPP * MgPP2[tt]
    - kOnMg * Mg[tt] * PP1[tt] + kOffMgPP * MgPP1[tt]
 }

;
```

```
    Eqns := {BufferDMn, BufferDMf, BufferDMs, BufferATP,
      BufferPP1, BufferPP2, FreeCa, FreeMg, BufferMB, BufferOG}
    ;
    Vars := {ATP, CaATP, MgATP, Ca, Mg, CaDMn, DMn, CaDMf, DMf, CaDMs,
      DMs, CaPP1, PP1, CaPP2, PP2, MgPP2, MgPP1, MB, CaMB, OG, CaOG}
    ;
    sol := NDSolve[Eqns, Vars, {tt, 0., TimeWindow}
      (*,Method→{"EquationSimplification"->"Solve"}*)]
    ;
    CafP = Extract[Ca[TimeWindow] /. sol, 1];
    CafOG = KdOG * CaOG[tt] / OG[tt];

    AppendTo[CaListReal, Evaluate[{Ca[tt]} /. sol]];
    AppendTo[CaListDye, Evaluate[{CafOG} /. sol]];

  ];
```

10 mM DMN

general parameters

```
In[•]:= TimeWindow = 0.006; (*End of simulation*)
tflash = 0.0;  (*Time of flash*)
PlStart = 0.; (*Plot start*)

af = 0.67; (*fast uncaging fraction; Faas et al*)

(*Select dye*)
OGB1 = 0;
OGB5N = 1;
OGB6F = 0;
Fluo5F = 0;

CaRest = 227. * 10^-9; (*Free pre-flash rersting Ca;
equilibrates with all buffers and DM*)
MgT = 0.5 * 10^-3; (*total Mg in pipette*)
γ = 0.; (*Pump rate*)

(*Concentrations of dye, buffers, DM*)
OGtotal = 200. * 10^-6 ;
ATPtotal = 5. * 10^-3 ;
MBtotal = 480. * 10^-6 ;(*(*Delvendahl, PNAS, 2015*)*)

DMT = 10. * 10^-3;  (*total concentration of DMn *)
(*uncaging efficiency*)
aStartDMN10 = 0.14;
aEndDMN10 = 0.25;
```

definitions and loop

```
In[•]:= (*Dye*)
If[OGB1 == 1,
 kOnOG = 4.3 * 10^8;
kOffOG = 103.;]

If[OGB5N == 1,
 kOnOG = 2.5 * 10^8;
kOffOG = 6000.;]

If[OGB6F == 1,
 kOnOG = 3. * 10^8;
kOffOG = 900.;]

If[Fluo5F == 1,
 kOnOG = 3. * 10^8;
kOffOG = 249.;] (*Delvendahl PNAS; before: 432*)
```

```
KdOG = kOffOG / kOnOG;
kappaOG = OGtotal / KdOG;

(*ATP*)
kOnATP  = 5. * 10^8;
kOffATP = 100 000.;
kOnMgATP  = 1. * 10^7; (*Bollmann Dissertation S. 59; *)
kOffMgATP = 1000.;

KdATP = kOffATP / kOnATP;
kappaATP = ATPtotal / KdATP;
KdMgATP = kOffMgATP / kOnMgATP;

(*DM*)
If[MgT == 0.,
 kOnDM = 1.98 * 10^7; (*Faas Plos Biol, 2007*)
kOffDM = 0.14;
 ,
 kOnDM = 2.9 * 10^7; (*Faas Biophys J, 2005*)
kOffDM = 0.19;
]

(*Mg binding constants for DMn, DMf, DMs*)
kOnMg = 1.3 * 10^5; (*all values for Mg are from Faas et al., 2005*)
kOffMg = 0.2;

(*Ca binding constants for PP*)
kOnPP2 = kOnPP1 = kOnDM;
kOffPP2 = 3.6 * 10^3;
If[MgT == 0.,
 kOffPP1 = 7. * 10^4;,
 kOffPP1 = 6.9 * 10^4; ]

(*Mg binding constants for PP1,PP2*)
kOffMgPP = 3. * 10^2; (*for PP1,PP2*)
konMgPP = kOnMg; (*koMgPP not used in below diff. eq., only kOnMg*)

(*Equilibrium constants (not complete)*)
KdDM = kOffDM / kOnDM;
KdPP1 = kOffPP1 / kOnPP1;
KdMg = kOffMg / kOnMg;
kappaDM = DMT / KdDM;

 (*Endogenous buffer*)
kOnMB = 5 * 10^8;(*Delvendahl, PNAS, 2015*)
kOffMB = 16 000;
```

```
KdMB = kOffMB / kOnMB;

TRest = 1000.;


(*---------------------------------  Loop  ----------
 ---------------------------------------*)
(*---------------------------------  Loop  ----------
 ---------------------------------------*)
(*---------------------------------  Loop  ----------
 ---------------------------------------*)

For[aCount = 1, aCount ≤ aNumberDMN10, aCount += 1,
  a = 10^ (Log10[aStartDMN10] +
      (aCount - 1) * (Log10[aEndDMN10] - Log10[aStartDMN10]) / (aNumberDMN10 - 1));

  (*------------------------- Resting
    Equations ------------------------------------------*)

  (*Dye*)
  OGRest := {

    OG[0] == OGtotal,
    CaOG[0] == 0,

    OG'[tt] == -kOnOG * CaRest * OG[tt] + kOffOG * CaOG[tt],
    CaOG'[tt] == kOnOG * CaRest * OG[tt] - kOffOG * CaOG[tt]
   }
  ;

  (*ATP*)
  ATPRest := {

    ATP[0] == ATPtotal,
    CaATP[0] == 0,
    MgATP[0] == 0,

    ATP'[tt] == -kOnATP * CaRest * ATP[tt] + kOffATP * CaATP[tt] -
      kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt],
    CaATP'[tt] == kOnATP * CaRest * ATP[tt] - kOffATP * CaATP[tt],
    MgATP'[tt] == kOnMgATP * Mg[tt] * ATP[tt] - kOffMgATP * MgATP[tt]

   }

  ;

  (*DM nitrophene*)
```

```
DMnRest := {

   DMn[0] == (1 - a) * DMT,
   CaDMn[0] == 0.,
   MgDMn[0] == 0.,

   DMn'[tt] == -kOnDM * CaRest * DMn[tt] +
     kOffDM * CaDMn[tt] - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt],
   CaDMn'[tt] == kOnDM * CaRest * DMn[tt] - kOffDM * CaDMn[tt],
   MgDMn'[tt] == kOnMg * Mg[tt] * DMn[tt] - kOffMg * MgDMn[tt]
  }

;
DMfRest := {

   DMf[0] == a * af * DMT,
   CaDMf[0] == 0.,
   MgDMf[0] == 0.,

   DMf'[tt] == -kOnDM * CaRest * DMf[tt] +
     kOffDM * CaDMf[tt] - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt],
   CaDMf'[tt] == kOnDM * CaRest * DMf[tt] - kOffDM * CaDMf[tt],
   MgDMf'[tt] == kOnMg * Mg[tt] * DMf[tt] - kOffMg * MgDMf[tt]
  }

;
DMsRest := {

   DMs[0] == a * (1 - af) * DMT,
   CaDMs[0] == 0.,
   MgDMs[0] == 0.,

   DMs'[tt] == -kOnDM * CaRest * DMs[tt] +
     kOffDM * CaDMs[tt] - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt],
   CaDMs'[tt] == kOnDM * CaRest * DMs[tt] - kOffDM * CaDMs[tt],
   MgDMs'[tt] == kOnMg * Mg[tt] * DMs[tt] - kOffMg * MgDMs[tt]
  }
;

(*Endogeneous buffer*)
MBRest := {

   MB[0] == MBtotal,
   CaMB[0] == 0,

   MB'[tt] == -kOnMB * CaRest * MB[tt] + kOffMB * CaMB[tt],
   CaMB'[tt] == kOnMB * CaRest * MB[tt] - kOffMB * CaMB[tt]
```

```
 }

;

(*Free Mg*)
MgfRest := {
  Mg[0] == MgT,

  Mg'[tt] ==
   -kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt]
    - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt]
    - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt]
    - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt]
 }

;
EqRest := {ATPRest, MgfRest, OGRest, DMnRest, DMfRest, DMsRest, MBRest};
VarsRest := {ATP, Mg, CaATP, MgATP, CaOG, OG, DMn,
  CaDMn, MgDMn, DMf, CaDMf, MgDMf, DMs, CaDMs, MgDMs, MB, CaMB}
;
solr := NDSolve[EqRest, VarsRest, {tt, 0, TRest}]
;

Ca0 = CaRest;
Mg0 = Extract[Mg[TRest] /. solr, 1];
ATP0 = Extract[ATP[TRest] /. solr, 1];
CaATP0 = Extract[CaATP[TRest] /. solr, 1];
MgATP0 = Extract[MgATP[TRest] /. solr, 1];
OG0 = Extract[OG[TRest] /. solr, 1];
CaOG0 = Extract[CaOG[TRest] /. solr, 1];
DMn0 = Extract[DMn[TRest] /. solr, 1];
CaDMn0 = Extract[CaDMn[TRest] /. solr, 1];
MgDMn0 = Extract[MgDMn[TRest] /. solr, 1];
DMf0 = Extract[DMf[TRest] /. solr, 1];
CaDMf0 = Extract[CaDMf[TRest] /. solr, 1];
MgDMf0 = Extract[MgDMf[TRest] /. solr, 1];
DMs0 = Extract[DMs[TRest] /. solr, 1];
CaDMs0 = Extract[CaDMs[TRest] /. solr, 1];
MgDMs0 = Extract[MgDMs[TRest] /. solr, 1];
MB0 = Extract[MB[TRest] /. solr, 1];
CaMB0 = Extract[CaMB[TRest] /. solr, 1];


ClearAll[EqRest, VarsRest];


(*------------------------- Flash
```

```
    Equations ------------------------------------------*)

   (*Dye*)
   BufferOG := {

     OG[0] == OG0,
     CaOG[0] == CaOG0,

     OG'[tt] == -kOnOG * Ca[tt] * OG[tt] + kOffOG * CaOG[tt],
     CaOG'[tt] == kOnOG * Ca[tt] * OG[tt] - kOffOG * CaOG[tt]}
   ;

   (*ATP*)
 BufferATP := {

     ATP[0] == ATP0,
     CaATP[0] == CaATP0,
     MgATP[0] == MgATP0,

     ATP'[tt] == -kOnATP * Ca[tt] * ATP[tt] + kOffATP * CaATP[tt] -
       kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt],
     CaATP'[tt] == kOnATP * Ca[tt] * ATP[tt] - kOffATP * CaATP[tt],
     MgATP'[tt] == kOnMgATP * Mg[tt] * ATP[tt] - kOffMgATP * MgATP[tt]
    }
   ;

   (*fast (tauf) and slow (taus) time constants for uncageing;
   Faas et al., 2005,2007*)
 If[MgT == 0.,
    tauf = 15.2 * 10^-6;  (*Faas, 2007*)
    taus = 1.9 * 10^-3;
    ,
    tauf = 15. * 10^-6;  (*Faas,2005*)
    taus = 2. * 10^-3; ]

   ;

   (*The differential equations*)
   (*non uncaging fraction of DMn*)
   BufferDMn := {

     DMn[0] == DMn0,
     CaDMn[0] == CaDMn0,
     MgDMn[0] == MgDMn0,

     DMn'[tt] == -kOnDM * Ca[tt] * DMn[tt] +
       kOffDM * CaDMn[tt] - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt],
```

```
  CaDMn'[tt] == kOnDM * Ca[tt] * DMn[tt] - kOffDM * CaDMn[tt],
  MgDMn'[tt] == kOnMg * Mg[tt] * DMn[tt] - kOffMg * MgDMn[tt]
 }
;

(*fast uncaging fraction of DMn*)
BufferDMf := {

  DMf[0] == DMf0,
  CaDMf[0] == CaDMf0,
  MgDMf[0] == MgDMf0,

  DMf'[tt] == -kOnDM * Ca[tt] * DMf[tt] + kOffDM * CaDMf[tt] - kOnMg * Mg[tt] *
      DMf[tt] + kOffMg * MgDMf[tt] - 1 / tauf * DMf[tt] * UnitStep[tt - tflash],
  CaDMf'[tt] == kOnDM * Ca[tt] * DMf[tt] - kOffDM * CaDMf[tt] -
    1 / tauf * CaDMf[tt] * UnitStep[tt - tflash],
  MgDMf'[tt] == kOnMg * Mg[tt] * DMf[tt] - kOffMg * MgDMf[tt] -
    1 / tauf * MgDMf[tt] * UnitStep[tt - tflash]
 }

;
(*slow uncaging fraction of DMn*)
BufferDMs := {

  DMs[0] == DMs0,
  CaDMs[0] == CaDMs0,
  MgDMs[0] == MgDMs0,

  DMs'[tt] == -kOnDM * Ca[tt] * DMs[tt] + kOffDM * CaDMs[tt] - kOnMg * Mg[tt] *
      DMs[tt] + kOffMg * MgDMs[tt] - 1 / taus * DMs[tt] * UnitStep[tt - tflash],
  CaDMs'[tt] == kOnDM * Ca[tt] * DMs[tt] - kOffDM * CaDMs[tt] -
    1 / taus * CaDMs[tt] * UnitStep[tt - tflash],
  MgDMs'[tt] == kOnMg * Mg[tt] * DMs[tt] - kOffMg * MgDMs[tt] -
    1 / taus * MgDMs[tt] * UnitStep[tt - tflash]
 }
;

(*Photoproducts*)
(*PP2: comes from DMf,DMs and MgDMf,MgDMs; but also binds Ca*)
BufferPP2 := {

  PP2[0] == 0,
  CaPP2[0] == 0,
  MgPP2[0] == 0,

  PP2'[tt] == -kOnPP2 * Ca[tt] * PP2[tt] + kOffPP2 * CaPP2[tt] -
    kOnMg * Mg[tt] * PP2[tt] + kOffMgPP * MgPP2[tt] + 2 * (1 / tauf * DMf[tt] *
```

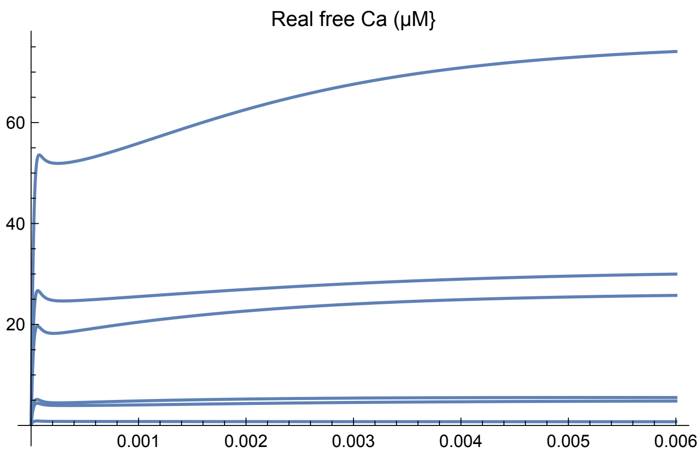
```
        UnitStep[tt - tflash] + 1 / taus * DMs[tt] * UnitStep[tt - tflash])
    + 1 / tauf * MgDMf[tt] * UnitStep[tt - tflash] +
    1 / taus * MgDMs[tt] * UnitStep[tt - tflash],

  CaPP2'[tt] == kOnPP2 * Ca[tt] * PP2[tt] - kOffPP2 * CaPP2[tt],

  MgPP2'[tt] == kOnMg * Mg[tt] * PP2[tt] - kOffMgPP * MgPP2[tt] + 1 / tauf *
     MgDMf[tt] * UnitStep[tt - tflash] + 1 / taus * MgDMs[tt] * UnitStep[tt - tflash]
 }
;

(*PP1: Comes from CaDMf,CaDMs and binds Ca and Mg*)
BufferPP1 := {

  PP1[0] == 0,
  CaPP1[0] == 0,
  MgPP1[0] == 0,

  PP1'[tt] == -kOnPP1 * Ca[tt] * PP1[tt] +
    kOffPP1 * CaPP1[tt] - kOnMg * Mg[tt] * PP1[tt] + kOffMgPP * MgPP1[tt]
    + 1 / tauf * CaDMf[tt] * UnitStep[tt - tflash] +
    1 / taus * CaDMs[tt] * UnitStep[tt - tflash],

  CaPP1'[tt] == kOnPP1 * Ca[tt] * PP1[tt] -
    kOffPP1 * CaPP1[tt] + 1 / tauf * CaDMf[tt] * UnitStep[tt - tflash] +
    1 / taus * CaDMs[tt] * UnitStep[tt - tflash],

  MgPP1'[tt] == kOnMg * Mg[tt] * PP1[tt] - kOffMgPP * MgPP1[tt]

 }
;

(*Endogeneous Buffer*)
BufferMB := {

  MB[0] == MB0,
  CaMB[0] == CaMB0,

  MB'[tt] == -kOnMB * Ca[tt] * MB[tt] + kOffMB * CaMB[tt],
  CaMB'[tt] == kOnMB * Ca[tt] * MB[tt] - kOffMB * CaMB[tt]}

;

(*Clear[Eqns,Vars,sol]*)

(*Free Ca*)
FreeCa := {
```

```
  Ca[0] == Ca0,

  Ca'[tt] == -γ * (Ca[tt] - CaRest)
    (*DMn*)
    - kOnPP1 * Ca[tt] * PP1[tt] + kOffPP1 * CaPP1[tt]
    - kOnPP2 * Ca[tt] * PP2[tt] + kOffPP2 * CaPP2[tt]
    - kOnDM * Ca[tt] * DMn[tt] + kOffDM * CaDMn[tt]
    - kOnDM * Ca[tt] * DMf[tt] + kOffDM * CaDMf[tt]
    - kOnDM * Ca[tt] * DMs[tt] + kOffDM * CaDMs[tt]
    (*buffers*)
    - kOnATP * Ca[tt] * ATP[tt] + kOffATP * CaATP[tt]
    - kOnMB * Ca[tt] * MB[tt] + kOffMB * CaMB[tt]
    (*dye*)
    - kOnOG * Ca[tt] * OG[tt] + kOffOG * CaOG[tt]
  }
;

(*Free Mg*)
FreeMg := {
  Mg[0] == Mg0,

  Mg'[tt] ==
   -kOnMgATP * Mg[tt] * ATP[tt] + kOffMgATP * MgATP[tt]
    - kOnMg * Mg[tt] * DMn[tt] + kOffMg * MgDMn[tt]
    - kOnMg * Mg[tt] * DMf[tt] + kOffMg * MgDMf[tt]
    - kOnMg * Mg[tt] * DMs[tt] + kOffMg * MgDMs[tt]
    - kOnMg * Mg[tt] * PP2[tt] + kOffMgPP * MgPP2[tt]
    - kOnMg * Mg[tt] * PP1[tt] + kOffMgPP * MgPP1[tt]
 }

;

Eqns := {BufferDMn, BufferDMf, BufferDMs, BufferATP,
  BufferPP1, BufferPP2, FreeCa, FreeMg, BufferMB, BufferOG}
;
Vars := {ATP, CaATP, MgATP, Ca, Mg, CaDMn, DMn, CaDMf, DMf, CaDMs,
  DMs, CaPP1, PP1, CaPP2, PP2, MgPP2, MgPP1, MB, CaMB, OG, CaOG}
;
sol := NDSolve[Eqns, Vars, {tt, 0., TimeWindow}
  (*,Method→{"EquationSimplification"->"Solve"}*)]
;
CafP = Extract[Ca[TimeWindow] /. sol, 1];
CafOG = KdOG * CaOG[tt] / OG[tt];


AppendTo[CaListReal, Evaluate[{Ca[tt]} /. sol]];
AppendTo[CaListDye, Evaluate[{CafOG} /. sol]];
```

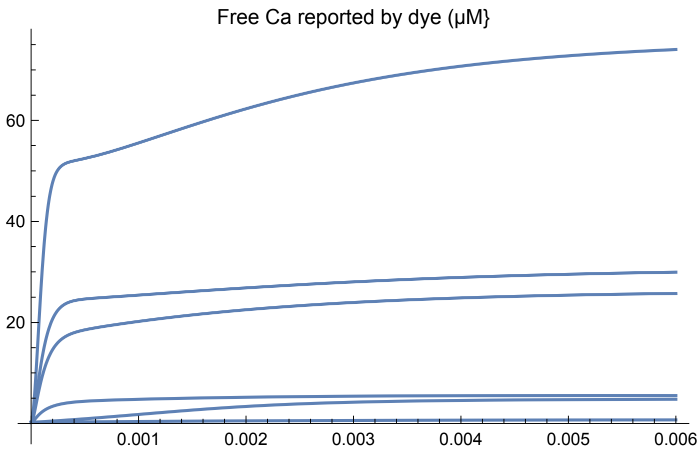
Plot and further processing

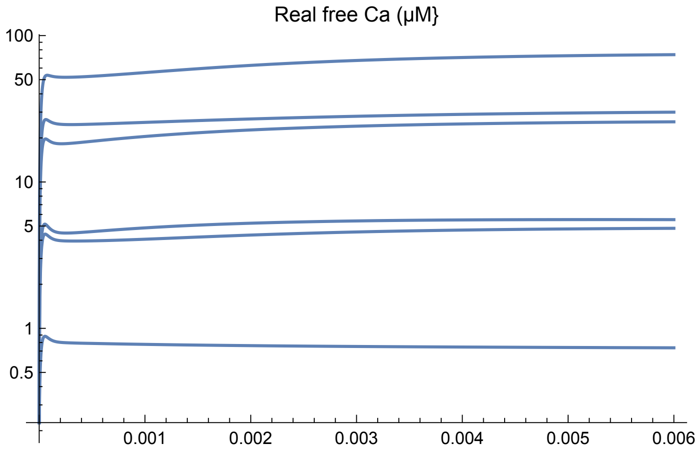
In[∘]:=
```
Plot[10^6 * CaListReal, {tt, 0, TimeWindow}, PlotLabel → "Real free Ca (μM}"]
Plot[10^6 * CaListDye, {tt, 0, TimeWindow},
 PlotLabel → "Free Ca reported by dye (μM}"]
LogPlot[10^6 * CaListReal, {tt, 0, TimeWindow}, PlotLabel → "Real free Ca (μM}"]
LogPlot[10^6 * CaListDye, {tt, 0, TimeWindow},
 PlotLabel → "Free Ca reported by dye (μM}"]
CaListDyePeak =
 Table[NMaximize[{CaListDye[[nn]][[1]][[1]], 0 ≤ tt ≤ TimeWindow}, tt][[1]],
  {nn, Length[CaListDye]}]
  (*"[[1]][[1]]" is neede to get rid of these brackets {{}}*)
```

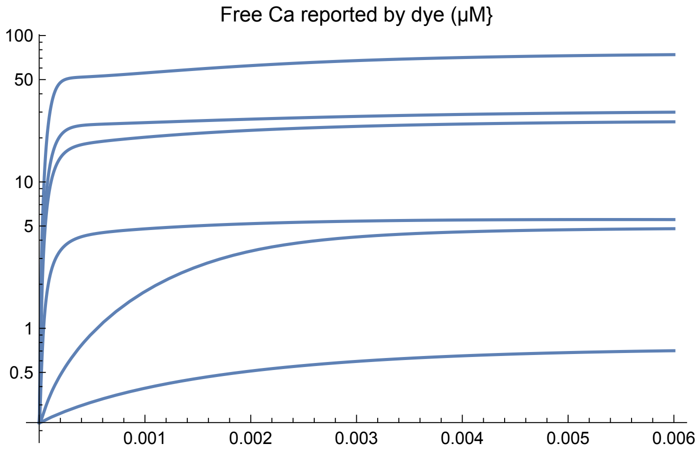
Out[∘]=



Out[∘]=



Out[•]= 

Out[•]= 

Out[•]= $\{7.03073\times10^{-7}, 4.79194\times10^{-6}, 5.53376\times10^{-6}, 0.0000257412, 0.0000299583, 0.0000740312\}$

In[•]:=
```
runs = Length[CaListDyePeak];
```

Release scheme and parameters

Define release scheme

In[•]:=
```
nStates = 4;
mat = Table[0, {nStates}, {nStates}];
```

forward rates

In[•]:=
```
from = 1; (*0 ca bound to 1 ca bound*)
kk = 2 kon;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;

from = 2; (*1 ca bound to 2 ca bound*)
kk = 1 kon;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;

from = 3; (*from 2 ca bound to fused*)
kk = gamma;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;
```

backwards rates

In[•]:=
```
from = 2; (*1 ca bound to 0 ca bound*)
kk = koff b^0;
mat[[from - 1, from]] += kk; mat[[from, from]] += -kk;

from = 3; (*2 ca bound to 1 ca bound*)
kk = 2 koff b^1;
mat[[from - 1, from]] += kk; mat[[from, from]] += -kk;
```

outflux from matrix

In[•]:=
```
mat[[1, 1]] += -kunprim;
```

influx in matrix

In[•]:=
```
mat[[1, 1]] += kprim / ss1[t];
```

Matrix

In[•]:=
```
mat // TableForm
```

Out[•]//TableForm=

$-2\,\text{kon} - \text{kunprim} + \frac{\text{kprim}}{\text{ss1}[t]}$	koff	0	0
2 kon	- koff - kon	2 b koff	0
0	kon	- gamma - 2 b koff	0
0	0	gamma	0

Parameters of release scheme

In[◦]:=
```
q10 = 2.3;
tempFact = q10 ^ ((37 - 24) / 10);
```

In[◦]:=
```
Clear[caFunc, kprimScheme];
(*Clear is needed if the cell is exectued for a 2nd time when
 caFunc is already set to a value or an Interpolationfunction*)

caRest = CaRest;(*227nM see above*)

affinityFactor = 1.0;
konScheme = 100. * caFunc[t] Sqrt[affinityFactor] tempFact 1.*^7;(*M^-1 s^-1*)
koffScheme = 100. * (1 / Sqrt[affinityFactor]) tempFact 1500;(*s^-1*)
gammaScheme = 10. * tempFact 6000;(*s^-1*)
bScheme = 0.25;


KdPrim = 2.*^-6;
kprimScheme = 0.6 + 30. (caFunc[t] / (KdPrim + caFunc[t]));
kunprimScheme = 0.6 + 30. (caRest / (KdPrim + caRest));


repl = {
   kon → konScheme,
   koff → koffScheme ,
   gamma → gammaScheme ,
    b → bScheme,

   kprim → kprimScheme ,
   kunprim → kunprimScheme

  };
```

In[◦]:=
```
tauOfDecayOfUncagedCa = 0.4;
```

Initial occupancy

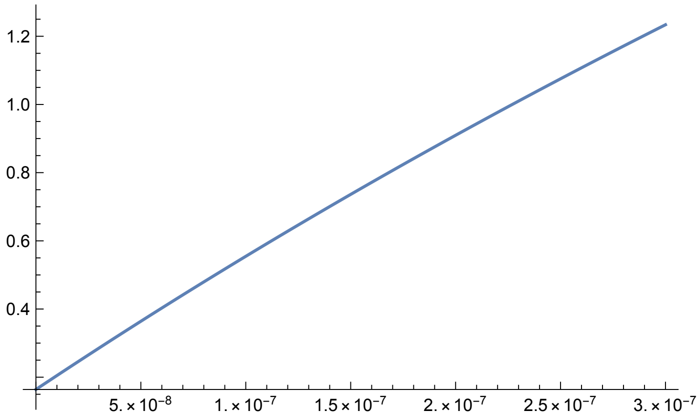
In[∘]:=
```
(*test initial equilibrium occupancy*)
caFunc[t_] := caTmp;
fillStateSSInitial = kprimScheme / kunprimScheme;
ss0Initial = fillStateSSInitial;
(ss0Initial /. caTmp → 180*^-9)
(ss0Initial /. caTmp → 30*^-9)
(ss0Initial /. caTmp → 180*^-9) / (ss0Initial /. caTmp → 30*^-9)
(*test initial *)
Plot[kprimScheme / kunprimScheme, {caTmp, 0, 300*^-9}]
```

Out[∘]= 0.841205

Out[∘]= 0.28523

Out[∘]= 2.94922

Out[∘]=



In[∘]:=
```
(*calualte initial equilibrium occupancy*)
caFunc[t_] := caRest;
kprimScheme
kunprimScheme
ss0Initial = kprimScheme / kunprimScheme
```

Out[∘]= 3.65793

Out[∘]= 3.65793

Out[∘]= 1.

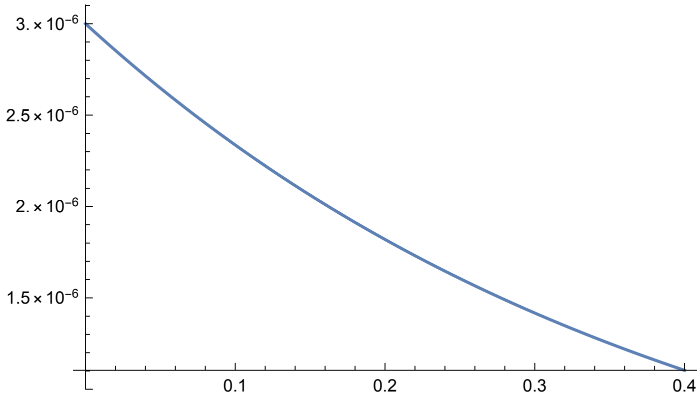
Diff eq.

In[∘]:=
```
Clear[caFunc, eq];(*Clear is needed if the cell is exectued for a 2nd time
 when caFunc is already set to a value or an Interpolationfunction*)
ss[t_] = {ss1[t], ss2[t], ss3[t], ss4[t]};
eq = {ss'[t] == (mat /. repl).ss[t],
   ss[0] == {ss0Initial, 0, 0, 0}};
```

Solve all states

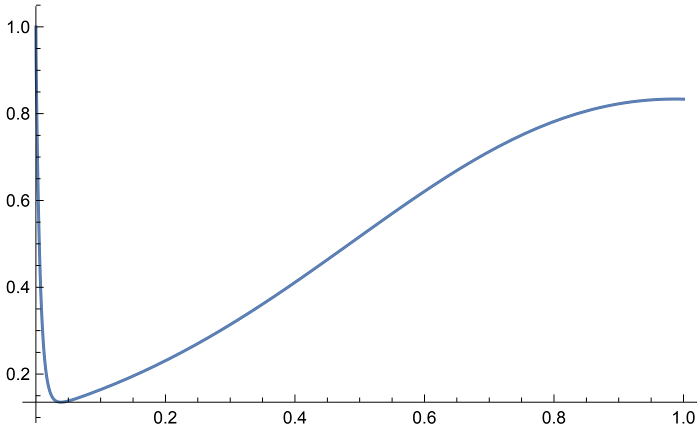
In[•]:=
```
caFunc[t_] := 3*^-6 * Exp[-t / tauOfDecayOfUncagedCa];;
Plot[caFunc[t], {t, 0, 0.4}, PlotRange → All]
```

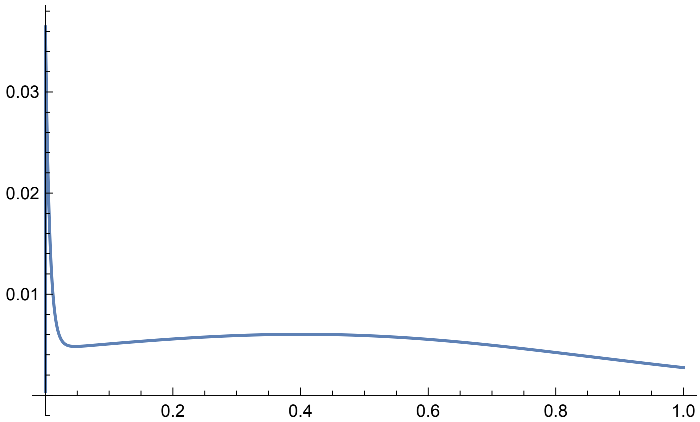
Out[•]=

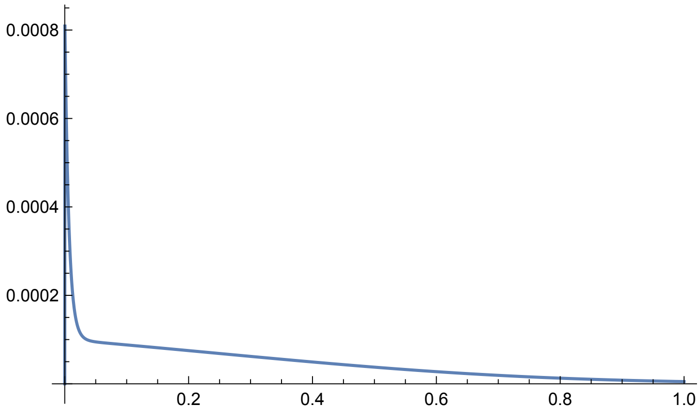


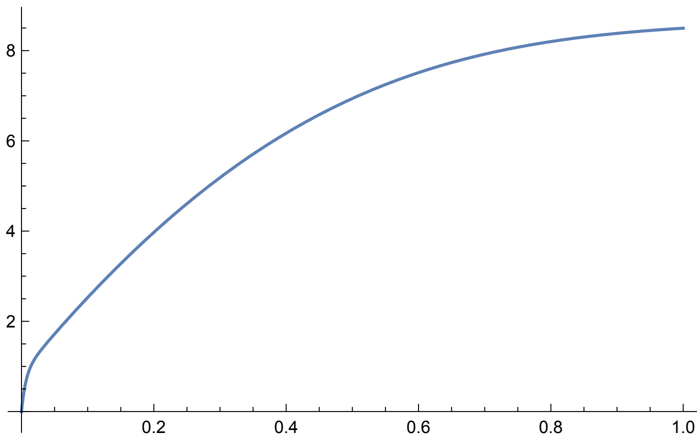
In[•]:=
```
myNDSolveResults = NDSolve[eq, {ss1, ss2, ss3, ss4}, {t, 0, 10.}];
tEndForPlot = 1.;
Plot[(ss1[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss2[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss3[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss4[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
```

Out[•]=



Out[ ]=


Out[ ]=


Out[ ]=


Loop

make lists for later

In[ ]:=
```
simCaList = Table[0, {runs}];
simParamNv = Table[0, {7}, {runs}];
```

C5

```
In[•]:= baselineC5 = Table[{ttt, 0}, {ttt, cursorStart, -1*^-6, dtOfDataC5}];
(*Lists for saving data within loop*)
simParamNoiseC5 = Table[0, {numberOfFitParamToBeSaved}, {noiseRepeats}];
simParamMedianC5 = Table[0, {numberOfFitParamToBeSaved}, {runs}];
simParamQuantile1C5 = Table[0, {numberOfFitParamToBeSaved}, {runs}];
simParamQuantile2C5 = Table[0, {numberOfFitParamToBeSaved}, {runs}];
```

C10

```
In[•]:= baselineC10 = Table[{ttt, 0}, {ttt, cursorStart, -1*^-6, dtOfDataC10}];
(*Lists for saving data within loop*)
simParamNoiseC10 = Table[0, {numberOfFitParamToBeSaved}, {noiseRepeats}];
simParamMedianC10 = Table[0, {numberOfFitParamToBeSaved}, {runs}];
simParamQuantile1C10 = Table[0, {numberOfFitParamToBeSaved}, {runs}];
simParamQuantile2C10 = Table[0, {numberOfFitParamToBeSaved}, {runs}];
```

D

```
In[•]:= baselineD = Table[{ttt, 0}, {ttt, cursorStart, -1*^-6, dtOfDataD}];
(*Lists for saving data within loop*)
simParamNoiseD = Table[0, {numberOfFitParamToBeSaved}, {noiseRepeats}];
simParamMedianD = Table[0, {numberOfFitParamToBeSaved}, {runs}];
simParamQuantile1D = Table[0, {numberOfFitParamToBeSaved}, {runs}];
simParamQuantile2D = Table[0, {numberOfFitParamToBeSaved}, {runs}];
```

Long

```
In[•]:= baselineLong = Table[{ttt, 0}, {ttt, -0.05, -1*^-6, dtOfDataLong}];
```

Loop

```
In[•]:= For[r = 1, r ≤ runs, r += 1,
  myCaNow = CaListDyePeak[[r]];
  lastSimulatedCaListReal = CaListReal[[r]][[1]][[1]] /. tt → TimeWindow;
  (*"[[1]][[1]]" is neede to get rid of these brackets {{}}*)
  Print[
   "-----------------------------------------------------------------------
     ----------------------------------"];
  Print["----------------     Ca  = ", 1*^6 myCaNow,
   " uM         -------------------------------------------------------"];
  Print[
   "-----------------------------------------------------------------------
     ----------------------------------"];
  simCaList[[r]] = myCaNow;
```

```
caFunc[ttt_] := If[ttt < TimeWindow,
  CaListReal[[r]][[1]][[1]] /. tt → ttt,
  (*tt because this is the symbol used in "Calculate Ca transients"*)
  lastSimulatedCaListReal * Exp[-ttt / tauOfDecayOfUncagedCa]
 ];
(* solve Diff Eq.: *)
myNDSolveResults = NDSolve[eq, ss4, {t, 0, 0.4}];
(* plot results: *)
fused[t_] := ss4[t];
Plot[(fused[t] /. myNDSolveResults),
  {t, 0, cursorEnd}, PlotRange → All] // Print;
Plot[(fused[t] /. myNDSolveResults), {t, 0, cursorEndLong},
  PlotRange → All] // Print;
If[exportYes == 1,
 toExport = Table[{t, (fused[t] /. myNDSolveResults)[[1]]},
   {t, 0., cursorEndLong, dtOfPlotsForExport}];
 Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
   " withoutNoise.txt", toExport, "Table"];
];
(* sample data and add baseline: --------*)
tmpCumRelC5 = Table[{ttt, (fused[ttt] /. myNDSolveResults)[[1]]},
  {ttt, 0., cursorEnd, dtOfDataC5}];
tmpToFitC5 = Catenate[{baselineC5, tmpCumRelC5}];
tmpCumRelC10 = Table[{ttt, (fused[ttt] /. myNDSolveResults)[[1]]},
  {ttt, 0., cursorEnd, dtOfDataC10}];
tmpToFitC10 = Catenate[{baselineC10, tmpCumRelC10}];
tmpCumRelD = Table[{ttt, (fused[ttt] /. myNDSolveResults)[[1]]},
  {ttt, 0., cursorEnd, dtOfDataD}];
tmpToFitD = Catenate[{baselineD, tmpCumRelD}];
tmpCumRelLong = Table[{ttt, (fused[ttt] /. myNDSolveResults)[[1]]},
  {ttt, 0., cursorEndLong, dtOfDataLong}];
tmpToFitLong = Catenate[{baselineLong, tmpCumRelLong}];

(*---------    get amplitude
  without noise and without fitting -----------------*)
For[NvCount = 1, NvCount ≤ 7, NvCount += 1,
 simParamNv[[NvCount, r]] =
  (fused[timeOfNv[[NvCount]]] /. myNDSolveResults)[[1]];
 (* the [[1]] is somehow needed to get rid of a list
  structure probably related to the interpolate function*)
];

(*--------------   Startvalues for
  fit the same for all C5 C10 and D -------------*)
caAdjustedTau1Guess = tau1Guess / ((myCaNow / 10.*^-6) ^4);
caAdjustedTau1Guess = tau1Guess / ((myCaNow / 10.*^-6) ^1);
```

```
caAdjustedTau2Guess = 10 caAdjustedTau1Guess;
caAdjustedDelayGuess = delayGuess / ((myCaNow / 10.*^-6) ^1);

(*---------    Fitting of data,
saving of results, and plotting-----------------*)
(*----------------------------------------------------------------------
                                    ----*)
(*------------------------------------    C5     -----------------------
                       ----*)
(*----------------------------------------------------------------------
                                    ----*)
Print[
 "-----------------------------------------------------------------------
   C5"];
(*check that signal is large enough relative to noise to obtain
 useful fit results. If not, do not do fitting and set everything to {}*)
If[simParamNv[[5, r]] > signalToNoiseRatioC5 myNoiseC5, (*add noise
  and do the fitting several times and then average the results*)
 For[noiseN = 1, noiseN ≤ noiseRepeats, noiseN += 1,
  (*Print[noiseN];*)
  tmpToFitNoise = Transpose[{tmpToFitC5[[All, 1]],
     # + RandomVariate[NormalDistribution[0, myNoiseC5]] & /@
      tmpToFitC5[[All, 2]]}];
  (*fit mono-exp*)
  fitResultsTMP = NonlinearModelFit[tmpToFitNoise, myFitMono[x1],
    {{delayMono, delayGuess}, {ampMono, ampGuess}, {tau1Mono,
      caAdjustedTau1Guess}}, x1, MaxIterations → myMaxIterations];
  fitResultMono = fitResultsTMP[{"BestFitParameters"}];
  simParamNoiseC5[[1, noiseN]] = 0; (*not used anymore*)
  simParamNoiseC5[[2, noiseN]] =
   fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
  (*Print[fitResultsTMP["ANOVATableSumsOfSquares"]];*)
  simParamNoiseC5[[3, noiseN]] = (delayMono /. fitResultMono)[[1]];
  simParamNoiseC5[[4, noiseN]] = ((ampMono /. fitResultMono))[[1]];
  simParamNoiseC5[[5, noiseN]] = (1 / (tau1Mono /. fitResultMono))[[1]];
  (*fit bi-exp*)
  fitResultsTMP =
   NonlinearModelFit[tmpToFitNoise, myFitBi[x1], {{delay, delayGuess},
     {amp, ampGuess}, {amp1, amp1Guess}, {tau1, caAdjustedTau1Guess},
     {tau2, caAdjustedTau2Guess}}, x1, MaxIterations → myMaxIterations];
  fitResultBi = fitResultsTMP[{"BestFitParameters"}];
  simParamNoiseC5[[6, noiseN]] = simParamNoiseC5[[2, noiseN]] /
    fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
  simParamNoiseC5[[7, noiseN]] = (delay /. fitResultBi)[[1]];
  simParamNoiseC5[[8, noiseN]] = ((amp /. fitResultBi))[[1]];
  simParamNoiseC5[[9, noiseN]] = ((amp amp1 /. fitResultBi))[[1]];
  (*relative amp1*)
```

```
 simParamNoiseC5[[10, noiseN]] = (1/(tau1 /. fitResultBi))[[1]];
 simParamNoiseC5[[11, noiseN]] = (1/(tau2 /. fitResultBi))[[1]];
 (*merge*)
 If[
  (*to use the bi-exp fit, the following cirteria should be fullfilled:*)
  (*chi2 should improve(=decrease) by >4%*)
  (simParamNoiseC5[[6, noiseN]] > 1.04)
   &&
   (*tau1 and tau2 of bi fit should be factor of >3 different*)
   ((simParamNoiseC5[[11, noiseN]] / simParamNoiseC5[[10, noiseN]]) < 3.)
   &&
   (*relative amplitude of 1st component should be > 5% *)
   (((amp1 /. fitResultBi))[[1]] > 0.05)
   &&
   (*relative amplitude of 1st component should be < 95% *)
   (((amp1 /. fitResultBi))[[1]] < 0.95)
  ,
  (*take bi*)
  Print["take bi"];
  simParamNoiseC5[[12, noiseN]] = simParamNoiseC5[[7, noiseN]];
  (*delay*)
  simParamNoiseC5[[13, noiseN]] = simParamNoiseC5[[8, noiseN]];
  (*amp*)
  simParamNoiseC5[[14, noiseN]] = simParamNoiseC5[[9, noiseN]];
  (*amp1*)
  simParamNoiseC5[[15, noiseN]] = simParamNoiseC5[[10, noiseN]];
  (*tau1*)
  simParamNoiseC5[[16, noiseN]] = simParamNoiseC5[[11, noiseN]];(*tau2*)
  ,
  (*take mono*)
  Print["take mono"];
  simParamNoiseC5[[12, noiseN]] = simParamNoiseC5[[3, noiseN]];
  (*delay*)
  simParamNoiseC5[[13, noiseN]] = simParamNoiseC5[[4, noiseN]];
  (*amp*)
  simParamNoiseC5[[14, noiseN]] = NaN; (*amp1*)
  simParamNoiseC5[[15, noiseN]] = simParamNoiseC5[[5, noiseN]];
  (*tau1*)
  simParamNoiseC5[[16, noiseN]] = NaN;(*tau2*)
 ];
];
(*plot last example of the noise loop*)
gr1 = ListPlot[tmpToFitNoise, PlotRange → All, PlotStyle → Black];
gr2 = Plot[myFitMono[x1] /. fitResultMono,
  {x1, cursorStart, cursorEnd}, PlotRange → All, PlotStyle → {Blue, Dashed}];
gr3 = Plot[myFitBi[x1] /. fitResultBi, {x1, cursorStart, cursorEnd},
  PlotRange → All, PlotStyle → {Green, Dashed}];
```

```
Show[gr1, gr2, gr3, PlotRange → All ] // Print;
If[exportYes == 1,
 Export["withinLoop r" <> ToString[r] <> " Ca" <>
   ToString[1*^6 myCaNow] <> " C5 data.txt", tmpToFitNoise, "Table"];
 toExport = Table[{t, (myFitMono[t] /. fitResultMono) [[1]]},
   {t, cursorStart, cursorEnd, dtOfPlotsForExport}];
 Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
   " C5 fitMono.txt", toExport, "Table"];
 toExport = Table[{t, (myFitBi[t] /. fitResultBi) [[1]]},
   {t, cursorStart, cursorEnd, dtOfPlotsForExport}];
 Export["withinLoop r" <> ToString[r] <> " Ca" <>
   ToString[1*^6 myCaNow] <> " C5 fitBi.txt", toExport, "Table"];
];
noiseN = noiseRepeats; (*fit parameter of last noisetrace*)
Print["Mono: chi2 = ", simParamNoiseC5[[2, noiseN]], "     d = ",
 simParamNoiseC5[[2, noiseN]], "     a = ", simParamNoiseC5[[4, noiseN]],
 "     t = ", 1/simParamNoiseC5[[5, noiseN]]];
Print["Bi: ratio chi2Mono/chi2Bi = ", simParamNoiseC5[[6, noiseN]],
 "     d = ", simParamNoiseC5[[7, noiseN]], "     a = ",
 simParamNoiseC5[[8, noiseN]], "     a1 = ", simParamNoiseC5[[9, noiseN]],
 "     t1 =", 1/simParamNoiseC5[[10, noiseN]],
 "     t2 = ", 1/simParamNoiseC5[[11, noiseN]]];
(*average fit results*)
For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
 simParamMedianC5[[p, r]] =
  Median[simParamNoiseC5[[p, All]] /. NaN → Sequence[]];
 simParamQuantile1C5[[p, r]] = Quantile[
   simParamNoiseC5[[p, All]] /. NaN → Sequence[], myQuantile1];
 simParamQuantile2C5[[p, r]] = Quantile[
   simParamNoiseC5[[p, All]] /. NaN → Sequence[], myQuantile2];
];

(*if tau1 merge > 10 ms, use long trace for fitting*)
If[(1/simParamMedianC5[[15, r]]) > 0.01,
 Print["Long trace was used for fitting."];
 For[noiseN = 1, noiseN ≤ noiseRepeats, noiseN += 1,
  tmpToFitNoiseLong = Transpose[{tmpToFitLong[[All, 1]],
     # + RandomVariate[NormalDistribution[0, myNoiseLong]] & /@
      tmpToFitLong[[All, 2]]}];
  (*fit mono-exp to Long trace*)
  fitResultsTMP = NonlinearModelFit[tmpToFitNoiseLong, myFitMono[x1],
    {{delayMono, delayGuess}, {ampMono, ampGuess}, {tau1Mono,
      caAdjustedTau1Guess}}, x1, MaxIterations → myMaxIterations];
  fitResultLongMono = fitResultsTMP[{"BestFitParameters"}];
  simParamNoiseC5[[2, noiseN]] =
   fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
```

```
(*Print[fitResultsTMP["ANOVATableSumsOfSquares"]];*)
simParamNoiseC5[[3, noiseN]] = (delayMono /. fitResultLongMono)[[1]];
simParamNoiseC5[[4, noiseN]] = ((ampMono /. fitResultLongMono))[[1]];
simParamNoiseC5[[5, noiseN]] = (1/(tau1Mono /. fitResultLongMono))[[1]];
(*fit bi-exp*)
fitResultsTMP =
 NonlinearModelFit[tmpToFitNoiseLong, myFitBi[x1], {{delay, delayGuess},
   {amp, ampGuess}, {amp1, amp1Guess}, {tau1, caAdjustedTau1Guess},
   {tau2, caAdjustedTau2Guess}}, x1, MaxIterations → myMaxIterations];
fitResultLongBi = fitResultsTMP[{"BestFitParameters"}];
simParamNoiseC5[[6, noiseN]] = simParamNoiseC5[[2, noiseN]] /
  fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
simParamNoiseC5[[7, noiseN]] = (delay /. fitResultLongBi)[[1]];
simParamNoiseC5[[8, noiseN]] = ((amp /. fitResultLongBi))[[1]];
simParamNoiseC5[[9, noiseN]] = ((amp amp1 /. fitResultLongBi))[[1]];
(*relative amp1*)
simParamNoiseC5[[10, noiseN]] = (1/(tau1 /. fitResultLongBi))[[1]];
simParamNoiseC5[[11, noiseN]] = (1/(tau2 /. fitResultLongBi))[[1]];
(*merge*)
If[
 (*to use the bi-exp fit,
 the following cirteria should be fullfilled:*)
 (*chi2 should improve(=decrease) by >4%*)
 (simParamNoiseC5[[6, noiseN]] > 1.04)
  &&
  (*tau1 and tau2 of bi fit should be factor of >3 different*)
  ((simParamNoiseC5[[11, noiseN]] / simParamNoiseC5[[10, noiseN]]) < 3.)
  &&
  (*relative amplitude of 1st component should be > 5% *)
  ((( amp1 /. fitResultLongBi))[[1]] > 0.05)
  &&
  (*relative amplitude of 1st component should be < 95% *)
  ((( amp1 /. fitResultLongBi))[[1]] < 0.95)
 ,
 (*take bi*)
 Print["take bi"];
 simParamNoiseC5[[12, noiseN]] = simParamNoiseC5[[7, noiseN]];
 (*delay*)
 simParamNoiseC5[[13, noiseN]] = simParamNoiseC5[[8, noiseN]];
 (*amp*)
 simParamNoiseC5[[14, noiseN]] = simParamNoiseC5[[9, noiseN]];
 (*amp1*)
 simParamNoiseC5[[15, noiseN]] = simParamNoiseC5[[10, noiseN]];
 (*tau1*)
 simParamNoiseC5[[16, noiseN]] = simParamNoiseC5[[11, noiseN]];(*tau2*)
 ,
```

```
    (*take mono*)
    Print["take mono"];
    simParamNoiseC5[[12, noiseN]] = simParamNoiseC5[[3, noiseN]];
    (*delay*)
    simParamNoiseC5[[13, noiseN]] = simParamNoiseC5[[4, noiseN]];
    (*amp*)
    simParamNoiseC5[[14, noiseN]] = NaN; (*amp1*)
    simParamNoiseC5[[15, noiseN]] = simParamNoiseC5[[5, noiseN]];
    (*tau1*)
    simParamNoiseC5[[16, noiseN]] = NaN;(*tau2*)
  ];
];
(*plot last example of the noise loop*)
gr1 = ListPlot[tmpToFitNoiseLong, PlotRange → All, PlotStyle → Black];
gr2 = Plot[myFitMono[x1] /. fitResultLongMono, {x1, cursorStart,
     cursorEndLong}, PlotRange → All, PlotStyle → {Blue, Dashed}];
gr3 = Plot[myFitBi[x1] /. fitResultLongBi, {x1, cursorStart, cursorEndLong},
   PlotRange → All, PlotStyle → {Green, Dashed}];
Show[gr1, gr2, gr3, PlotRange → All ] // Print;
If[exportYes == 1,
  Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
     " C5 dataLong.txt", tmpToFitNoiseLong, "Table"];
  toExport = Table[{t, (myFitMono[t] /. fitResultLongMono) [[1]]},
     {t, cursorStart, cursorEndLong, dtOfPlotsForExport}];
  Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
     " C5 fitLongMono.txt", toExport, "Table"];
  toExport = Table[{t, (myFitBi[t] /. fitResultLongBi) [[1]]},
     {t, cursorStart, cursorEndLong, dtOfPlotsForExport}];
  Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
     " C5 fitLongBi.txt", toExport, "Table"];

];
noiseN = noiseRepeats; (*fit parameter of last noisetrace*)
Print["Mono: chi2 = ", simParamNoiseC5[[2, noiseN]], "     d = ",
  simParamNoiseC5[[3, noiseN]], "     a = ", simParamNoiseC5[[4, noiseN]],
  "     t = ", 1/simParamNoiseC5[[5, noiseN]]];
Print["Bi: ratio chi2Mono/chi2Bi = ", simParamNoiseC5[[6, noiseN]],
  "     d = ", simParamNoiseC5[[7, noiseN]], "     a = ",
  simParamNoiseC5[[8, noiseN]], "     a1 = ", simParamNoiseC5[[9, noiseN]],
  "     t1 =", 1/simParamNoiseC5[[10, noiseN]],
  "     t2 = ", 1/simParamNoiseC5[[11, noiseN]]];
(*average fit results*)
For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
  simParamMedianC5[[p, r]] =
   Median[simParamNoiseC5[[p, All]] /. NaN → Sequence[]];
  simParamQuantile1C5[[p, r]] = Quantile[
```

```
      simParamNoiseC5[[p, All]] /. NaN → Sequence[], myQuantile1];
    simParamQuantile2C5[[p, r]] = Quantile[
      simParamNoiseC5[[p, All]] /. NaN → Sequence[], myQuantile2];
  ];
 ];

 , (*else: signal is not large enough*)
 For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
   simParamMedianC5[[p, r]] = {};
   simParamQuantile1C5[[p, r]] = {};
   simParamQuantile2C5[[p, r]] = {};
  ];
];


(*---------    Fitting of data,
saving of results, and plotting-----------------*)
(*------------------------------------------------------------------
                                         ----*)
(*----------------------------------------    C10     -----------------------
                           ----*)
(*------------------------------------------------------------------
                                         ----*)
Print[
 "------------------------------------------------------------------
   C10"];
(*check that signal is large enough relative to noise to obtain
 useful fit results. If not, do not do fitting and set everything to {}*)
If[simParamNv[[5, r]] > signalToNoiseRatioC10 myNoiseC10, (*add noise
  several times and do the fitting and than average the results*)
 For[noiseN = 1, noiseN ≤ noiseRepeats, noiseN += 1,
  (*Print[noiseN];*)
  tmpToFitNoise = Transpose[{tmpToFitC10[[All, 1]],
     # + RandomVariate[NormalDistribution[0, myNoiseC10]] & /@
      tmpToFitC10[[All, 2]]}];
  (*fit mono-exp*)
  fitResultsTMP = NonlinearModelFit[tmpToFitNoise, myFitMono[x1],
    {{delayMono, delayGuess}, {ampMono, ampGuess}, {tau1Mono,
      caAdjustedTau1Guess}}, x1, MaxIterations → myMaxIterations];
  fitResultMono = fitResultsTMP[{"BestFitParameters"}];
  simParamNoiseC10[[1, noiseN]] = 0; (*not used anymore*)
  simParamNoiseC10[[2, noiseN]] =
   fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
  (*Print[fitResultsTMP["ANOVATableSumsOfSquares"]];*)
  simParamNoiseC10[[3, noiseN]] = (delayMono /. fitResultMono)[[1]];
  simParamNoiseC10[[4, noiseN]] = ((ampMono /. fitResultMono))[[1]];
  simParamNoiseC10[[5, noiseN]] = (1/(tau1Mono /. fitResultMono))[[1]];
```

```
(*fit bi-exp*)
fitResultsTMP =
 NonlinearModelFit[tmpToFitNoise, myFitBi[x1], {{delay, delayGuess},
   {amp, ampGuess}, {amp1, amp1Guess}, {tau1, caAdjustedTau1Guess},
   {tau2, caAdjustedTau2Guess}}, x1, MaxIterations → myMaxIterations];
fitResultBi = fitResultsTMP[{"BestFitParameters"}];
simParamNoiseC10[[6, noiseN]] = simParamNoiseC10[[2, noiseN]] /
  fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
simParamNoiseC10[[7, noiseN]] = (delay /. fitResultBi)[[1]];
simParamNoiseC10[[8, noiseN]] = ((amp /. fitResultBi))[[1]];
simParamNoiseC10[[9, noiseN]] = ((amp amp1 /. fitResultBi))[[1]];
(*relative amp1*)
simParamNoiseC10[[10, noiseN]] = (1/ (tau1 /. fitResultBi))[[1]];
simParamNoiseC10[[11, noiseN]] = (1/ (tau2 /. fitResultBi))[[1]];
(*merge*)
If[
 (*to use the bi-exp fit, the following cirteria should be fullfilled:*)
 (*chi2 should improve(=decrease) by >4%*)
 (simParamNoiseC10[[6, noiseN]] > 1.04)
  &&
  (*tau1 and tau2 of bi fit should be factor of >3 different*)
  ((simParamNoiseC10[[11, noiseN]] / simParamNoiseC10[[10, noiseN]]) < 3.)
  &&
  (*relative amplitude of 1st component should be > 5% *)
  ((( amp1 /. fitResultBi)) [[1]] > 0.05)
  &&
  (*relative amplitude of 1st component should be < 95% *)
  ((( amp1 /. fitResultBi)) [[1]] < 0.95)
 ,
 (*take bi*)
 Print["take bi"];
 simParamNoiseC10[[12, noiseN]] = simParamNoiseC10[[7, noiseN]];
 (*delay*)
 simParamNoiseC10[[13, noiseN]] = simParamNoiseC10[[8, noiseN]];
 (*amp*)
 simParamNoiseC10[[14, noiseN]] = simParamNoiseC10[[9, noiseN]];
 (*amp1*)
 simParamNoiseC10[[15, noiseN]] = simParamNoiseC10[[10, noiseN]];
 (*tau1*)
 simParamNoiseC10[[16, noiseN]] = simParamNoiseC10[[11, noiseN]];(*tau2*)
 ,
 (*take mono*)
 Print["take mono"];
 simParamNoiseC10[[12, noiseN]] = simParamNoiseC10[[3, noiseN]];
 (*delay*)
 simParamNoiseC10[[13, noiseN]] = simParamNoiseC10[[4, noiseN]];
 (*amp*)
```

```
    simParamNoiseC10[[14, noiseN]] = NaN; (*amp1*)
    simParamNoiseC10[[15, noiseN]] = simParamNoiseC10[[5, noiseN]];
    (*tau1*)
    simParamNoiseC10[[16, noiseN]] = NaN;(*tau2*)
  ];
];
(*plot last example of the noise loop*)
gr1 = ListPlot[tmpToFitNoise, PlotRange → All, PlotStyle → Black];
gr2 = Plot[myFitMono[x1] /. fitResultMono,
    {x1, cursorStart, cursorEnd}, PlotRange → All, PlotStyle → {Blue, Dashed}];
gr3 = Plot[myFitBi[x1] /. fitResultBi, {x1, cursorStart, cursorEnd},
    PlotRange → All, PlotStyle → {Green, Dashed}];
Show[gr1, gr2, gr3, PlotRange → All ] // Print;
If[exportYes == 1,
  Export["withinLoop r" <> ToString[r] <> " Ca" <>
     ToString[1*^6 myCaNow] <> " C10 data.txt", tmpToFitNoise, "Table"];
  toExport = Table[{t, (myFitMono[t] /. fitResultMono) [[1]]},
     {t, cursorStart, cursorEnd, dtOfPlotsForExport}];
  Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
     " C10 fitMono.txt", toExport, "Table"];
  toExport = Table[{t, (myFitBi[t] /. fitResultBi) [[1]]},
     {t, cursorStart, cursorEnd, dtOfPlotsForExport}];
  Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
     " C10 fitBi.txt", toExport, "Table"];
];
noiseN = noiseRepeats; (*fit parameter of last noisetrace*)
Print["Mono: chi2 = ", simParamNoiseC10[[2, noiseN]], "     d = ",
  simParamNoiseC10[[2, noiseN]], "     a = ", simParamNoiseC10[[4, noiseN]],
  "     t = ", 1/simParamNoiseC10[[5, noiseN]]];
Print["Bi: ratio chi2Mono/chi2Bi = ", simParamNoiseC10[[6, noiseN]],
  "     d = ", simParamNoiseC10[[7, noiseN]], "     a = ",
  simParamNoiseC10[[8, noiseN]], "     a1 = ", simParamNoiseC10[[9, noiseN]],
  "     t1 =", 1/simParamNoiseC10[[10, noiseN]],
  "     t2 = ", 1/simParamNoiseC10[[11, noiseN]]];
(*average fit results*)
For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
  simParamMedianC10[[p, r]] =
   Median[simParamNoiseC10[[p, All]] /. NaN → Sequence[]];
  simParamQuantile1C10[[p, r]] = Quantile[
     simParamNoiseC10[[p, All]] /. NaN → Sequence[], myQuantile1];
  simParamQuantile2C10[[p, r]] = Quantile[
     simParamNoiseC10[[p, All]] /. NaN → Sequence[], myQuantile2];
];

(*if tau1 merge > 10 ms, use long trace for fitting*)
If[(1/simParamMedianC10[[15, r]]) > 0.01,
```

```
Print["Long trace was used for fitting."];
For[noiseN = 1, noiseN ≤ noiseRepeats, noiseN += 1,
 tmpToFitNoiseLong = Transpose[{tmpToFitLong[[All, 1]],
    # + RandomVariate[NormalDistribution[0, myNoiseLong]] & /@
     tmpToFitLong[[All, 2]]}];
 (*fit mono-exp to Long trace*)
 fitResultsTMP = NonlinearModelFit[tmpToFitNoiseLong, myFitMono[x1],
   {{delayMono, delayGuess}, {ampMono, ampGuess}, {tau1Mono,
     caAdjustedTau1Guess}}, x1, MaxIterations → myMaxIterations];
 fitResultLongMono = fitResultsTMP[{"BestFitParameters"}];
 simParamNoiseC10[[2, noiseN]] =
  fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
 (*Print[fitResultsTMP["ANOVATableSumsOfSquares"]];*)
 simParamNoiseC10[[3, noiseN]] = (delayMono /. fitResultLongMono)[[1]];
 simParamNoiseC10[[4, noiseN]] = ((ampMono /. fitResultLongMono))[[1]];
 simParamNoiseC10[[5, noiseN]] = (1 / (tau1Mono /. fitResultLongMono))[[1]];
 (*fit bi-exp*)
 fitResultsTMP =
  NonlinearModelFit[tmpToFitNoiseLong, myFitBi[x1], {{delay, delayGuess},
    {amp, ampGuess}, {amp1, amp1Guess}, {tau1, caAdjustedTau1Guess},
    {tau2, caAdjustedTau2Guess}}, x1, MaxIterations → myMaxIterations];
 fitResultLongBi = fitResultsTMP[{"BestFitParameters"}];
 simParamNoiseC10[[6, noiseN]] = simParamNoiseC10[[2, noiseN]] /
   fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
 simParamNoiseC10[[7, noiseN]] = (delay /. fitResultLongBi)[[1]];
 simParamNoiseC10[[8, noiseN]] = ((amp /. fitResultLongBi))[[1]];
 simParamNoiseC10[[9, noiseN]] = ((amp amp1 /. fitResultLongBi))[[1]];
 (*relative amp1*)
 simParamNoiseC10[[10, noiseN]] = (1 / (tau1 /. fitResultLongBi))[[1]];
 simParamNoiseC10[[11, noiseN]] = (1 / (tau2 /. fitResultLongBi))[[1]];
 (*merge*)
 If[
  (*to use the bi-exp fit,
  the following cirteria should be fullfilled:*)
  (*chi2 should improve(=decrease) by >4%*)
  (simParamNoiseC10[[6, noiseN]] > 1.04)
   &&
   (*tau1 and tau2 of bi fit should be factor of >3 different*)
   ((simParamNoiseC10[[11, noiseN]] / simParamNoiseC10[[10, noiseN]]) < 3.)
   &&
   (*relative amplitude of 1st component should be > 5% *)
   ((( amp1 /. fitResultLongBi))[[1]] > 0.05)
   &&
   (*relative amplitude of 1st component should be < 95% *)
   ((( amp1 /. fitResultLongBi))[[1]] < 0.95)
  ,
```

```
  (*take bi*)
  Print["take bi"];
  simParamNoiseC10[[12, noiseN]] = simParamNoiseC10[[7, noiseN]];
  (*delay*)
  simParamNoiseC10[[13, noiseN]] = simParamNoiseC10[[8, noiseN]];
  (*amp*)
  simParamNoiseC10[[14, noiseN]] = simParamNoiseC10[[9, noiseN]];
  (*amp1*)
  simParamNoiseC10[[15, noiseN]] = simParamNoiseC10[[10, noiseN]];
  (*tau1*)
  simParamNoiseC10[[16, noiseN]] = simParamNoiseC10[[11, noiseN]];(*tau2*)
  ,
  (*take mono*)
  Print["take mono"];
  simParamNoiseC10[[12, noiseN]] = simParamNoiseC10[[3, noiseN]];
  (*delay*)
  simParamNoiseC10[[13, noiseN]] = simParamNoiseC10[[4, noiseN]];
  (*amp*)
  simParamNoiseC10[[14, noiseN]] = NaN; (*amp1*)
  simParamNoiseC10[[15, noiseN]] = simParamNoiseC10[[5, noiseN]];
  (*tau1*)
  simParamNoiseC10[[16, noiseN]] = NaN;(*tau2*)
 ];
];
(*plot last example of the noise loop*)
gr1 = ListPlot[tmpToFitNoiseLong, PlotRange → All, PlotStyle → Black];
gr2 = Plot[myFitMono[x1] /. fitResultLongMono, {x1, cursorStart,
    cursorEndLong}, PlotRange → All, PlotStyle → {Blue, Dashed}];
gr3 = Plot[myFitBi[x1] /. fitResultLongBi, {x1, cursorStart, cursorEndLong},
   PlotRange → All, PlotStyle → {Green, Dashed}];
Show[gr1, gr2, gr3, PlotRange → All ] // Print;
If[exportYes == 1,
 Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
    " C10 dataLong.txt", tmpToFitNoiseLong, "Table"];
 toExport = Table[{t, (myFitMono[t] /. fitResultLongMono)[[1]]},
    {t, cursorStart, cursorEndLong, dtOfPlotsForExport}];
 Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
    " C10 fitLongMono.txt", toExport, "Table"];
 toExport = Table[{t, (myFitBi[t] /. fitResultLongBi)[[1]]},
    {t, cursorStart, cursorEndLong, dtOfPlotsForExport}];
 Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
    " C10 fitLongBi.txt", toExport, "Table"];

];
noiseN = noiseRepeats; (*fit parameter of last noisetrace*)
Print["Mono: chi2 = ", simParamNoiseC10[[2, noiseN]], "     d = ",
 simParamNoiseC10[[3, noiseN]], "     a = ", simParamNoiseC10[[4, noiseN]],
```

```
    "     t = ", 1/simParamNoiseC10[[5, noiseN]]];
   Print["Bi: ratio chi2Mono/chi2Bi = ", simParamNoiseC10[[6, noiseN]],
    "     d = ", simParamNoiseC10[[7, noiseN]], "     a = ",
    simParamNoiseC10[[8, noiseN]], "     a1 = ", simParamNoiseC10[[9, noiseN]],
    "     t1 =", 1/simParamNoiseC10[[10, noiseN]],
    "     t2 = ", 1/simParamNoiseC10[[11, noiseN]]];
   (*average fit results*)
   For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
    simParamMedianC10[[p, r]] =
     Median[simParamNoiseC10[[p, All]] /. NaN → Sequence[]];
    simParamQuantile1C10[[p, r]] = Quantile[
      simParamNoiseC10[[p, All]] /. NaN → Sequence[], myQuantile1];
    simParamQuantile2C10[[p, r]] = Quantile[
      simParamNoiseC10[[p, All]] /. NaN → Sequence[], myQuantile2];
   ];
  ];

  , (*else: signal is not large enough*)
  For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
    simParamMedianC10[[p, r]] = {};
    simParamQuantile1C10[[p, r]] = {};
    simParamQuantile2C10[[p, r]] = {};
   ];
 ];

(*---------    Fitting of data,
saving of results, and plotting-----------------*)
(*--------------------------------------------------------------------
                                  ----*)
(*-----------------------------------    D     ------------------------
                     --*)
(*--------------------------------------------------------------------
                                  ----*)
Print[
 "---------------------------------------------------------------------
   D"];
(*check that signal is large enough relative to noise to obtain
 useful fit results. If not, do not do fitting and set everything to {}*)
If[simParamNv[[5, r]] > signalToNoiseRatioD myNoiseD, (*add noise
  several times and do the fitting and than average the results*)
 For[noiseN = 1, noiseN ≤ noiseRepeats, noiseN += 1,
  (*Print[noiseN];*)
  tmpToFitNoise = Transpose[{tmpToFitD[[All, 1]],
     # + RandomVariate[NormalDistribution[0, myNoiseD]] & /@
      tmpToFitD[[All, 2]]}];
  (*fit mono-exp*)
  fitResultsTMP = NonlinearModelFit[tmpToFitNoise, myFitMono[x1],
```

```
  {{delayMono, delayGuess}, {ampMono, ampGuess}, {tau1Mono,
    caAdjustedTau1Guess}}, x1, MaxIterations → myMaxIterations];
fitResultMono = fitResultsTMP[{"BestFitParameters"}];
simParamNoiseD[[1, noiseN]] = 0; (*not used anymore*)
simParamNoiseD[[2, noiseN]] =
 fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
(*Print[fitResultsTMP["ANOVATableSumsOfSquares"]];*)
simParamNoiseD[[3, noiseN]] = (delayMono /. fitResultMono)[[1]];
simParamNoiseD[[4, noiseN]] = ((ampMono /. fitResultMono))[[1]];
simParamNoiseD[[5, noiseN]] = (1/(tau1Mono /. fitResultMono))[[1]];
(*fit bi-exp*)
fitResultsTMP =
 NonlinearModelFit[tmpToFitNoise, myFitBi[x1], {{delay, delayGuess},
   {amp, ampGuess}, {amp1, amp1Guess}, {tau1, caAdjustedTau1Guess},
   {tau2, caAdjustedTau2Guess}}, x1, MaxIterations → myMaxIterations];
fitResultBi = fitResultsTMP[{"BestFitParameters"}];
simParamNoiseD[[6, noiseN]] = simParamNoiseD[[2, noiseN]] /
  fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
simParamNoiseD[[7, noiseN]] = (delay /. fitResultBi)[[1]];
simParamNoiseD[[8, noiseN]] = ((amp /. fitResultBi))[[1]];
simParamNoiseD[[9, noiseN]] = ((amp amp1 /. fitResultBi))[[1]];
(*relative amp1*)
simParamNoiseD[[10, noiseN]] = (1/(tau1 /. fitResultBi))[[1]];
simParamNoiseD[[11, noiseN]] = (1/(tau2 /. fitResultBi))[[1]];
(*merge*)
If[
 (*to use the bi-exp fit, the following cirteria should be fullfilled:*)
 (*chi2 should improve(=decrease) by >4%*)
 (simParamNoiseD[[6, noiseN]] > 1.04)
  &&
  (*tau1 and tau2 of bi fit should be factor of >3 different*)
  ((simParamNoiseD[[11, noiseN]] / simParamNoiseD[[10, noiseN]]) < 3.)
  &&
  (*relative amplitude of 1st component should be > 5% *)
  ((( amp1 /. fitResultBi))[[1]] > 0.05)
  &&
  (*relative amplitude of 1st component should be < 95% *)
  ((( amp1 /. fitResultBi))[[1]] < 0.95)
 ,
 (*take bi*)
 Print["take bi"];
 simParamNoiseD[[12, noiseN]] = simParamNoiseD[[7, noiseN]];
 (*delay*)
 simParamNoiseD[[13, noiseN]] = simParamNoiseD[[8, noiseN]];
 (*amp*)
 simParamNoiseD[[14, noiseN]] = simParamNoiseD[[9, noiseN]];
```

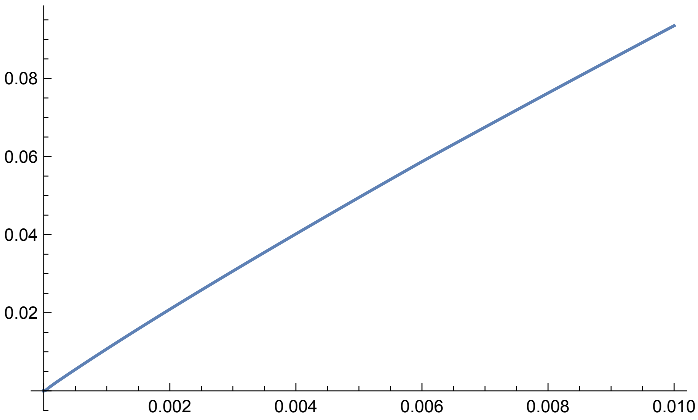
```
  (*amp1*)
  simParamNoiseD[[15, noiseN]] = simParamNoiseD[[10, noiseN]];
  (*tau1*)
  simParamNoiseD[[16, noiseN]] = simParamNoiseD[[11, noiseN]];(*tau2*)
  ,
  (*take mono*)
  Print["take mono"];
  simParamNoiseD[[12, noiseN]] = simParamNoiseD[[3, noiseN]];
  (*delay*)
  simParamNoiseD[[13, noiseN]] = simParamNoiseD[[4, noiseN]];
  (*amp*)
  simParamNoiseD[[14, noiseN]] = NaN; (*amp1*)
  simParamNoiseD[[15, noiseN]] = simParamNoiseD[[5, noiseN]];
  (*tau1*)
  simParamNoiseD[[16, noiseN]] = NaN;(*tau2*)
 ];
];
(*plot last example of the noise loop*)
gr1 = ListPlot[tmpToFitNoise, PlotRange → All, PlotStyle → Black];
gr2 = Plot[myFitMono[x1] /. fitResultMono,
  {x1, cursorStart, cursorEnd}, PlotRange → All, PlotStyle → {Blue, Dashed}];
gr3 = Plot[myFitBi[x1] /. fitResultBi, {x1, cursorStart, cursorEnd},
  PlotRange → All, PlotStyle → {Green, Dashed}];
Show[gr1, gr2, gr3, PlotRange → All ] // Print;
If[exportYes == 1,
 Export["withinLoop r" <> ToString[r] <> " Ca" <>
   ToString[1*^6 myCaNow] <> " D data.txt", tmpToFitNoise, "Table"];
 toExport = Table[{t, (myFitMono[t] /. fitResultMono) [[1]]},
   {t, cursorStart, cursorEnd, dtOfPlotsForExport}];
 Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
   " D fitMono.txt", toExport, "Table"];
 toExport = Table[{t, (myFitBi[t] /. fitResultBi) [[1]]},
   {t, cursorStart, cursorEnd, dtOfPlotsForExport}];
 Export["withinLoop r" <> ToString[r] <> " Ca" <>
   ToString[1*^6 myCaNow] <> " D fitBi.txt", toExport, "Table"];
];
noiseN = noiseRepeats; (*fit parameter of last noisetrace*)
Print["Mono: chi2 = ", simParamNoiseD[[2, noiseN]],
 "     d = ", simParamNoiseD[[2, noiseN]], "     a = ",
 simParamNoiseD[[4, noiseN]], "     t = ", 1/simParamNoiseD[[5, noiseN]]];
Print["Bi: ratio chi2Mono/chi2Bi = ", simParamNoiseD[[6, noiseN]],
 "     d = ", simParamNoiseD[[7, noiseN]], "     a = ",
 simParamNoiseD[[8, noiseN]], "     a1 = ", simParamNoiseD[[9, noiseN]],
 "     t1 =", 1/simParamNoiseD[[10, noiseN]],
 "     t2 = ", 1/simParamNoiseD[[11, noiseN]]];
(*average fit results*)
```

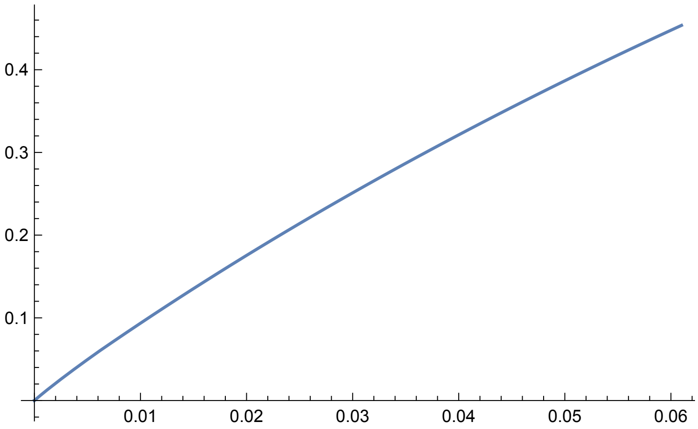
```
For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
 simParamMedianD[[p, r]] =
  Median[simParamNoiseD[[p, All]] /. NaN → Sequence[]];
 simParamQuantile1D[[p, r]] = Quantile[
   simParamNoiseD[[p, All]] /. NaN → Sequence[], myQuantile1];
 simParamQuantile2D[[p, r]] = Quantile[
   simParamNoiseD[[p, All]] /. NaN → Sequence[], myQuantile2];
];

(*if tau1 merge > 10 ms, use long trace for fitting*)
If[(1/simParamMedianD[[15, r]]) > 0.01,
 Print["Long trace was used for fitting."];
 For[noiseN = 1, noiseN ≤ noiseRepeats, noiseN += 1,
  tmpToFitNoiseLong = Transpose[{tmpToFitLong[[All, 1]],
     # + RandomVariate[NormalDistribution[0, myNoiseLong]] & /@
      tmpToFitLong[[All, 2]]}];
  (*fit mono-exp to Long trace*)
  fitResultsTMP = NonlinearModelFit[tmpToFitNoiseLong, myFitMono[x1],
    {{delayMono, delayGuess}, {ampMono, ampGuess}, {tau1Mono,
      caAdjustedTau1Guess}}, x1, MaxIterations → myMaxIterations];
  fitResultLongMono = fitResultsTMP[{"BestFitParameters"}];
  simParamNoiseD[[2, noiseN]] =
   fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
  (*Print[fitResultsTMP["ANOVATableSumsOfSquares"]];*)
  simParamNoiseD[[3, noiseN]] = (delayMono /. fitResultLongMono)[[1]];
  simParamNoiseD[[4, noiseN]] = ((ampMono /. fitResultLongMono))[[1]];
  simParamNoiseD[[5, noiseN]] = (1/(tau1Mono /. fitResultLongMono))[[1]];
  (*fit bi-exp*)
  fitResultsTMP =
   NonlinearModelFit[tmpToFitNoiseLong, myFitBi[x1], {{delay, delayGuess},
     {amp, ampGuess}, {amp1, amp1Guess}, {tau1, caAdjustedTau1Guess},
     {tau2, caAdjustedTau2Guess}}, x1, MaxIterations → myMaxIterations];
  fitResultLongBi = fitResultsTMP[{"BestFitParameters"}];
  simParamNoiseD[[6, noiseN]] = simParamNoiseD[[2, noiseN]] /
    fitResultsTMP["ANOVATableSumsOfSquares"][[2]];
  simParamNoiseD[[7, noiseN]] = (delay /. fitResultLongBi)[[1]];
  simParamNoiseD[[8, noiseN]] = ((amp /. fitResultLongBi))[[1]];
  simParamNoiseD[[9, noiseN]] = ((amp amp1 /. fitResultLongBi))[[1]];
  (*relative amp1*)
  simParamNoiseD[[10, noiseN]] = (1/(tau1 /. fitResultLongBi))[[1]];
  simParamNoiseD[[11, noiseN]] = (1/(tau2 /. fitResultLongBi))[[1]];
  (*merge*)
  If[
   (*to use the bi-exp fit,
   the following cirteria should be fullfilled:*)
   (*chi2 should improve(=decrease) by >4%*)
```

```
  (simParamNoiseD[[6, noiseN]] > 1.04)
   &&
   (*tau1 and tau2 of bi fit should be factor of >3 different*)
   ((simParamNoiseD[[11, noiseN]] / simParamNoiseD[[10, noiseN]]) < 3.)
   &&
   (*relative amplitude of 1st component should be > 5% *)
   ((( amp1 /. fitResultLongBi)) [[1]] > 0.05)
   &&
   (*relative amplitude of 1st component should be < 95% *)
   ((( amp1 /. fitResultLongBi)) [[1]] < 0.95)
  ,
  (*take bi*)
  Print["take bi"];
  simParamNoiseD[[12, noiseN]] = simParamNoiseD[[7, noiseN]];
  (*delay*)
  simParamNoiseD[[13, noiseN]] = simParamNoiseD[[8, noiseN]];
  (*amp*)
  simParamNoiseD[[14, noiseN]] = simParamNoiseD[[9, noiseN]];
  (*amp1*)
  simParamNoiseD[[15, noiseN]] = simParamNoiseD[[10, noiseN]];
  (*tau1*)
  simParamNoiseD[[16, noiseN]] = simParamNoiseD[[11, noiseN]];(*tau2*)
  ,
  (*take mono*)
  Print["take mono"];
  simParamNoiseD[[12, noiseN]] = simParamNoiseD[[3, noiseN]];
  (*delay*)
  simParamNoiseD[[13, noiseN]] = simParamNoiseD[[4, noiseN]];
  (*amp*)
  simParamNoiseD[[14, noiseN]] = NaN; (*amp1*)
  simParamNoiseD[[15, noiseN]] = simParamNoiseD[[5, noiseN]];
  (*tau1*)
  simParamNoiseD[[16, noiseN]] = NaN;(*tau2*)
 ];
];
(*plot last example of the noise loop*)
gr1 = ListPlot[tmpToFitNoiseLong, PlotRange → All, PlotStyle → Black];
gr2 = Plot[myFitMono[x1] /. fitResultLongMono, {x1, cursorStart,
    cursorEndLong}, PlotRange → All, PlotStyle → {Blue, Dashed}];
gr3 = Plot[myFitBi[x1] /. fitResultLongBi, {x1, cursorStart, cursorEndLong},
   PlotRange → All, PlotStyle → {Green, Dashed}];
Show[gr1, gr2, gr3, PlotRange → All ] // Print;
If[exportYes == 1,
 Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
    " D dataLong.txt", tmpToFitNoiseLong, "Table"];
 toExport = Table[{t, (myFitMono[t] /. fitResultLongMono) [[1]]},
    {t, cursorStart, cursorEndLong, dtOfPlotsForExport}];
```

```
      Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
        " D fitLongMono.txt", toExport, "Table"];
      toExport = Table[{t, (myFitBi[t] /. fitResultLongBi) [[1]]},
        {t, cursorStart, cursorEndLong, dtOfPlotsForExport}];
      Export["withinLoop r" <> ToString[r] <> " Ca" <> ToString[1*^6 myCaNow] <>
        " D fitLongBi.txt", toExport, "Table"];

    ];
    noiseN = noiseRepeats; (*fit parameter of last noisetrace*)
    Print["Mono: chi2 = ", simParamNoiseD[[2, noiseN]],
     "     d = ", simParamNoiseD[[3, noiseN]], "     a = ",
     simParamNoiseD[[4, noiseN]], "     t = ", 1/simParamNoiseD[[5, noiseN]]];
    Print["Bi: ratio chi2Mono/chi2Bi = ", simParamNoiseD[[6, noiseN]],
     "     d = ", simParamNoiseD[[7, noiseN]], "     a = ",
     simParamNoiseD[[8, noiseN]], "     a1 = ", simParamNoiseD[[9, noiseN]],
     "     t1 =", 1/simParamNoiseD[[10, noiseN]],
     "     t2 = ", 1/simParamNoiseD[[11, noiseN]]];
    (*average fit results*)
    For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
     simParamMedianD[[p, r]] =
      Median[simParamNoiseD[[p, All]] /. NaN → Sequence[]];
     simParamQuantile1D[[p, r]] = Quantile[
       simParamNoiseD[[p, All]] /. NaN → Sequence[], myQuantile1];
     simParamQuantile2D[[p, r]] = Quantile[
       simParamNoiseD[[p, All]] /. NaN → Sequence[], myQuantile2];
    ];
   ];

   , (*else: signal is not large enough*)
   For[p = 1, p ≤ numberOfFitParamToBeSaved, p += 1,
     simParamMedianD[[p, r]] = {};
     simParamQuantile1D[[p, r]] = {};
     simParamQuantile2D[[p, r]] = {};
    ];
  ];
 ];
```

```
-----------------------------------------------------------------------------
  -----------------------
----------------    Ca = 0.703073
  uM         ---------------------------------------------------
-----------------------------------------------------------------------------
  -----------------------
```

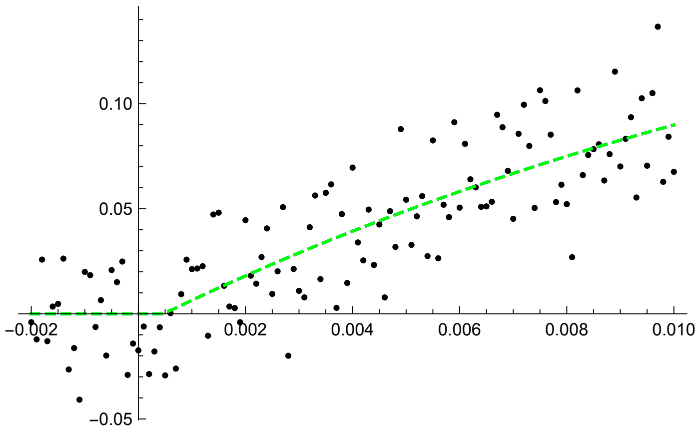





```
------------------------------------------------------------------------------ C5
------------------------------------------------------------------------------ C10
------------------------------------------------------------------------------ D
take mono
take mono
```

NonlinearModelFit: Failed to converge to the requested accuracy or precision within 100 iterations.

```
take mono
```




```
Mono: chi2 = 0.052073     d = 0.052073     a = 0.207514     t = 0.0167936
Bi: ratio chi2Mono/chi2Bi = 1.     d = 0.000470026     a =
 0.21825     a1 = 0.207217     t1 =0.0167806     t2 = 1.443
```

Quantile: Argument {} should be a non−empty list.

Quantile: Argument {} should be a non−empty list.

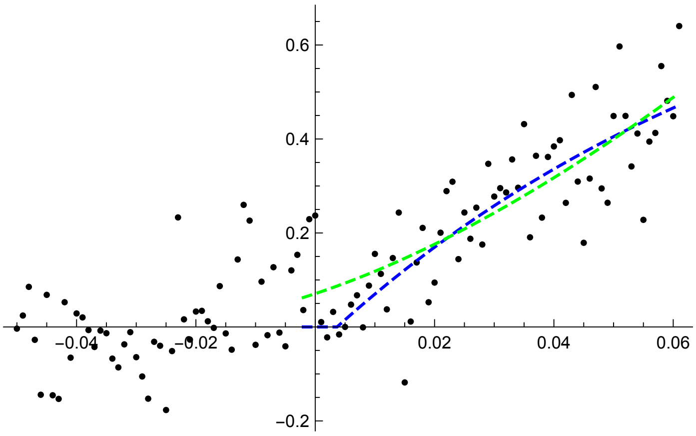
Quantile: Argument {} should be a non−empty list.

General: Further output of Quantile::empt will be suppressed during this calculation.

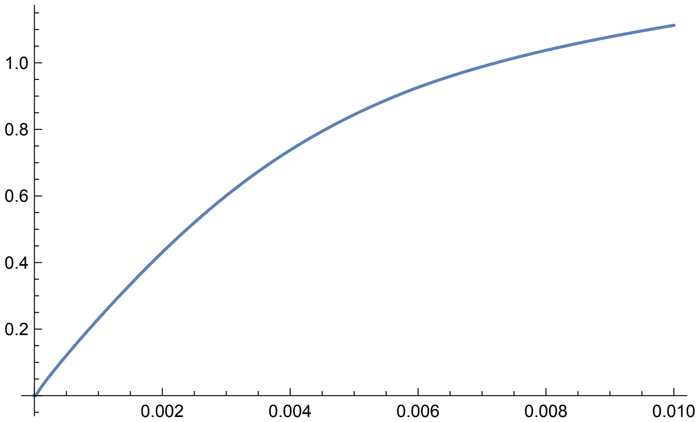
```
Long trace was used for fitting.

take mono
```

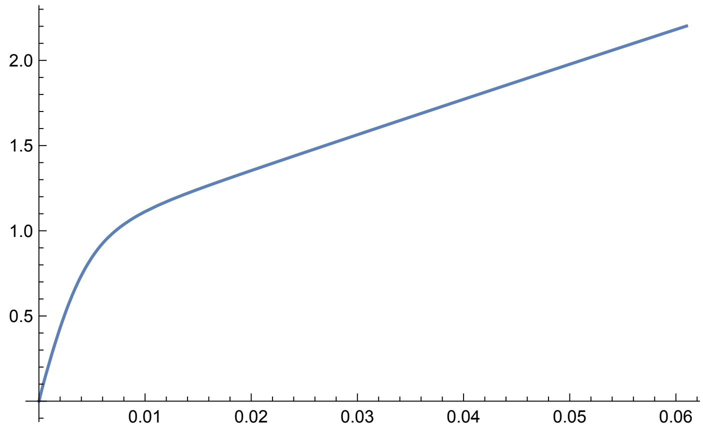
NonlinearModelFit: Failed to converge to the requested accuracy or precision within 100 iterations.

```
take mono

take mono
```




```
Mono: chi2 = 1.03411     d = 0.00366323     a = 0.933623     t = 0.0814763

Bi: ratio chi2Mono/chi2Bi = 1.05217     d = -0.028     a =
 9.46705     a1 = -4.83606     t1 =0.147526     t2 = 0.427475

---------------------------------------------------------------------------
  ----------------------

----------------     Ca = 4.79194
  uM          --------------------------------------------------

---------------------------------------------------------------------------
  ----------------------
```





--- C5

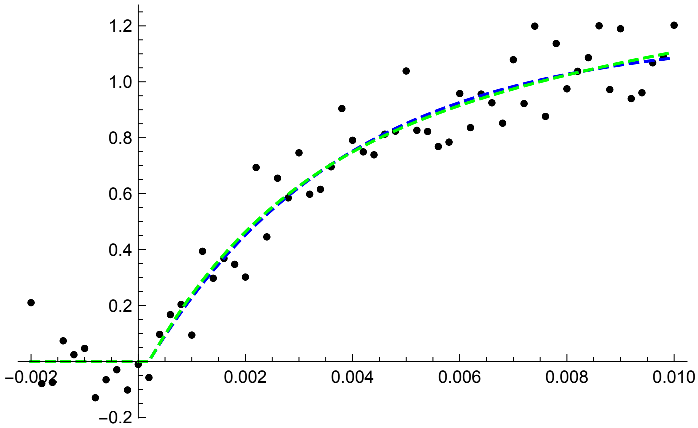
take mono

take mono

NonlinearModelFit: Failed to converge to the requested accuracy or precision within 100 iterations.

General: Further output of NonlinearModelFit::cvmit will be suppressed during this calculation.

take mono



Mono: chi2 = 0.558169   d = 0.558169   a = 1.16632   t = 0.00367285

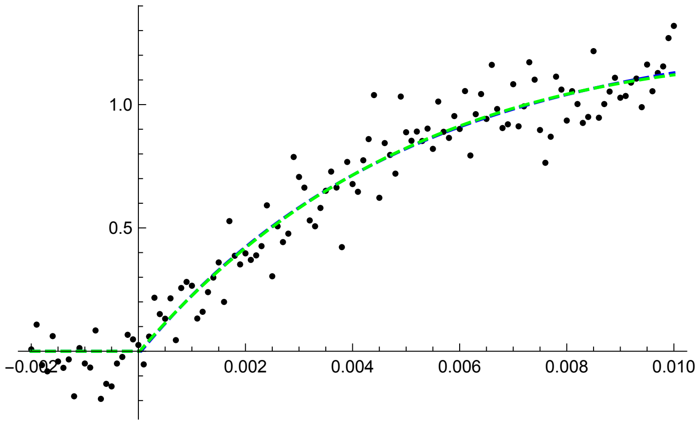
Bi: ratio chi2Mono/chi2Bi = 1.00805   d = 0.00020429   a = 7.96209   a1 = 0.840996   t1 =0.00268227   t2 = 0.238056

--- C10

take mono

take mono

take mono



Mono: chi2 = 1.20884   d = 1.20884   a = 1.30731   t = 0.0049998

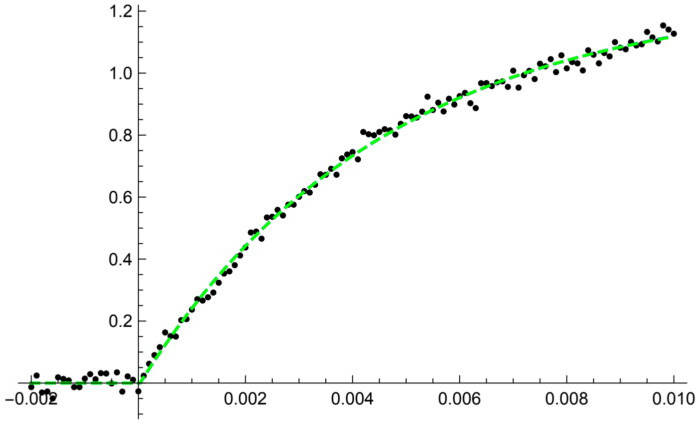
Bi: ratio chi2Mono/chi2Bi = 1.00234   d = 0.0000239968   a =
 0.777713   a1 = 2.85899   t1 =0.00736634   t2 = 0.0152262

--- D

take mono

take mono

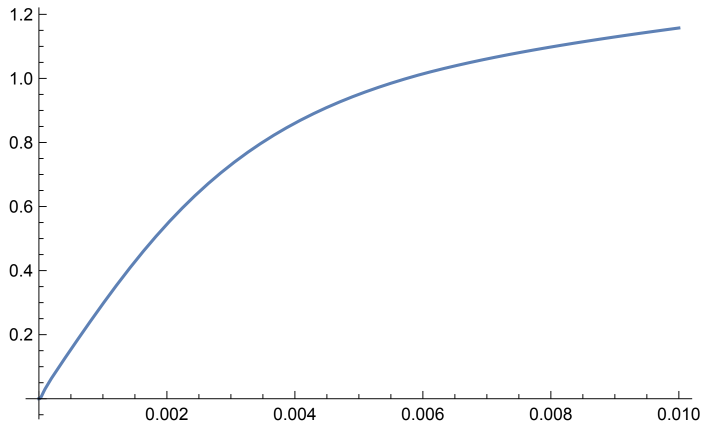
take mono

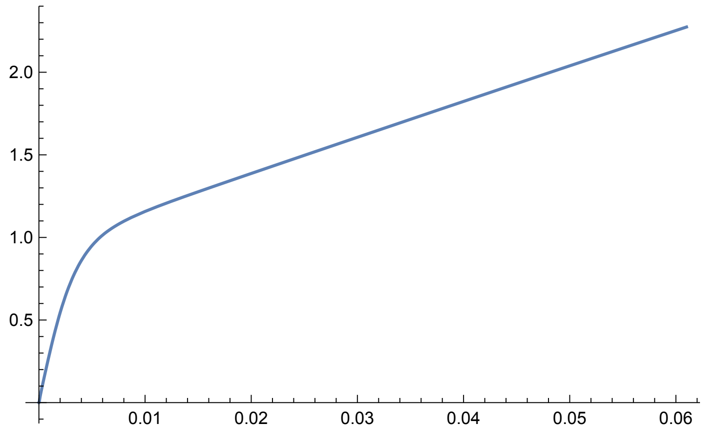


Mono: chi2 = 0.0558425   d = 0.0558425   a = 1.2585   t = 0.00453768

Bi: ratio chi2Mono/chi2Bi = 1.00026   d = 0.0000301442   a =
 1.06289   a1 = 1.3005   t1 =0.00465986   t2 = 0.0742347

----------------   Ca = 5.53376
 uM   --



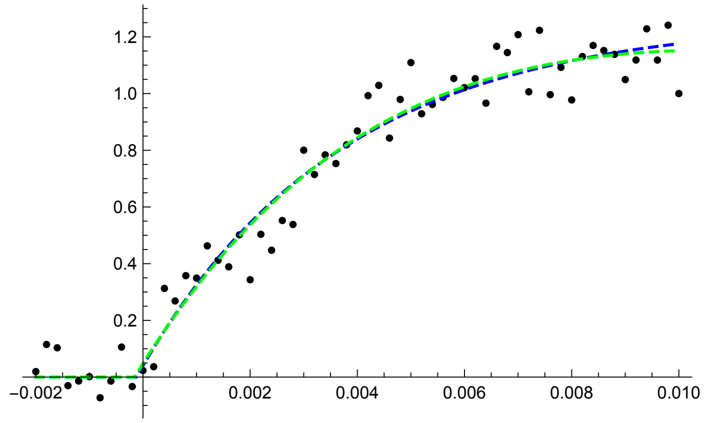


-- C5

take mono

take mono

take mono



Mono: chi2 = 0.442238   d = 0.442238   a = 1.26134   t = 0.00375974

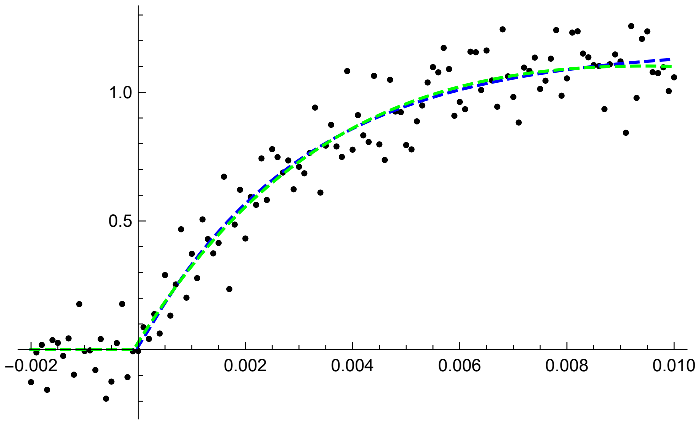
Bi: ratio chi2Mono/chi2Bi = 1.04856   d = -0.00015499   a = 0.436132   a1 = 3.67211   t1 =0.00659847   t2 = 0.0132433

-- C10

take mono

take mono

take mono



Mono: chi2 = 1.28054 d = 1.28054 a = 1.1716 t = 0.00304015

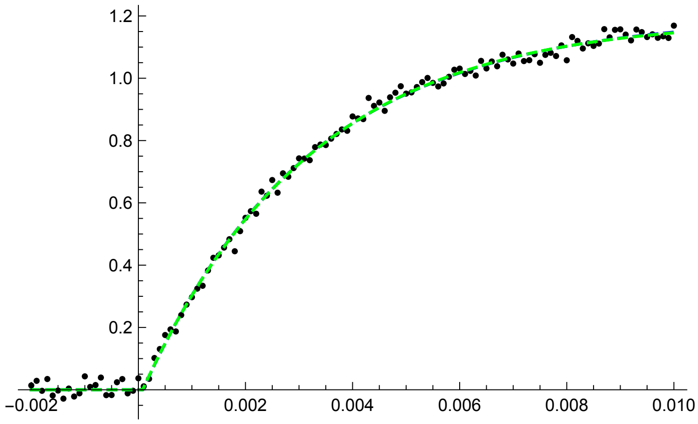
Bi: ratio chi2Mono/chi2Bi = 1.01083 d = -0.0000854457 a = 0.405774 a1 = 2.90733 t1 =0.00543144 t2 = 0.0129581

-- D

take mono

take mono

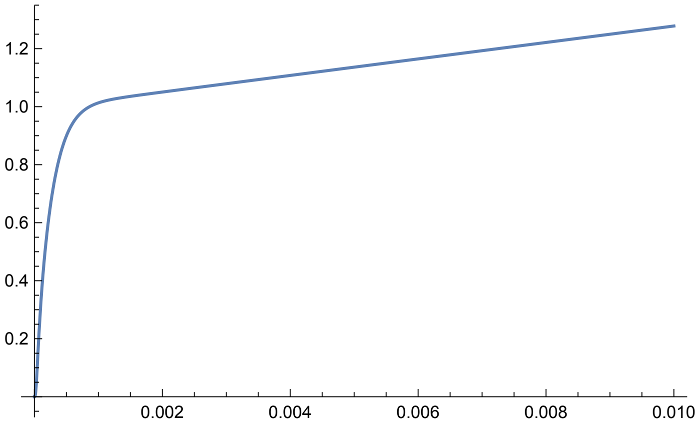
take mono

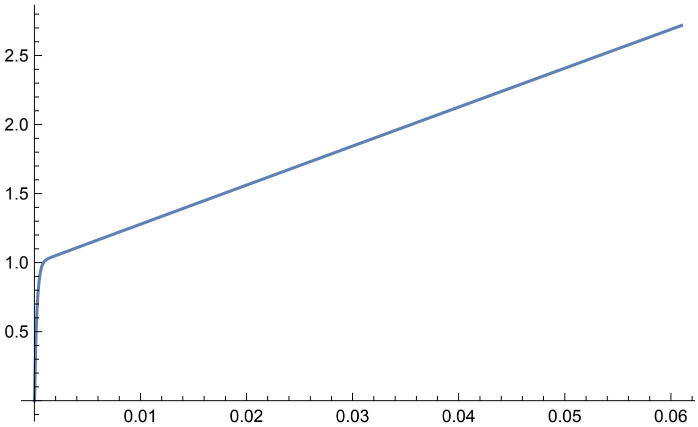


Mono: chi2 = 0.0445167 d = 0.0445167 a = 1.19823 t = 0.00312855

Bi: ratio chi2Mono/chi2Bi = 1.00155 d = 0.0000802138 a = 0.694394 a1 = 1.23061 t1 =0.00321519 t2 = 0.181744

---------------- Ca = 25.7412 uM --






```
------------------------------------------------------------------------------ C5
take bi
```

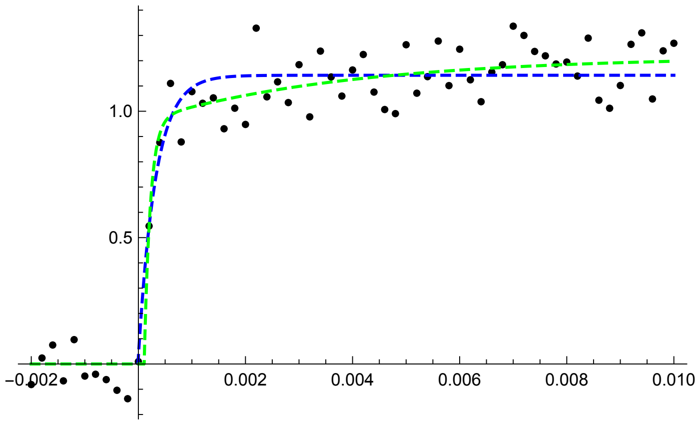
General: Exp[−747.003] is too small to represent as a normalized machine number; precision may be lost.

General: Exp[−814.867] is too small to represent as a normalized machine number; precision may be lost.

General: Exp[−882.732] is too small to represent as a normalized machine number; precision may be lost.

General: Further output of General::munfl will be suppressed during this calculation.

```
take bi
take bi
```

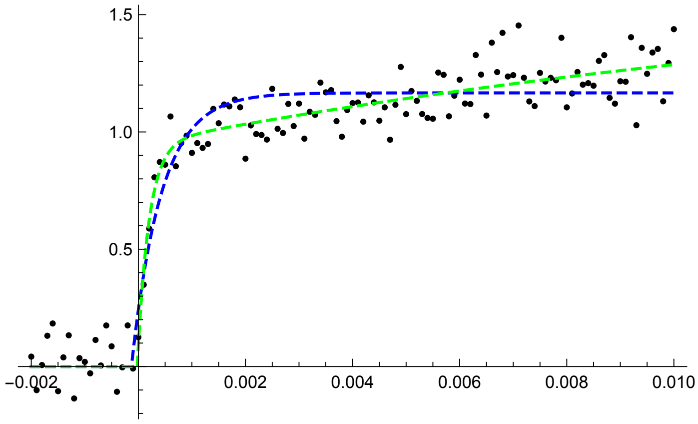



```
Mono: chi2 = 0.649345     d = 0.649345     a = 1.14232     t = 0.000320833
Bi: ratio chi2Mono/chi2Bi = 1.22491     d = 0.000108196     a =
 1.21659     a1 = 0.964012     t1 =0.000112704     t2 = 0.00380826
------------------------------------------------------------------------------ C10
```

take bi

take bi

take bi



Mono: chi2 = 1.58283 d = 1.58283 a = 1.16647 t = 0.000557984

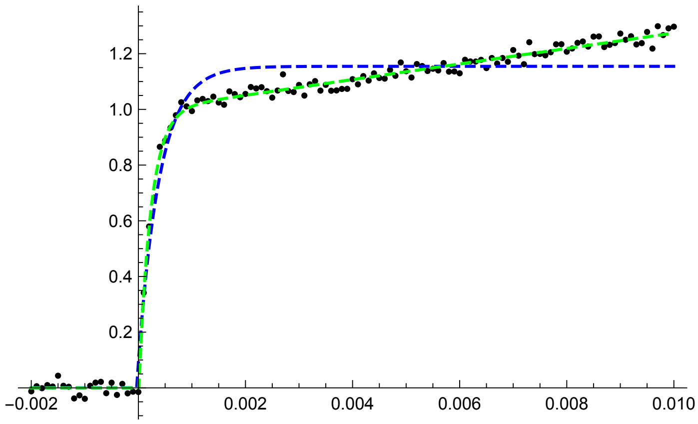
Bi: ratio chi2Mono/chi2Bi = 1.57304 d = -0.0000213642 a = 1.71711 a1 = 0.947993 t1 =0.000214065 t2 = 0.017239

-- D

take bi

take bi

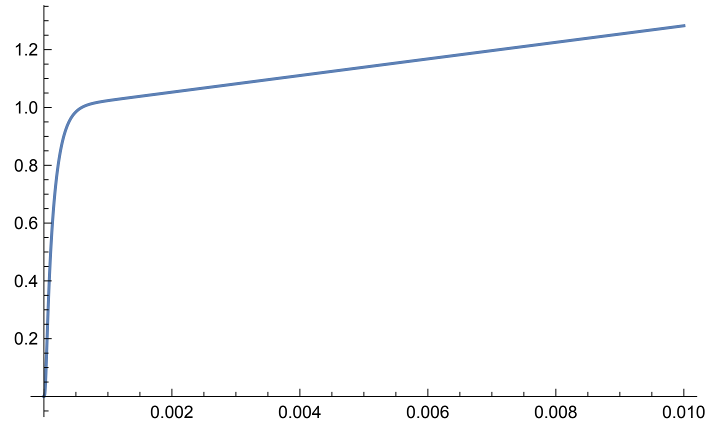
take bi

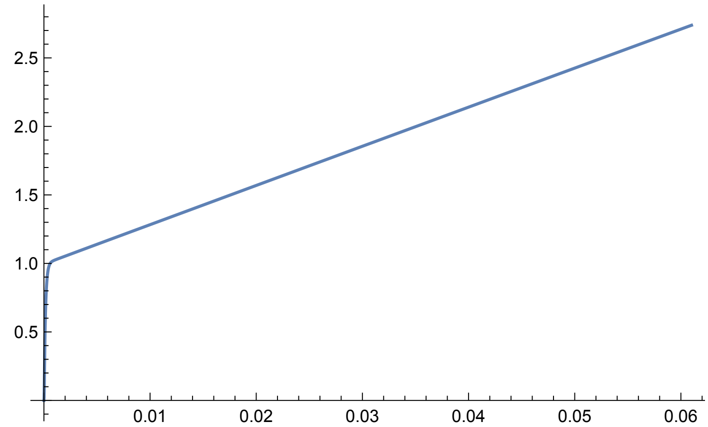


Mono: chi2 = 0.507636 d = 0.507636 a = 1.15462 t = 0.000401872

Bi: ratio chi2Mono/chi2Bi = 10.5369 d = 9.09647×10^{-6} a = 10.4532 a1 = 0.994364 t1 =0.000224212 t2 = 0.332725

---------------- Ca = 29.9583 uM --



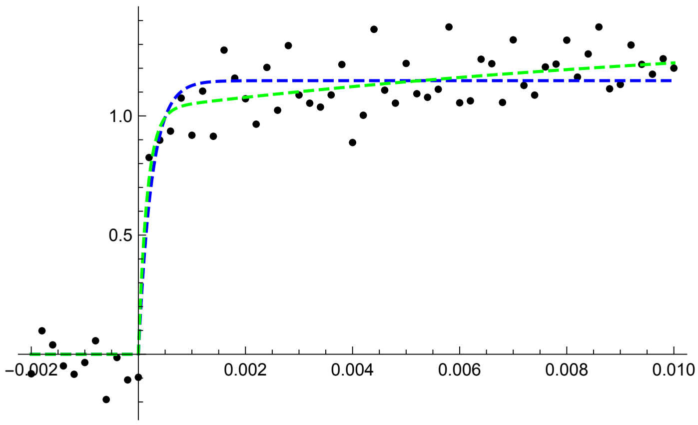


--- C5

take bi

take bi

take bi



Mono: chi2 = 0.786886   d = 0.786886   a = 1.14792   t = 0.000248599

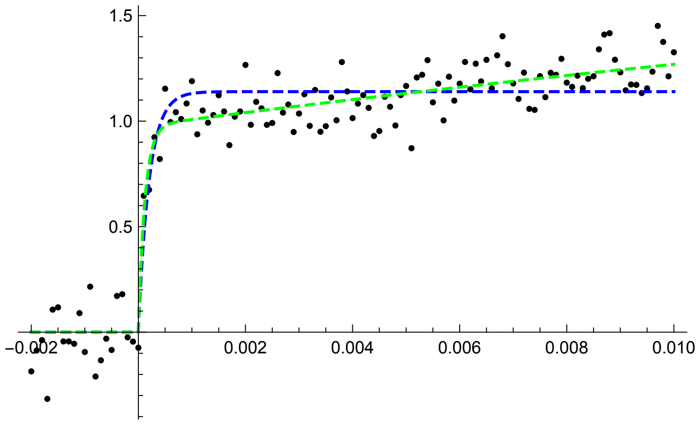
Bi: ratio chi2Mono/chi2Bi = 1.24222   d = -1.03232×10^{-15} a = 1.38662   a1 = 1.02517   t1 =0.000160952   t2 = 0.0126743

--- C10

take bi

take bi

take bi



Mono: chi2 = 1.91997 d = 1.91997 a = 1.13967 t = 0.00020587

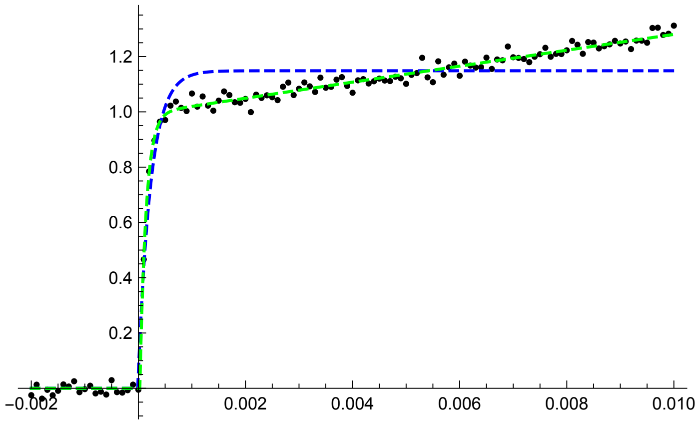
Bi: ratio chi2Mono/chi2Bi = 1.4426 d = -7.85951×10^{-18} a = 2.24612 a1 = 0.97525 t1 =0.000120365 t2 = 0.0380236

--- D

take bi

take bi

take bi



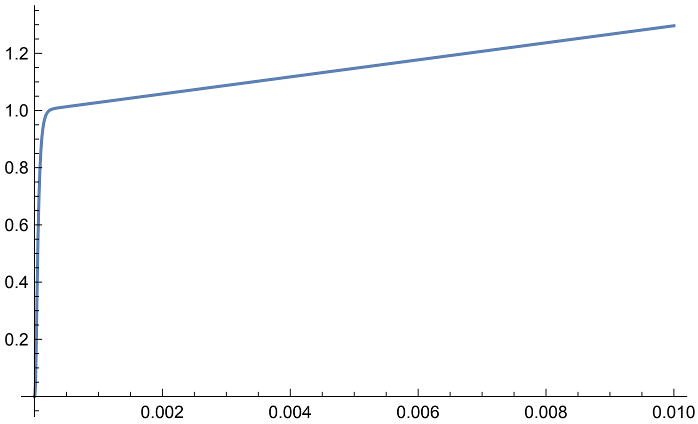
Mono: chi2 = 0.614661 d = 0.614661 a = 1.14859 t = 0.000235357

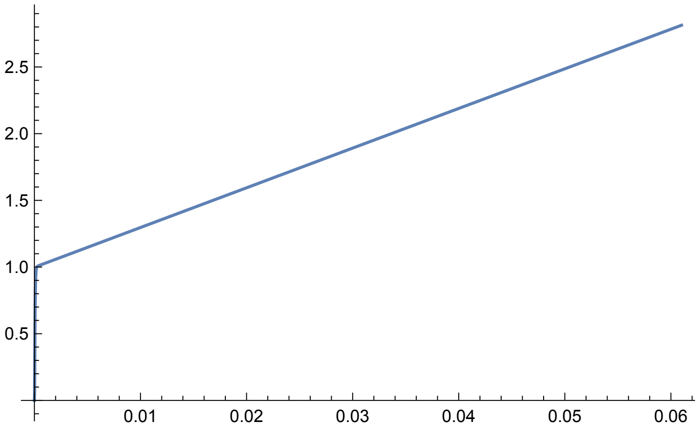
Bi: ratio chi2Mono/chi2Bi = 13.2444 d = 0.0000270937 a = 11.6767 a1 = 0.991481 t1 =0.000114976 t2 = 0.364136

--- -------------------------

---------------- Ca = 74.0312 uM --

--- -------------------------



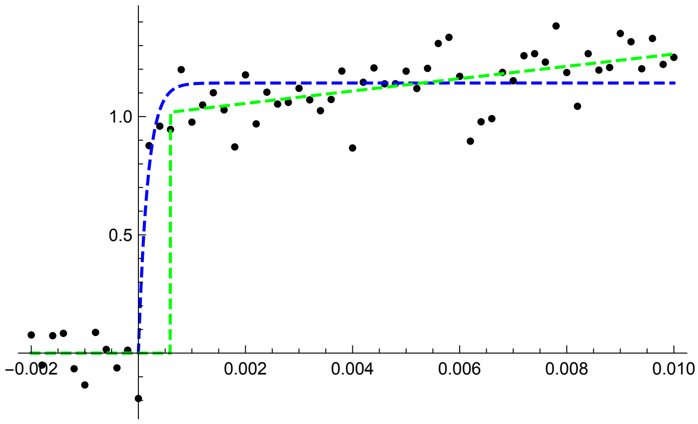


--- C5

take bi

take bi

take mono



Mono: chi2 = 0.857236 d = 0.857236 a = 1.14183 t = 0.000173996

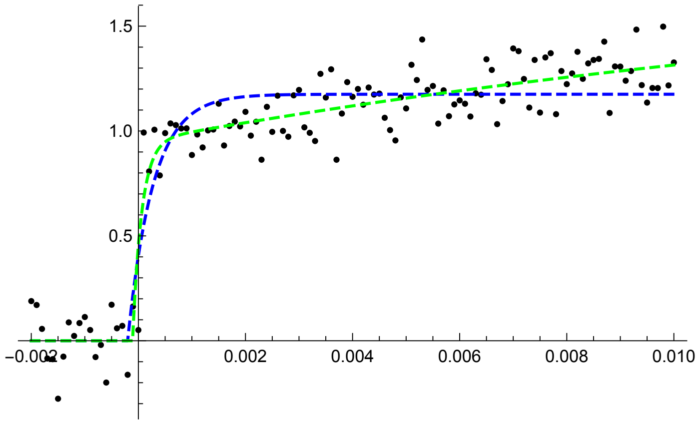
Bi: ratio chi2Mono/chi2Bi = 0.37743 d = 0.000595672 a = 10.783 a1 = 1.01854 t1 = 1.64419×10^{-6} t2 = 0.369272

--- C10

take bi

take bi

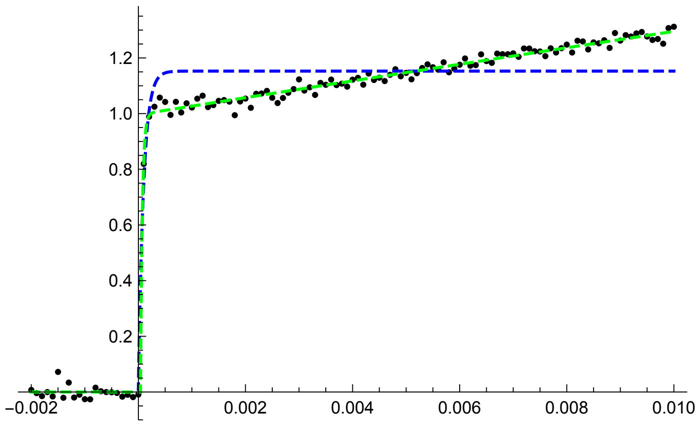
take bi




```
Mono: chi2 = 2.45429      d = 2.45429      a = 1.17529      t = 0.000473998

Bi: ratio chi2Mono/chi2Bi = 1.49977      d = -0.000108107      a =
 1.83289      a1 = 0.94555      t1 =0.000168777      t2 = 0.0188063

--------------------------------------------------------------------------- D
```

NonlinearModelFit: The step size in the search has become less than the tolerance prescribed by the PrecisionGoal option, but the gradient is larger than the tolerance specified by the AccuracyGoal option. There is a possibility that the method has stalled at a point that is not a local minimum.

```
take bi

take bi

take bi
```




```
Mono: chi2 = 0.729864      d = 0.729864      a = 1.15262      t = 0.000096565

Bi: ratio chi2Mono/chi2Bi = 17.9428      d = 0.0000391999      a =
 8.27077      a1 = 0.997597      t1 =0.0000355141      t2 = 0.238329
```

Plots

In[∘]:=
```
rrp = 10;
```

In[∘]:=
```
caFact = 1*^6;
```

In[∘]:=
```
colorA = Green;
colorB = Red;
colorC = Blue;
```

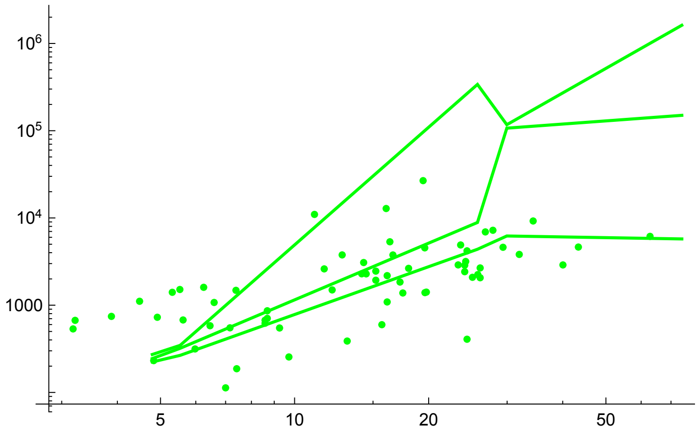
release rate 1/tau1 (merge of mono 1/tau and bi 1/tau1)

In[∘]:=
```
simParam = 15;
```

C5

In[∘]:=
```
gr1a = ListLogLogPlot[
    Transpose[{dataT1C5Ca, dataT1C5RelRate}], PlotStyle → {colorA}];
gr2a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamMedianC5[[simParam, All]]}],
    PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr3a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1C5[[simParam, All]]}],
    PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr4a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2C5[[simParam, All]]}],
    PlotStyle → {colorA}, Joined → True, PlotRange → All];
Show[gr1a, gr2a, gr3a, gr4a, PlotRange → All ]
If[exportYes == 1,
   Export["plot InvTau1 C5 data.txt",
    Transpose[{dataT1C5Ca, dataT1C5RelRate}], "Table"];
   toExport = Transpose[{caFact simCaList, simParamQuantile1C5[[simParam, All]],
      simParamMedianC5[[simParam, All]], simParamQuantile2C5[[simParam, All]]}];
   Export["plot InvTau1 C5 fit - quantiles and median.txt", toExport, "Table"];
  ];
```

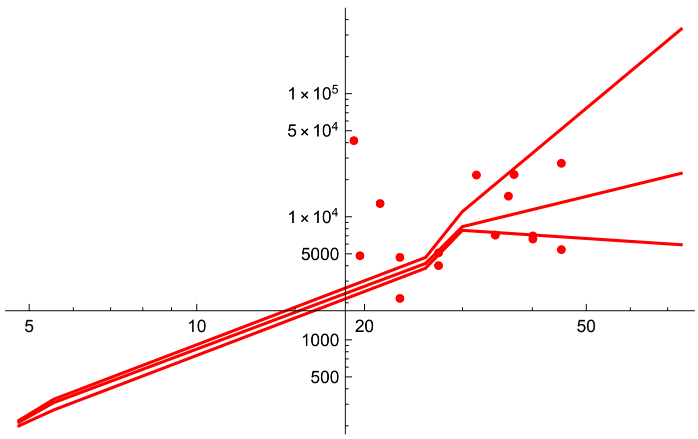
Out[∘]=



C10

In[•]:=
```
gr1b = ListLogLogPlot[
   Transpose[{dataT1C10Ca, dataT1C10RelRate}], PlotStyle → {colorB}];
gr2b = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamMedianC10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr3b = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1C10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr4b = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2C10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
Show[gr1b, gr2b, gr3b, gr4b, PlotRange → All ]
If[exportYes == 1,
  Export["plot InvTau1 C10 data.txt",
   Transpose[{dataT1C10Ca, dataT1C10RelRate}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1C10[[simParam, All]],
      simParamMedianC10[[simParam, All]],
      simParamQuantile2C10[[simParam, All]]}];
  Export["plot InvTau1 C10 fit - quantiles and median.txt", toExport, "Table"];
 ];
```

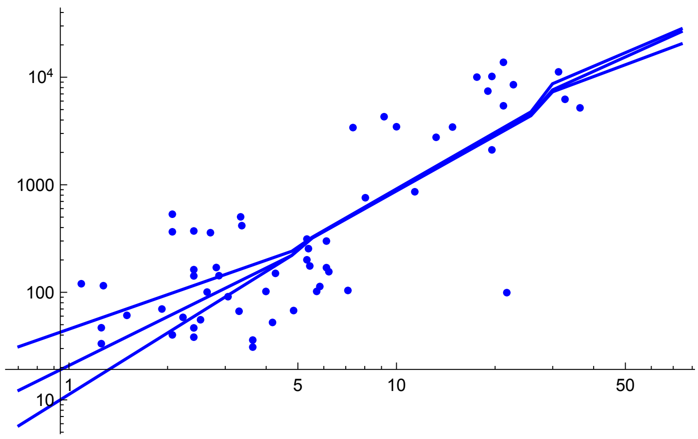
Out[•]=



D

In[•]:=
```
gr1c =
  ListLogLogPlot[Transpose[{dataT1DCa, dataT1DRelRate}], PlotStyle → {colorC}];
gr2c = ListLogLogPlot[Transpose[
     {caFact simCaList, simParamMedianD[[simParam, All]]}],
   PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr3c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1D[[simParam, All]]}],
   PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr4c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2D[[simParam, All]]}],
   PlotStyle → { colorC}, Joined → True, PlotRange → All];
Show[gr1c, gr2c, gr3c, gr4c, PlotRange → All ]
If[exportYes == 1,
  Export["plot InvTau1 D data.txt",
   Transpose[{dataT1DCa, dataT1DRelRate}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1D[[simParam, All]],
     simParamMedianD[[simParam, All]], simParamQuantile2D[[simParam, All]]}];
  Export["plot InvTau1 D fit - quantiles and median.txt", toExport, "Table"];
 ];
```

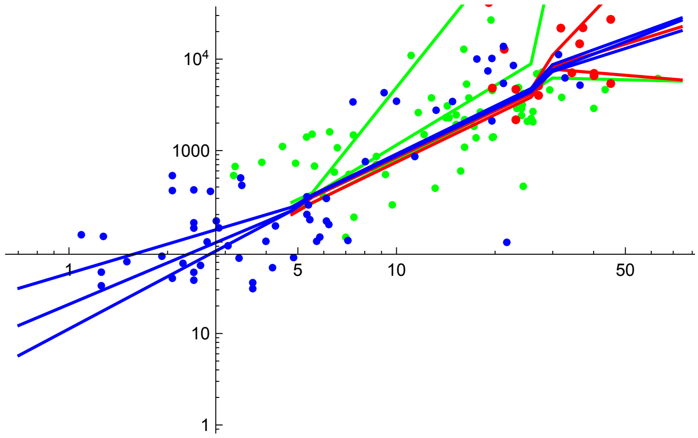
Out[•]=



C5 and C10 and D

In[∘]:=
```
Show[gr1a, gr2a, gr3a, gr4a, gr1b, gr2b, gr3b,
 gr4b, gr1c, gr2c, gr3c, gr4c, PlotRange → {All, {0, 10}}]
```

Out[∘]=



In[∘]:=
```
Show[gr1a, gr1b, gr1c, PlotRange → {All, {2, 10}}];
```

delay (mono and bi merged)

In[∘]:=
```
simParam = 12;
```

In[∘]:=
```
Transpose[{caFact simCaList, simParamMedianC5[[simParam, All]]}] // TableForm
```

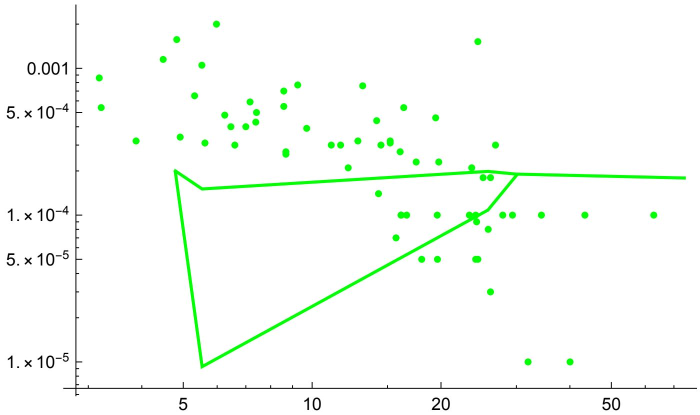
Out[∘]//TableForm=

0.703073	
4.79194	0.000196264
5.53376	9.28401×10^{-6}
25.7412	0.000108196
29.9583	0.00018539
74.0312	-8.5×10^{-18}

C5

In[∘]:=
```
gr1a =
  ListLogLogPlot[Transpose[{dataT1C5Ca, dataT1C5Delay}], PlotStyle → {colorA}];
gr2a = ListLogLogPlot[Transpose[
     {caFact simCaList, simParamMedianC5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr3a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1C5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr4a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2C5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
Show[gr1a, gr2a, gr3a, gr4a, PlotRange → All ]
If[exportYes == 1,
  Export["plot delay C5 data.txt",
   Transpose[{dataT1C5Ca, dataT1C5Delay}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1C5[[simParam, All]],
      simParamMedianC5[[simParam, All]], simParamQuantile2C5[[simParam, All]]}];
  Export["plot delay C5 fit - quantiles and median.txt", toExport, "Table"];
 ];
```

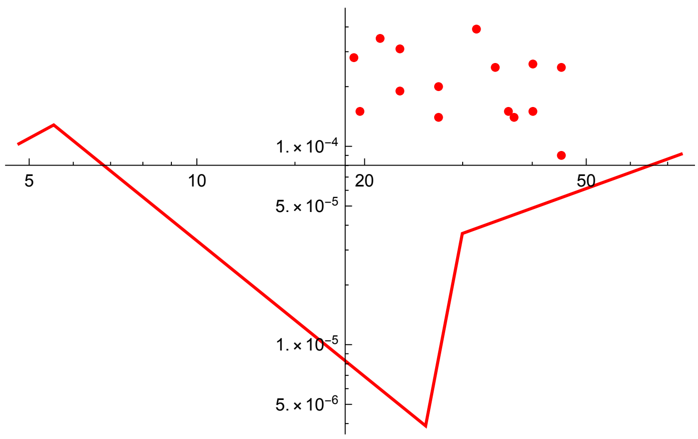
Out[∘]=



C10

In[•]:=
```
gr1b = ListLogLogPlot[
   Transpose[{dataT1C10Ca, dataT1C10Delay}], PlotStyle → {colorB}];
gr2b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamMedianC10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr3b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile1C10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr4b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile2C10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
Show[gr1b, gr2b, gr3b, gr4b, PlotRange → All ]
If[exportYes == 1,
  Export["plot delay C10 data.txt",
   Transpose[{dataT1C10Ca, dataT1C10Delay}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1C10[[simParam, All]],
     simParamMedianC10[[simParam, All]],
     simParamQuantile2C10[[simParam, All]]}];
  Export["plot delay C10 fit - quantiles and median.txt", toExport, "Table"];
 ];
```

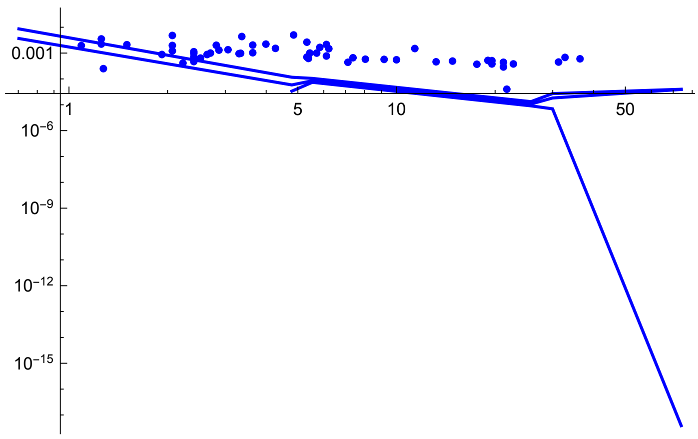
Out[•]=



D

In[•]:=
```
gr1c =
  ListLogLogPlot[Transpose[{dataT1DCa, dataT1DDelay}], PlotStyle → {colorC}];
gr2c = ListLogLogPlot[Transpose[
     {caFact simCaList, simParamMedianD[[simParam, All]]}],
   PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr3c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1D[[simParam, All]]}],
   PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr4c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2D[[simParam, All]]}],
   PlotStyle → { colorC}, Joined → True, PlotRange → All];
Show[gr1c, gr2c, gr3c, gr4c, PlotRange → All ]
If[exportYes == 1,
  Export["plot delay D data.txt",
   Transpose[{dataT1DCa, dataT1DDelay}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1D[[simParam, All]],
      simParamMedianD[[simParam, All]], simParamQuantile2D[[simParam, All]]}];
  Export["plot delay D fit - quantiles and median.txt", toExport, "Table"];
 ];
```

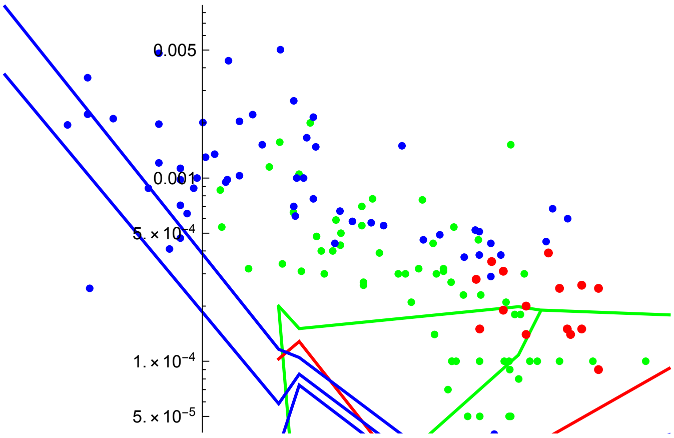
Out[•]=



C5 and C10 and D

In[•]:=
```
Show[gr1a, gr2a, gr3a, gr4a, gr1b, gr2b, gr3b,
  gr4b, gr1c, gr2c, gr3c, gr4c, PlotRange → {-10, -5}]
```

Out[•]=



In[•]:=
```
Show[gr1a, gr1b, gr1c, PlotRange → All];
```

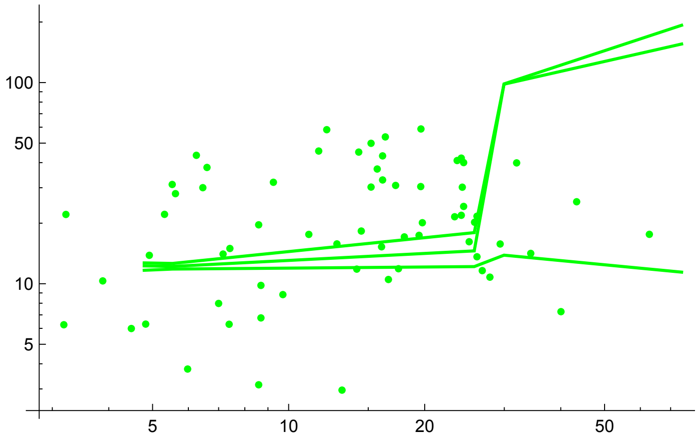
amp (merge of mono amp and bi amp)

In[•]:=
```
simParam = 13;
```

C5

In[•]:=
```
gr1a = ListLogLogPlot[
   Transpose[{dataT1C5Ca, dataT1C5Amplitude}], PlotStyle → {colorA}];
gr2a = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamMedianC5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr3a = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamQuantile1C5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr4a = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamQuantile2C5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
Show[gr1a, gr2a, gr3a, gr4a, PlotRange → All ]
```

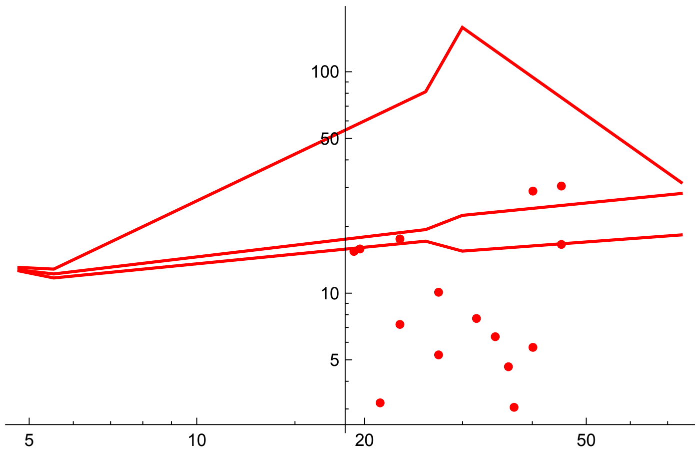
Out[•]=



C10

```
In[•]:= gr1b = ListLogLogPlot[
          Transpose[{dataT1C10Ca, dataT1C10Amplitude}], PlotStyle → {colorB}];
        gr2b = ListLogLogPlot[Transpose[{caFact simCaList,
             rrp simParamMedianC10[[simParam, All]]}],
          PlotStyle → { colorB}, Joined → True, PlotRange → All];
        gr3b = ListLogLogPlot[Transpose[{caFact simCaList,
             rrp simParamQuantile1C10[[simParam, All]]}],
          PlotStyle → { colorB}, Joined → True, PlotRange → All];
        gr4b = ListLogLogPlot[Transpose[{caFact simCaList,
             rrp simParamQuantile2C10[[simParam, All]]}],
          PlotStyle → { colorB}, Joined → True, PlotRange → All];
        Show[gr1b, gr2b, gr3b, gr4b, PlotRange → All ]
```

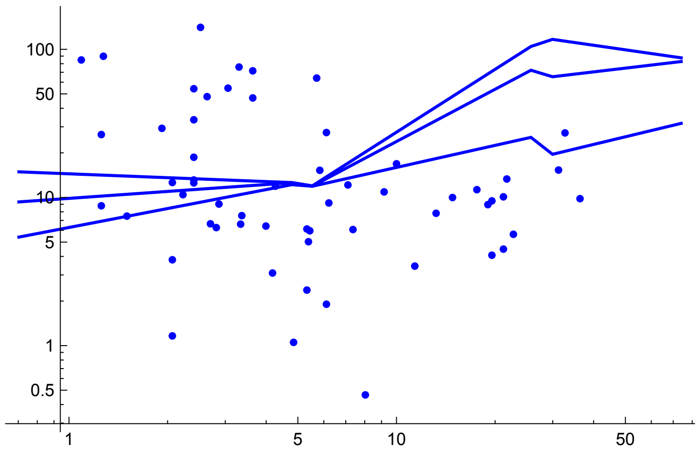
Out[•]=



D

In[•]:=
```
gr1c = ListLogLogPlot[
    Transpose[{dataT1DCa, dataT1DAmplitude}], PlotStyle → {colorC}];
gr2c = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamMedianD[[simParam, All]]}],
    PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr3c = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamQuantile1D[[simParam, All]]}],
    PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr4c = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamQuantile2D[[simParam, All]]}],
    PlotStyle → { colorC}, Joined → True, PlotRange → All];
Show[gr1c, gr2c, gr3c, gr4c, PlotRange → All ]
```

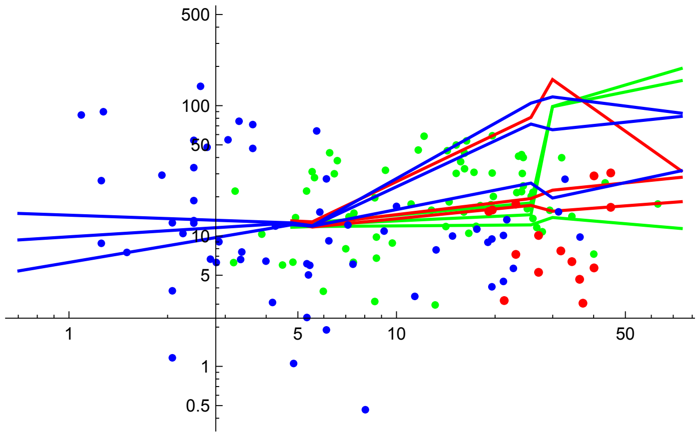
Out[•]=



C5 and C10 and D

In[•]:=
```
Show[gr1a, gr2a, gr3a, gr4a, gr1b, gr2b, gr3b,
 gr4b, gr1c, gr2c, gr3c, gr4c, PlotRange → {-1, 6} ]
```

Out[•]=



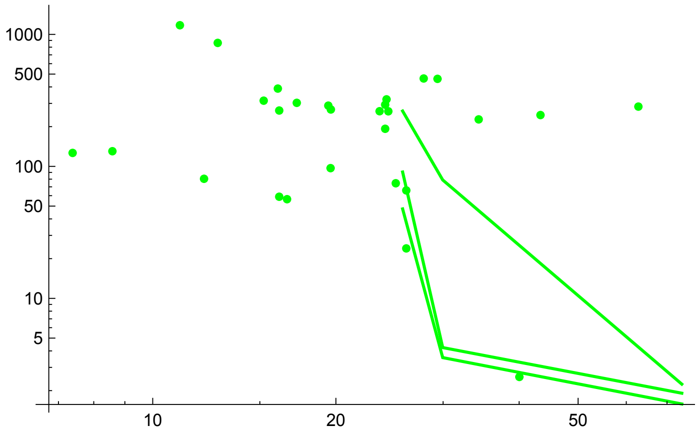
release rate 1/tau2 of bi fits (if bi is justified)

In[•]:=
```
simParam = 16;
```

C5

In[•]:=
```
gr1a = ListLogLogPlot[
   Transpose[{dataT2C5Ca, dataT2C5RelRate}], PlotStyle → {colorA}];
gr2a = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamMedianC5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr3a = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile1C5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr4a = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile2C5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
Show[gr1a, gr2a, gr3a, gr4a, PlotRange → All ]
If[exportYes == 1,
  Export["plot InvTau2 C5 data.txt",
   Transpose[{dataT2C5Ca, dataT2C5RelRate}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1C5[[simParam, All]],
     simParamMedianC5[[simParam, All]], simParamQuantile2C5[[simParam, All]]}];
  Export["plot InvTau2 C5 fit - quantiles and median.txt", toExport, "Table"];
 ];
```

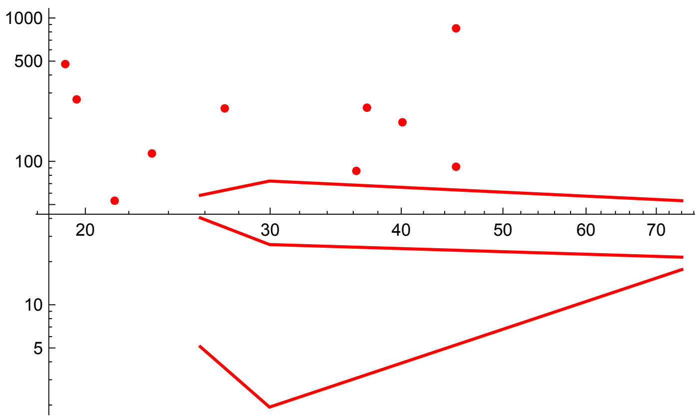
Out[•]=



C10

In[•]:=
```
gr1b = ListLogLogPlot[
   Transpose[{dataT2C10Ca, dataT2C10RelRate}], PlotStyle → {colorB}];
gr2b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamMedianC10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr3b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile1C10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr4b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile2C10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
Show[gr1b, gr2b, gr3b, gr4b, PlotRange → All ]
If[exportYes == 1,
  Export["plot InvTau2 C10 data.txt",
   Transpose[{dataT2C10Ca, dataT2C10RelRate}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1C10[[simParam, All]],
     simParamMedianC10[[simParam, All]],
     simParamQuantile2C10[[simParam, All]]}];
  Export["plot InvTau2 C10 fit - quantiles and median.txt", toExport, "Table"];
 ];
```

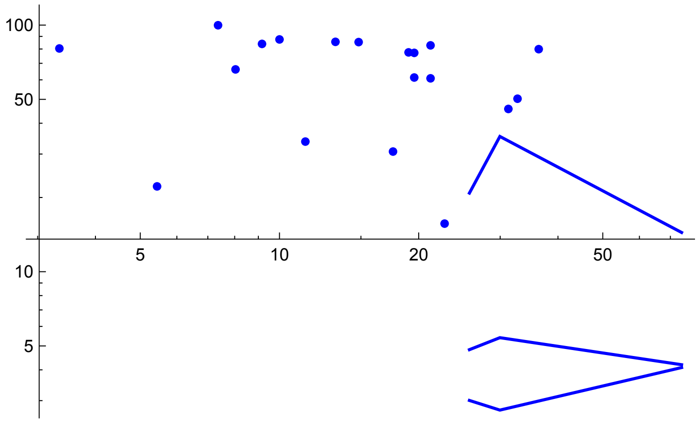
Out[•]=



D

In[•]:=
```
gr1c =
  ListLogLogPlot[Transpose[{dataT2DCa, dataT2DRelRate}], PlotStyle → {colorC}];
gr2c = ListLogLogPlot[Transpose[
     {caFact simCaList, simParamMedianD[[simParam, All]]}],
    PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr3c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1D[[simParam, All]]}],
    PlotStyle → { colorC}, Joined → True, PlotRange → All];
gr4c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2D[[simParam, All]]}],
    PlotStyle → { colorC}, Joined → True, PlotRange → All];
Show[gr1c, gr2c, gr3c, gr4c, PlotRange → All ]
If[exportYes == 1,
  Export["plot InvTau2 D data.txt",
   Transpose[{dataT2DCa, dataT2DRelRate}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1D[[simParam, All]],
     simParamMedianD[[simParam, All]], simParamQuantile2D[[simParam, All]]}];
  Export["plot InvTau2 D fit - quantiles and median.txt", toExport, "Table"];
 ];
```

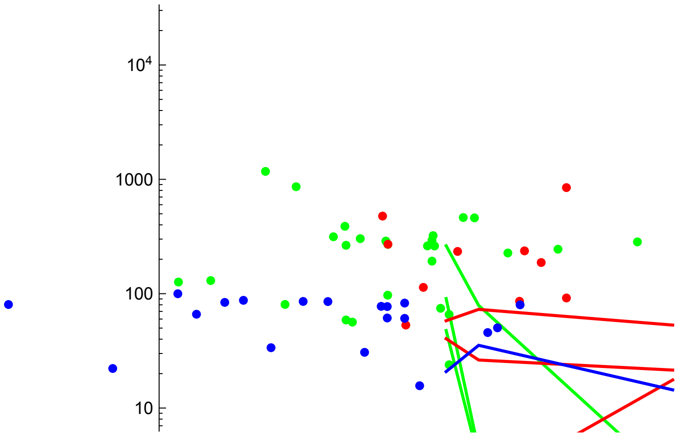
Out[•]=



C5 and C10 and D

In[•]:=
```
Show[gr1a, gr2a, gr3a, gr4a, gr1b, gr2b, gr3b,
  gr4b, gr1c, gr2c, gr3c, gr4c, PlotRange → {All, {2, 10}}]
```

Out[•]=



In[•]:=
```
Show[gr1a, gr1b, gr1c, PlotRange → All];
```

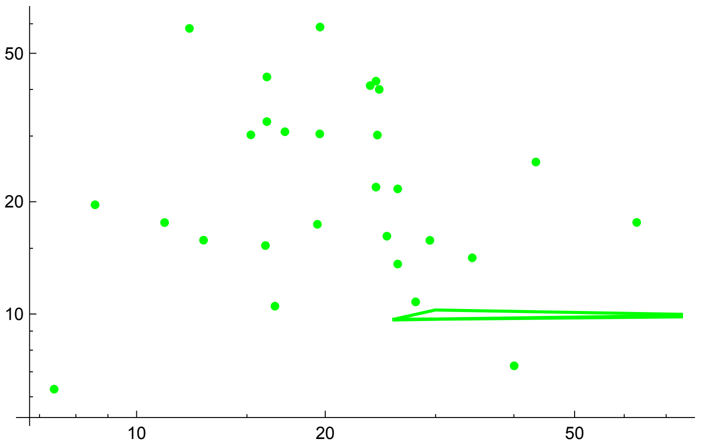
amp1 of bi fits (if bi is justified)

In[•]:=
```
simParam = 14;
```

C5

In[*]:=
```
gr1a = ListLogLogPlot[
   Transpose[{dataT2C5Ca, dataT2C5Amplitude1}], PlotStyle → {colorA}];
gr2a = ListLogLogPlot[Transpose[{caFact simCaList,
     rrp simParamMedianC5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr3a = ListLogLogPlot[Transpose[{caFact simCaList,
     rrp simParamQuantile1C5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr4a = ListLogLogPlot[Transpose[{caFact simCaList,
     rrp simParamQuantile2C5[[simParam, All]]}],
   PlotStyle → { colorA}, Joined → True, PlotRange → All];
Show[gr1a, gr2a, gr3a, gr4a, PlotRange → All ]
```

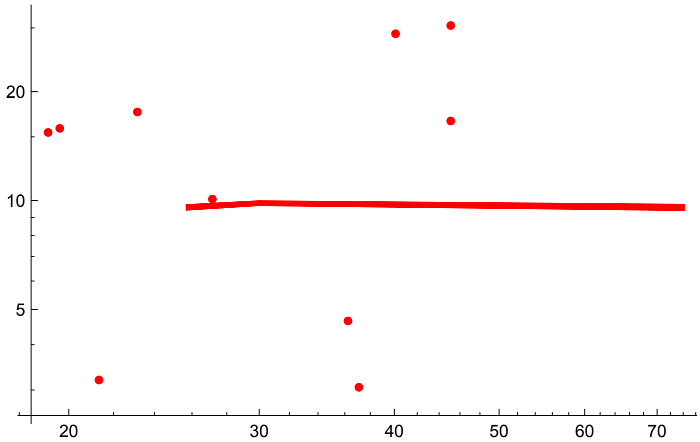
Out[*]=



C10

In[•]:=
```
gr1b = ListLogLogPlot[
   Transpose[{dataT2C10Ca, dataT2C10Amplitude1}], PlotStyle → {colorB}];
gr2b = ListLogLogPlot[Transpose[{caFact simCaList,
     rrp simParamMedianC10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr3b = ListLogLogPlot[Transpose[{caFact simCaList,
     rrp simParamQuantile1C10[[simParam, All]]}],
   PlotStyle →{colorB}, Joined → True, PlotRange → All];
gr4b = ListLogLogPlot[Transpose[{caFact simCaList,
     rrp simParamQuantile2C10[[simParam, All]]}],
   PlotStyle →{colorB}, Joined → True, PlotRange → All];
Show[gr1b, gr2b, gr3b, gr4b, PlotRange → All ]
```

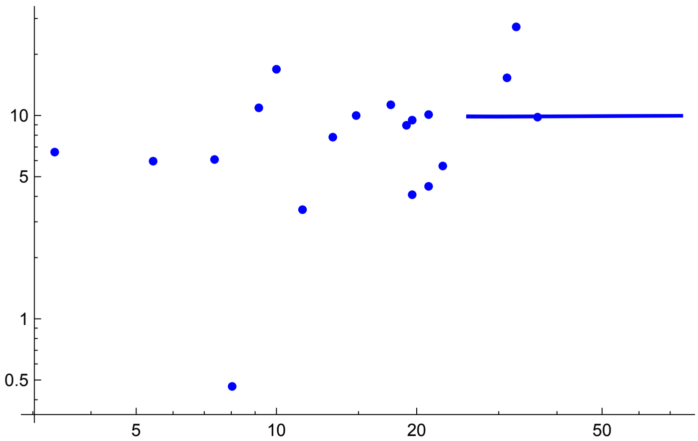
Out[•]=



D

In[•]:=
```
gr1c = ListLogLogPlot[
    Transpose[{dataT2DCa, dataT2DAmplitude1}], PlotStyle → {colorC}];
gr2c = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamMedianD[[simParam, All]]}],
    PlotStyle → {colorC}, Joined → True, PlotRange → All];
gr3c = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamQuantile1D[[simParam, All]]}],
    PlotStyle → {colorC}, Joined → True, PlotRange → All];
gr4c = ListLogLogPlot[Transpose[{caFact simCaList,
      rrp simParamQuantile2D[[simParam, All]]}],
    PlotStyle → {colorC}, Joined → True, PlotRange → All];
Show[gr1c, gr2c, gr3c, gr4c, PlotRange → All ]
```

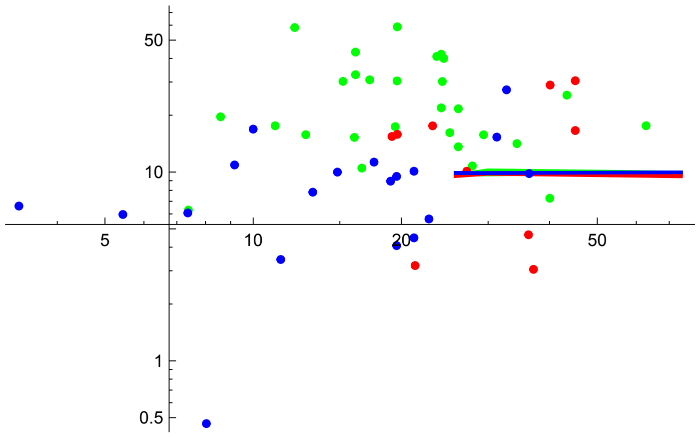
Out[•]=



C5 and C10 and D

In[•]:=
```
Show[gr1a, gr2a, gr3a, gr4a, gr1b, gr2b,
  gr3b, gr4b, gr1c, gr2c, gr3c, gr4c, PlotRange → All]
Show[gr1a, gr1b, gr1c, PlotRange → All];
```

Out[•]=



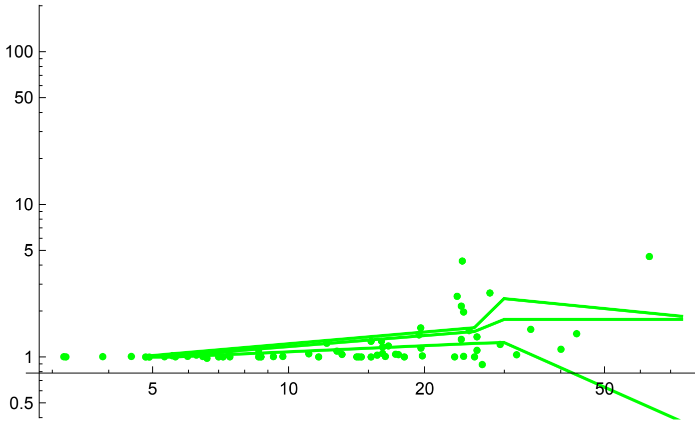
chi2 mono/bi ratio

In[•]:=
```
simParam = 6;
```

C5

In[•]:=
```
gr1a = ListLogLogPlot[
    Transpose[{dataT1C5Ca, dataT1C5ChiRatio}], PlotStyle → {colorA}];
gr2a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamMedianC5[[simParam, All]]}],
    PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr3a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1C5[[simParam, All]]}],
    PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr4a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2C5[[simParam, All]]}],
    PlotStyle → {colorA}, Joined → True, PlotRange → All];
Show[gr1a, gr2a, gr3a, gr4a, PlotRange → {All, {-0.8, 5}} ]
If[exportYes == 1,
   Export["plot chi2Ratio C5 data.txt",
    Transpose[{dataT1C5Ca, dataT1C5ChiRatio}], "Table"];
   toExport = Transpose[{caFact simCaList, simParamQuantile1C5[[simParam, All]],
      simParamMedianC5[[simParam, All]], simParamQuantile2C5[[simParam, All]]}];
   Export["plot chi2Ratio C5 fit - quantiles and median.txt",
    toExport, "Table"];
  ];
```

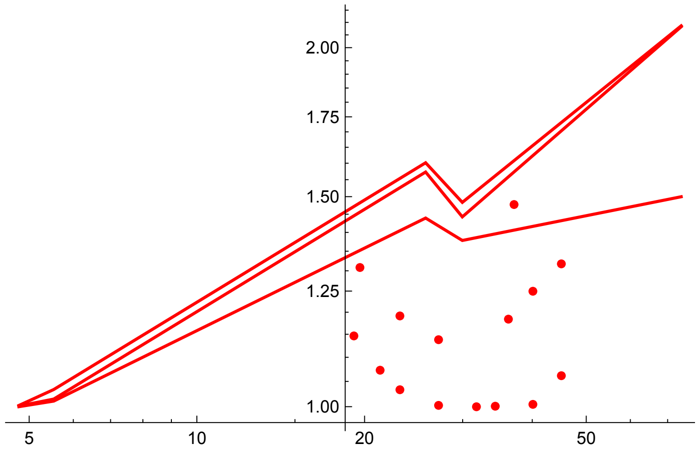
Out[•]=



C10

In[∘]:=
```
gr1b = ListLogLogPlot[
   Transpose[{dataT1C10Ca, dataT1C10ChiRatio}], PlotStyle → {colorB}];
gr2b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamMedianC10[[simParam, All]]}],
   PlotStyle → {colorB}, Joined → True, PlotRange → All];
gr3b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile1C10[[simParam, All]]}],
   PlotStyle → {colorB}, Joined → True, PlotRange → All];
gr4b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamQuantile2C10[[simParam, All]]}],
   PlotStyle → {colorB}, Joined → True, PlotRange → All];
Show[gr1b, gr2b, gr3b, gr4b, PlotRange → All ]
If[exportYes == 1,
  Export["plot chi2Ratio C10 data.txt",
   Transpose[{dataT1C10Ca, dataT1C10ChiRatio}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1C10[[simParam, All]],
     simParamMedianC10[[simParam, All]],
     simParamQuantile2C10[[simParam, All]]}];
  Export["plot chi2Ratio C10 fit - quantiles and median.txt",
   toExport, "Table"];
 ];
```

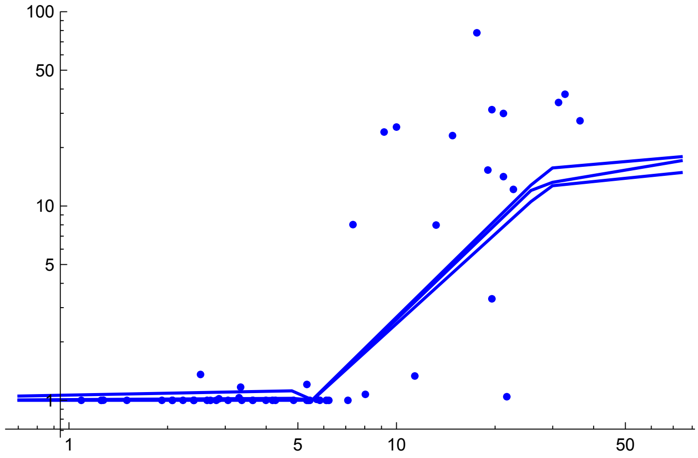
Out[∘]=



D

In[∘]:=
```
gr1c =
  ListLogLogPlot[Transpose[{dataT1DCa, dataT1DChiRatio}], PlotStyle → {colorC}];
gr2c = ListLogLogPlot[Transpose[
     {caFact simCaList, simParamMedianD[[simParam, All]]}],
   PlotStyle → {colorC}, Joined → True, PlotRange → All];
gr3c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile1D[[simParam, All]]}],
   PlotStyle → {colorC}, Joined → True, PlotRange → All];
gr4c = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamQuantile2D[[simParam, All]]}],
   PlotStyle → {colorC}, Joined → True, PlotRange → All];
Show[gr1c, gr2c, gr3c, gr4c, PlotRange → All ]
If[exportYes == 1,
  Export["plot chi2Ratio D data.txt",
   Transpose[{dataT1DCa, dataT1DChiRatio}], "Table"];
  toExport = Transpose[{caFact simCaList, simParamQuantile1D[[simParam, All]],
     simParamMedianD[[simParam, All]], simParamQuantile2D[[simParam, All]]}];
  Export["plot chi2Ratio D fit - quantiles and median.txt", toExport, "Table"];
 ];
```

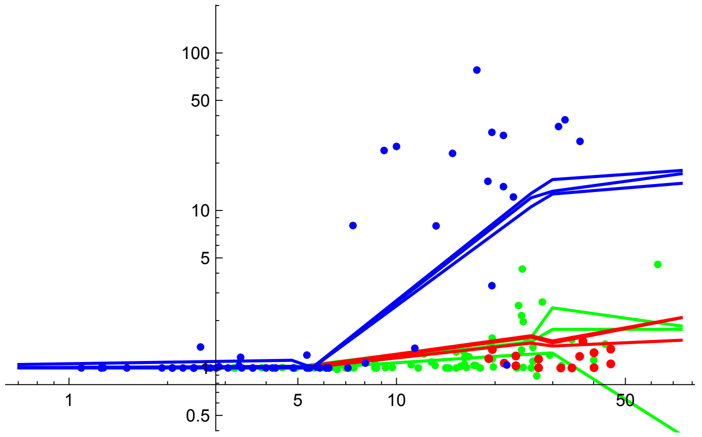
Out[∘]=



C5 and C10 and D

```
In[•]:= Show[gr1a, gr2a, gr3a, gr4a, gr1b, gr2b, gr3b,
         gr4b, gr1c, gr2c, gr3c, gr4c, PlotRange → {All, {-0.8, 5}}]
        Show[gr1a, gr1b, gr1c, PlotRange → All];
```

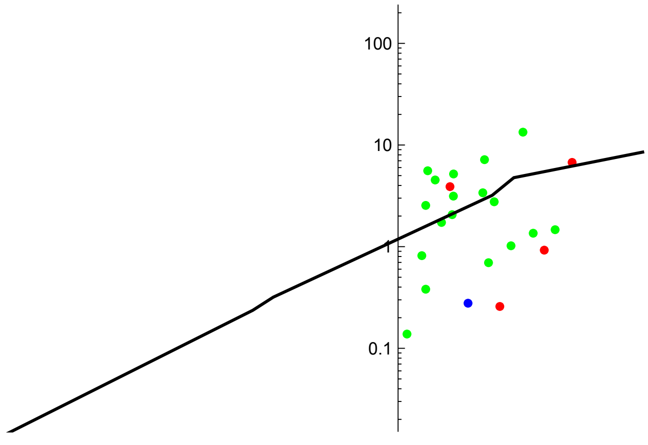
Out[•]=



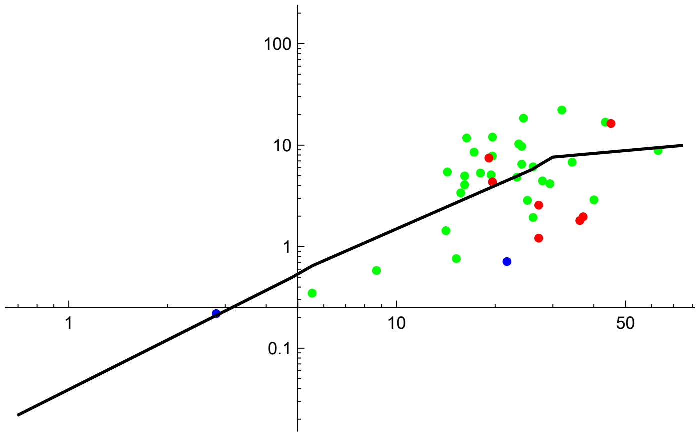
Nv

```
In[•]:= For[NvCount = 1, NvCount ≤ 7, NvCount += 1,
          Print[" time for Nv (ms) = ", 1000 * timeOfNv[[NvCount]]];
          gr1a = ListLogLogPlot[
            Transpose[{dataT1C5Ca, dataT1C5Nv[[NvCount]]}], PlotStyle → {colorA}];
          gr1b = ListLogLogPlot[Transpose[{dataT1C10Ca, dataT1C10Nv[[NvCount]]}],
            PlotStyle → {colorB}];
          gr1c = ListLogLogPlot[Transpose[{dataT1DCa, dataT1DNv[[NvCount]]}],
            PlotStyle → {colorC}];
          gr2 = ListLogLogPlot[Transpose[{caFact simCaList, rrp simParamNv[[NvCount,
                All]]}], PlotStyle → { Black}, Joined → True, PlotRange → All];
          Show[gr1a, gr1b, gr1c, gr2, PlotRange → {All, {-4, 5}} ] // Print;
        ];
```

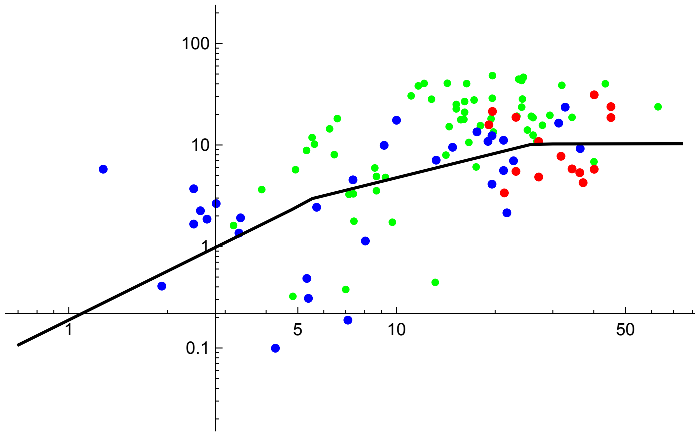
time for Nv (ms) = 0.1



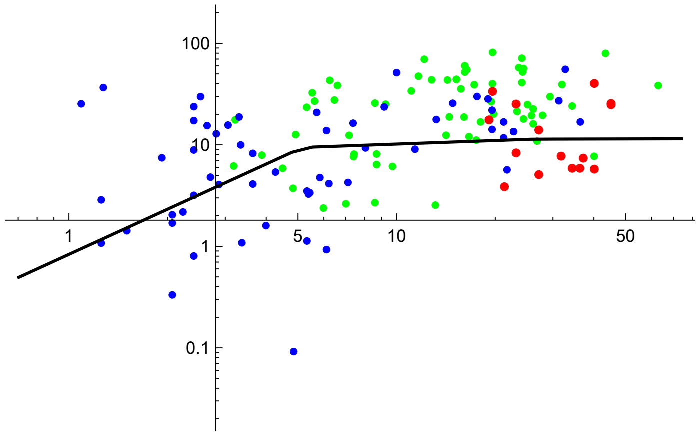
time for Nv (ms) = 0.2



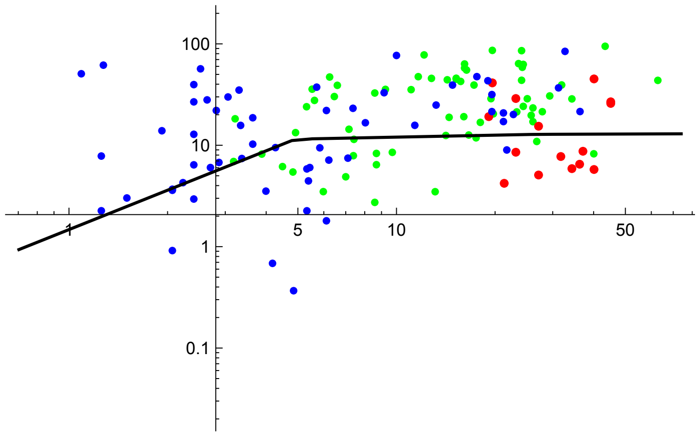
time for Nv (ms) = 1.



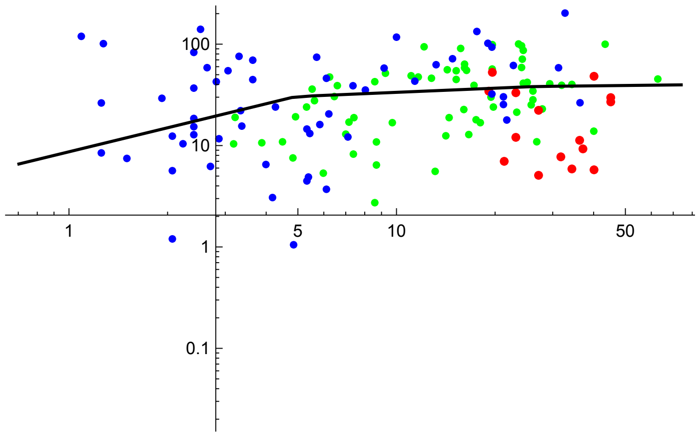
time for Nv (ms) = 5.



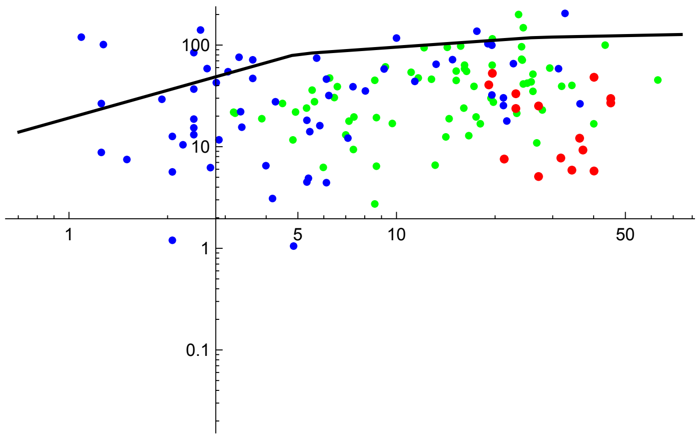
time for Nv (ms) = 10.



time for Nv (ms) = 100.

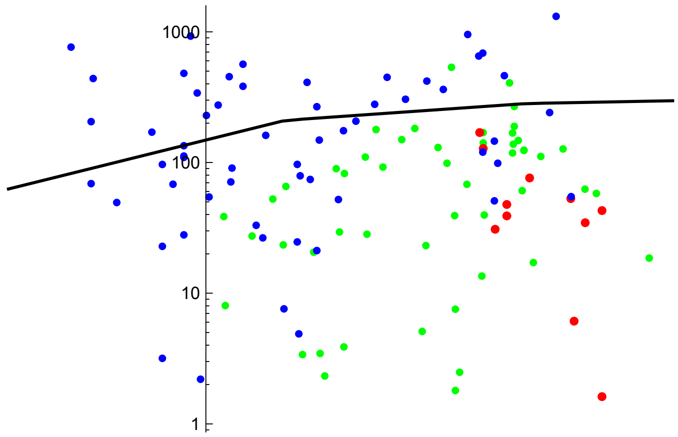


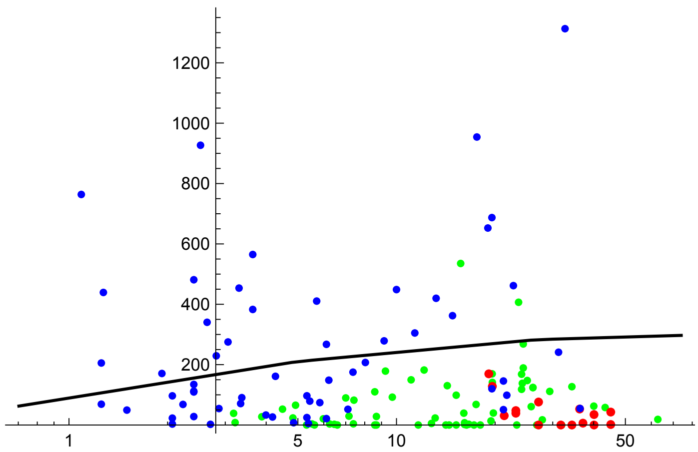
time for Nv (ms) = 400.



sustained release 10 to 100 ms

```
In[•]:= ttt1 = Transpose[{dataT1C5Ca, (dataT1C5Nv[[6]] - dataT1C5Nv[[5]]) / 0.09}];
ttt2 = Transpose[{dataT1C10Ca, (dataT1C10Nv[[6]] - dataT1C10Nv[[5]]) / 0.09}];
ttt3 = Transpose[{dataT1DCa, (dataT1DNv[[6]] - dataT1DNv[[5]]) / 0.09}];
ttt4 = Transpose[
   {caFact simCaList, rrp (simParamNv[[6, All]] - simParamNv[[5, All]]) / 0.09}];

gr1a = ListLogLogPlot[ttt1, PlotStyle → {colorA}];
gr1b = ListLogLogPlot[ttt2, PlotStyle → {colorB}];
gr1c = ListLogLogPlot[ttt3, PlotStyle → {colorC}];
gr2 = ListLogLogPlot[ttt4, PlotStyle → { Black}, Joined → True, PlotRange → All];
Show[gr1a, gr1b, gr1c, gr2, PlotRange → {All, {0, 7}} ] // Print;

gr1a = ListLogLinearPlot[ttt1, PlotStyle → {colorA}];
gr1b = ListLogLinearPlot[ttt2, PlotStyle → {colorB}];
gr1c = ListLogLinearPlot[ttt3, PlotStyle → {colorC}];
gr2 = ListLogLinearPlot[ttt4,
   PlotStyle → { Black}, Joined → True, PlotRange → All];
Show[gr1a, gr1b, gr1c, gr2, PlotRange → {All, All} ] // Print;
```





In[∘]:=
```
If[exportYes == 1,
  Export["plot sustained release Cm5 data.txt", ttt1, "Table"];
  Export["plot sustained release Cm10 data.txt", ttt2, "Table"];
  Export["plot sustained release D data.txt", ttt3, "Table"];
  Export["plot sustained release sim.txt", ttt4, "Table"]
 ];
```

Export Nv

In[∘]:=
```
If[exportYes == 1,
  Export["Nv export Ca,0.0001,0.0002,0.001,0.005,0.01,0.1,0.4.txt",
   Transpose[Prepend[simParamNv, caFact simCaList]], "Table"];
 ];
```

Print some values

C5

In[∘]:=
```
Transpose[simParamMedianC5] // TableForm
Transpose[simParamQuantile1C5] // TableForm
Transpose[simParamQuantile2C5] // TableForm
```

Out[∘]//TableForm=

0	0.558169	0.000196264	1.22645	244.494	1.00456	0.0002
0	0.442238	9.28401×10^{-6}	1.21939	320.467	1.01348	-0.00013109
0	0.691305	-7.7468×10^{-6}	1.15806	2638.91	1.46508	0.000108196
0	0.82562	-7.25179×10^{-6}	1.14792	4022.54	1.75847	0.00018539
0	0.857236	-1.32507×10^{-8}	1.143	15481.	1.75957	0.00017904

Out[∘]//TableForm=

0	0.535	0.000108148	1.16632	223.507	0.996897	0.0002
0	0.419633	-0.00012179	1.18265	265.976	0.997228	-0.00015499
0	0.649345	-0.0000558478	1.14232	2156.84	1.22491	-1.09854×10^{-18}
0	0.786886	-0.0000125089	1.12785	3704.23	1.24222	-1.03232×10^{-15}
0	0.795738	-4.77651×10^{-6}	1.14183	5747.24	0.37743	-5.05312×10^{-7}

Out[∘]//TableForm=

0	0.577463	0.0002	1.26918	272.268	1.00805	0.00020429
0	0.599915	0.000150731	1.26134	346.413	1.04856	0.000204061
0	0.815492	-1.3188×10^{-6}	1.15818	3116.89	1.55272	0.000198536
0	0.852301	1.51466×10^{-18}	1.16416	6069.04	2.40935	0.000190291
0	0.928748	-8.5×10^{-18}	1.14538	4.9648×10^{6}	1.84609	0.000595672

C10

In[•]:=
```
Transpose[simParamMedianC10] // TableForm
Transpose[simParamQuantile1C10] // TableForm
Transpose[simParamQuantile2C10] // TableForm
```

Out[•]//TableForm=

0	1.11476	0.0000484428	1.27367	214.143	1.00129	0.0000261636
0	1.02481	-7.15539×10^{-6}	1.22143	308.766	1.01479	-0.0000569535
0	1.69268	-0.000129442	1.17196	1792.17	1.57304	-0.0000213642
0	1.79081	-3.41449×10^{-6}	1.14068	4857.44	1.4426	-7.85951×10^{-18}
0	2.2687	-0.000117644	1.16258	3994.8	2.08245	0.0000134971

Out[•]//TableForm=

0	1.05691	0.0000261636	1.261	200.008	1.	0.0000239968
0	0.951601	-0.0000134287	1.1716	269.382	1.01083	-0.0000854457
0	1.58283	-0.000130109	1.16647	1587.15	1.43932	-0.000049544
0	1.77225	-0.000063172	1.13967	3033.16	1.37836	-3.92754×10^{-6}
0	1.93837	-0.0002	1.15261	2109.71	1.49977	-0.000108107

Out[•]//TableForm=

0	1.20884	0.000102995	1.30731	221.396	1.00234	0.0001
0	1.28054	0.00012816	1.28444	328.931	1.03365	0.0003
0	1.71333	-0.000105122	1.17977	1803.73	1.60145	3.89543×10^{-6}
0	1.91997	-4.23888×10^{-18}	1.17302	5613.36	1.48355	0.0000363526
0	2.45429	-2.17565×10^{-18}	1.17529	10044.1	2.08614	0.0000913627

D

In[•]:=
```
Transpose[simParamMedianD] // TableForm
Transpose[simParamQuantile1D] // TableForm
Transpose[simParamQuantile2D] // TableForm
```

Out[•]//TableForm=

0	1.07522	0.00366323	0.933623	12.2735	1.00524	-0.003
0	0.0470871	0.0000586294	1.2585	220.807	1.02416	0.0000301442
0	0.0445167	0.0000850033	1.19294	321.725	1.00325	0.0000802138
0	0.530804	-0.0000355205	1.15689	2444.95	12.023	0.0000107076
0	0.611601	-0.0000171127	1.1509	3815.31	13.2444	0.000018316
0	0.729864	8.15023×10^{-18}	1.15388	10355.7	17.105	0.0000391999

Out[•]//TableForm=

0	1.03411	-0.00337928	0.54024	5.75488	1.0002	-0.028
0	0.0454326	0.0000336663	1.2204	220.377	1.00026	0.0000272162
0	0.0390724	0.0000740578	1.19059	319.637	1.00155	0.0000700207
0	0.507636	-0.0000453135	1.15462	2250.41	10.5369	9.09647×10^{-6}
0	0.577697	-0.0000285742	1.14859	3546.18	12.7172	6.97549×10^{-6}
0	0.703231	-7.14717×10^{-7}	1.15262	9383.21	14.8626	3.86005×10^{-18}

Out[•]//TableForm=

0	1.12516	0.00862974	1.48961	31.2373	1.05217	0.0110829
0	0.0558425	0.00011618	1.26081	241.017	1.11916	0.0000628942
0	0.0464539	0.00010479	1.19823	325.886	1.00597	0.0000949808
0	0.543468	-0.00003188	1.15839	2488.35	12.8128	0.0000132203
0	0.614661	-0.0000117758	1.15154	4248.87	15.7052	0.0000270937
0	0.784491	1.52571×10^{-17}	1.15582	11243.3	17.9428	0.0000397785

Nv

In[•]:=
```
Transpose[simParamNv] // TableForm
```

Out[•]//TableForm=

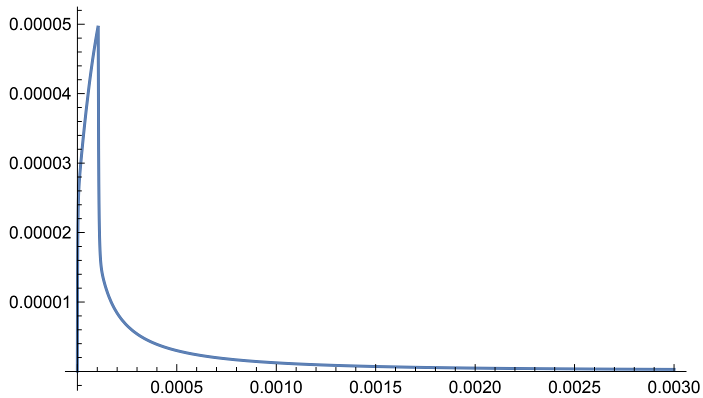
0.00105711	0.00221298	0.0107502	0.0495193	0.093503	0.658054	1.394
0.0236597	0.0497429	0.230838	0.844272	1.11259	2.97902	7.902
0.0318492	0.0648821	0.296443	0.950337	1.15738	3.09028	8.361
0.319936	0.570673	1.01314	1.13623	1.27814	3.8082	11.86
0.477046	0.762426	1.02364	1.13927	1.28265	3.84227	11.99
0.851423	0.991712	1.02808	1.14729	1.29626	3.96853	12.76

EPSC with different caRest

Interpolate

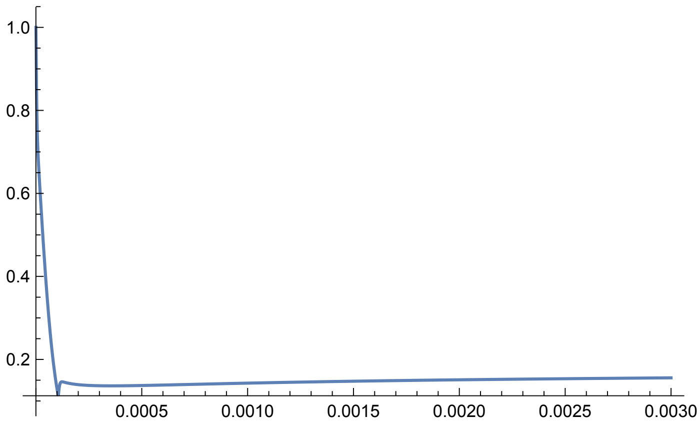
In[•]:=
```
locaCa = Transpose[{dataLocalCaTime, dataLocalCa}];
locaCaWithoutdublictes = Mean /@ GatherBy[locaCa, First];
interpolFunc = Interpolation[locaCaWithoutdublictes, InterpolationOrder → 1];
caFunc[t_] := interpolFunc[t];
Plot[caFunc[t], {t, 0.00, 0.003}, PlotRange → All]
```

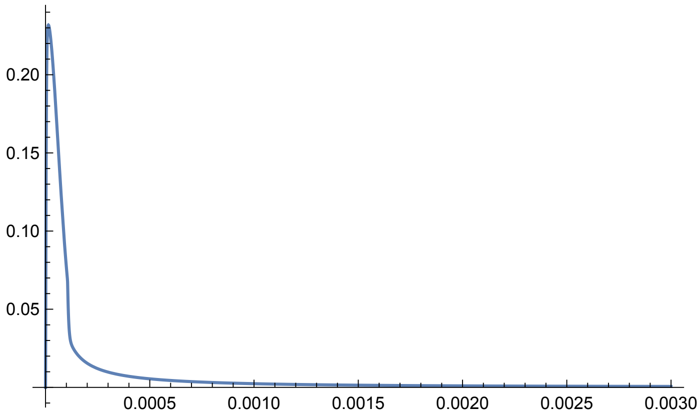
Out[•]=



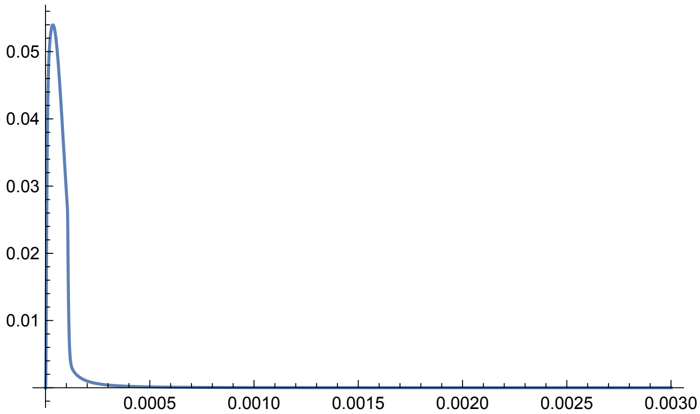
NDSolve

In[∘]:=
```
timeStartForPLot = 0.0;
timeEndForPLot = 0.003;
myNDSolveResults = NDSolve[eq, {ss1, ss2, ss3, ss4}, {t, 0, 0.003}];
Plot[(ss1[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss2[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss3[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss4[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
```

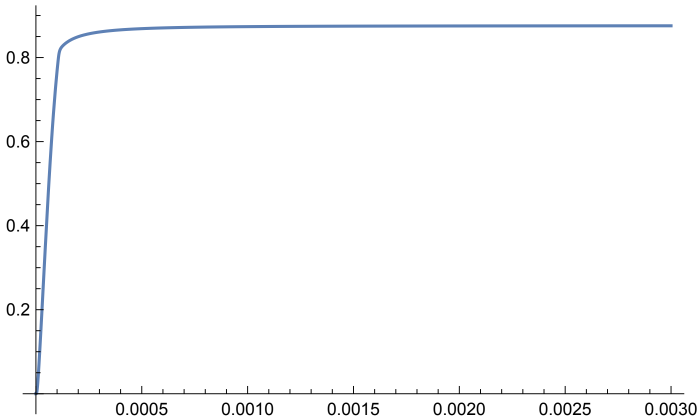
Out[∘]=


Out[∘]=


Out[•]=



Out[•]=



different caRest

In[•]:=
```
caRestLow = 30*^-9;
caRestHigh = 180*^-9;
```

Low Ca

Initial occupancy

In[•]:=
```
(*calualte initial equilibrium occupancy*)
caFunc[t_] := caRestLow;
kprimScheme
kunprimScheme
ss0Initial = kprimScheme / kunprimScheme
```

Out[•]= 1.04335

Out[•]= 3.65793

Out[•]= 0.28523

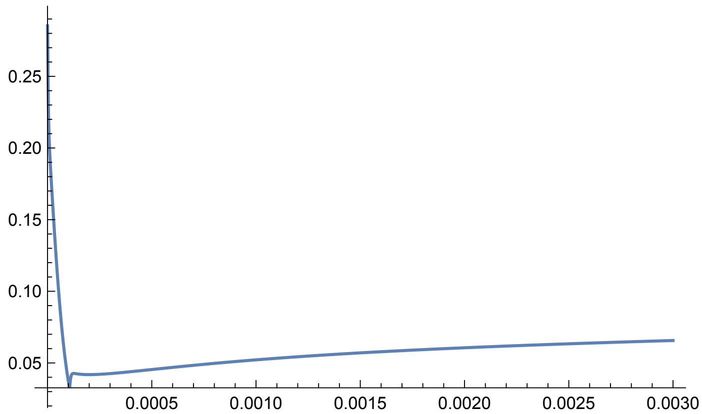
Diff eq.

In[∘]:=
```
Clear[caFunc, eq];(*Clear is needed if the cell is exectued for a 2nd time
 when caFunc is already set to a value or an Interpolationfunction*)
caFunc[t_] := interpolFunc[t];
ss[t_] = {ss1[t], ss2[t], ss3[t], ss4[t]};
eq = {ss'[t] == (mat /. repl).ss[t],
   ss[0] == {ss0Initial, 0, 0, 0}};
```

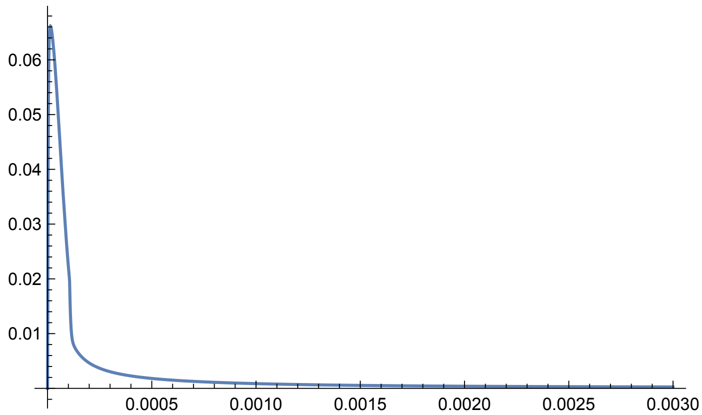
NDSolve

In[∘]:=
```
myNDSolveResults = NDSolve[eq, {ss1, ss2, ss3, ss4}, {t, 0, 0.003}];
Plot[(ss1[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss2[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss3[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss4[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
```

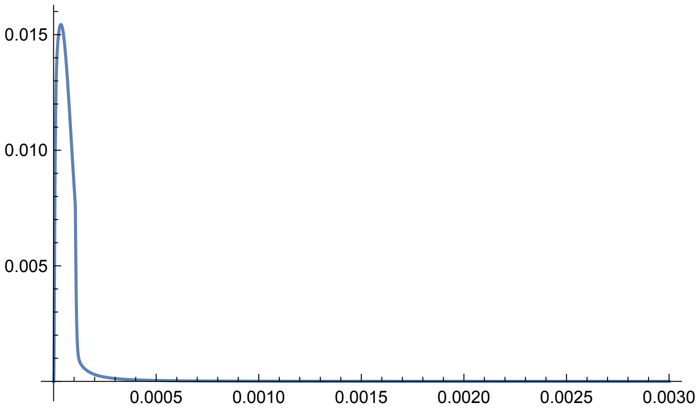
Out[∘]=



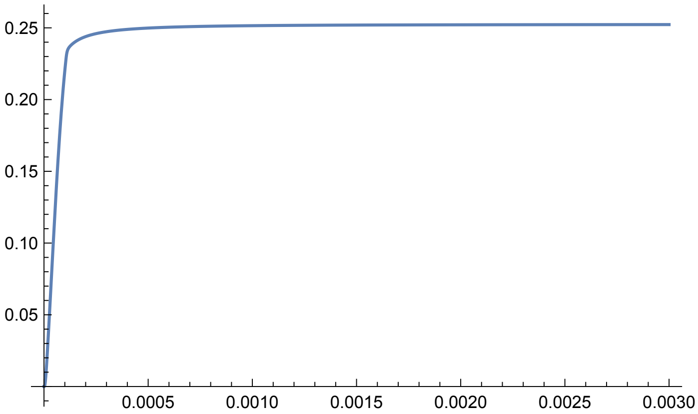
Out[∘]=



Out[∘]=



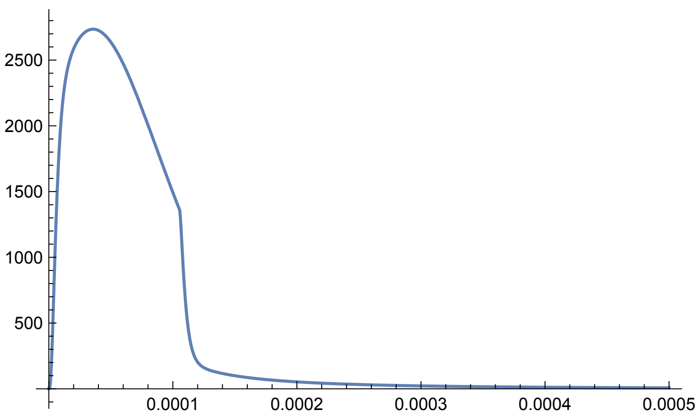
Out[∘]=



Plot EPSC

In[∘]:=
```
epscLowCa = D[(ss4[t] /. myNDSolveResults), t];
Plot[(ss4[t] /. myNDSolveResults), {t, 0, 2*^-3}, PlotRange → All];
Plot[epscLowCa, {t, 0, 0.5*^-3}, PlotRange → All]
```

Out[∘]=



High Ca

Initial occupancy

In[•]:=
```
(*calualte initial equilibrium occupancy*)
caFunc[t_] := caRestHigh;
kprimScheme
kunprimScheme
ss0Initial = kprimScheme / kunprimScheme
```

Out[•]= 3.07706

Out[•]= 3.65793

Out[•]= 0.841205

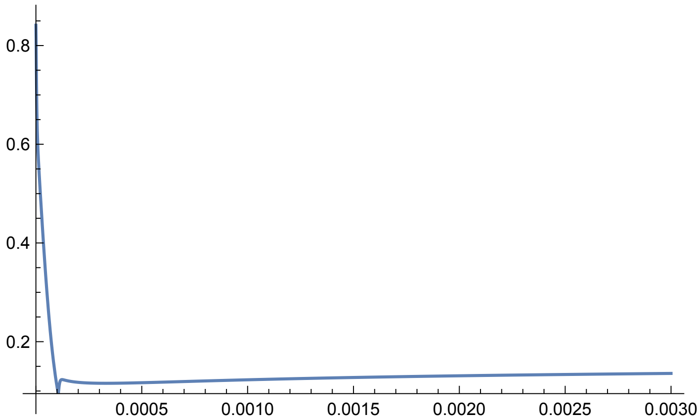
Diff eq.

In[•]:=
```
Clear[caFunc, eq];(*Clear is needed if the cell is exectued for a 2nd time
 when caFunc is already set to a value or an Interpolationfunction*)
caFunc[t_] := interpolFunc[t];
ss[t_] = {ss1[t], ss2[t], ss3[t], ss4[t]};
eq = {ss'[t] == (mat /. repl).ss[t],
   ss[0] == {ss0Initial, 0, 0, 0}};
```

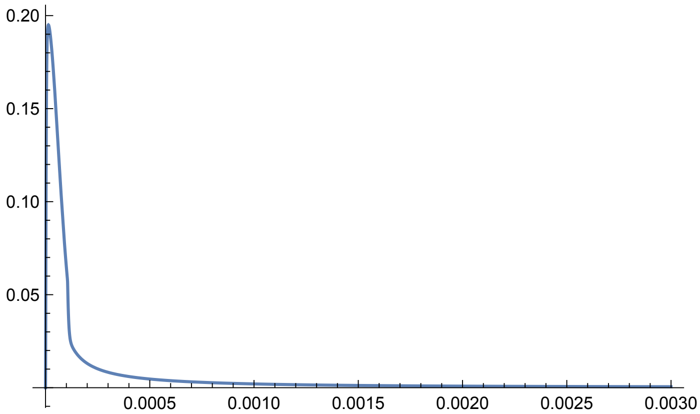
NDSolve

In[•]:=
```
myNDSolveResults = NDSolve[eq, {ss1, ss2, ss3, ss4}, {t, 0, 0.003}];
Plot[(ss1[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss2[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss3[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss4[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
```

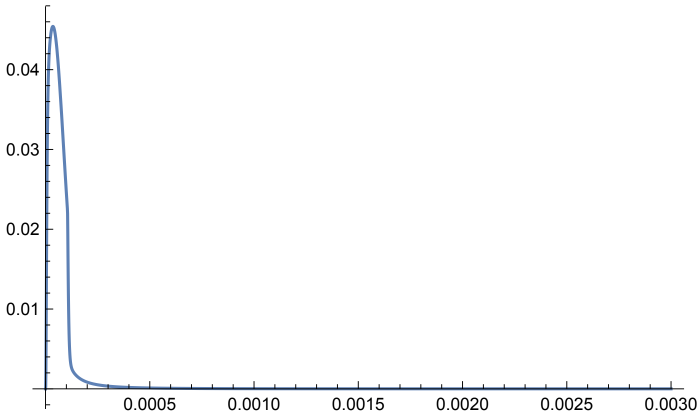
Out[•]=



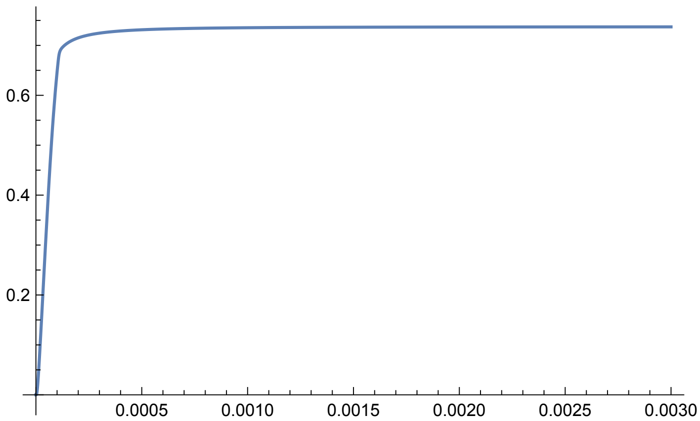
Out[•]=



Out[•]=



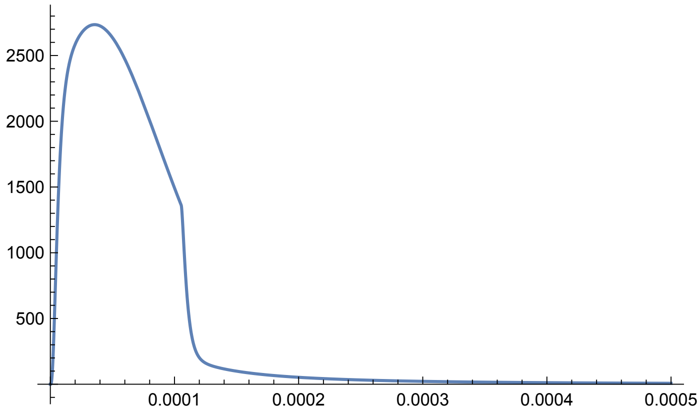
Out[•]=



Plot EPSC

In[•]:=
```
epscHighCa = D[(ss4[t] /. myNDSolveResults), t];
Plot[(ss4[t] /. myNDSolveResults), {t, 0, 2*^-3}, PlotRange → All];
Plot[epscLowCa, {t, 0, 0.5*^-3}, PlotRange → All]
```

Out[•]=

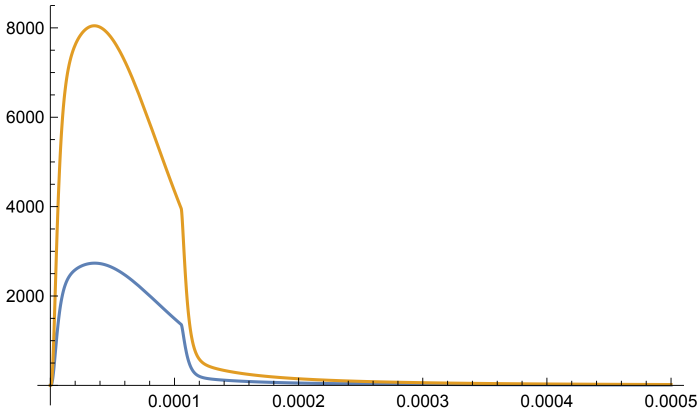


Compare

Plot both release rates

In[•]:=
```
Plot[{epscLowCa, epscHighCa}, {t, 0, 0.5*^-3}, PlotRange → All]
```

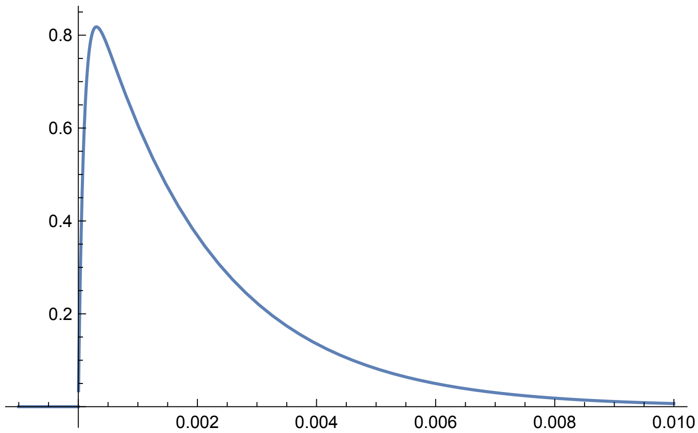
Out[•]=



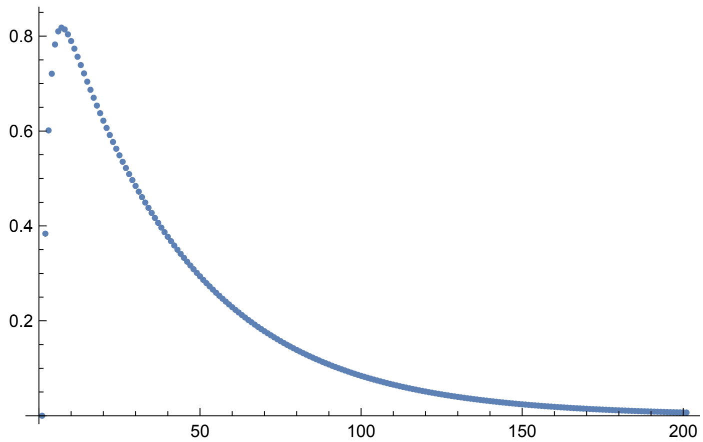
Convolution RelRate => EPSC

In[•]:=
```
miniKernel[t_] := If[t ≤ 0, 0, (1 - Exp[-t / 0.0001]) * Exp[-t / 0.002]];
Plot[miniKernel[t], {t, -.001, .01}]
dtForConvolve = 0.00005;
tEndConv = 0.01;
miniKernelList = Table[miniKernel[t], {t, 0.0, tEndConv, dtForConvolve}];
epscHighCaList = {Table[0, {t, 0, tEndConv, dtForConvolve}],
   Table[epscHighCa, {t, 0.0, 0.0025, dtForConvolve}],
   Table[0, {t, 0, tEndConv, dtForConvolve}]} // Flatten;
epscLowCaList = {Table[0, {t, 0, tEndConv, dtForConvolve}],
   Table[epscLowCa, {t, 0.0, 0.0025, dtForConvolve}],
   Table[0, {t, 0, tEndConv, dtForConvolve}]} // Flatten;
ListPlot[miniKernelList]
ListPlot[epscLowCaList, PlotRange → All]
```

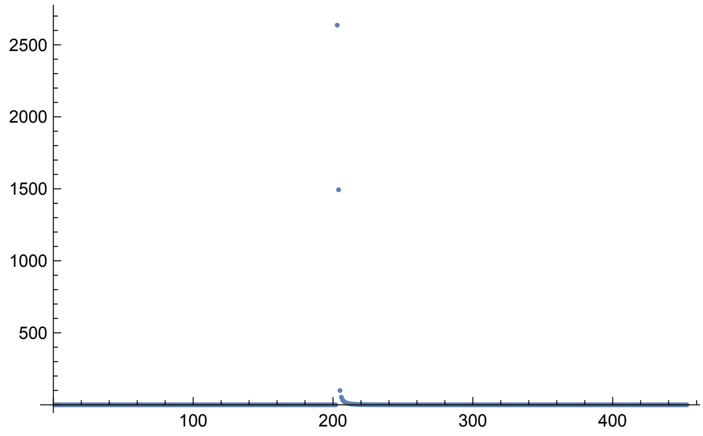
Out[•]=



Out[•]=

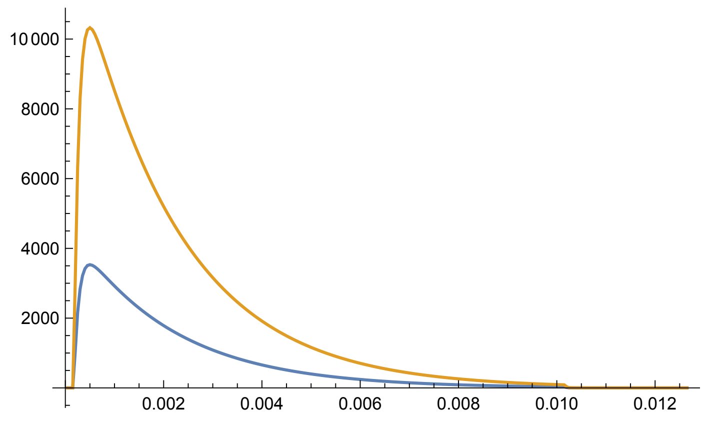


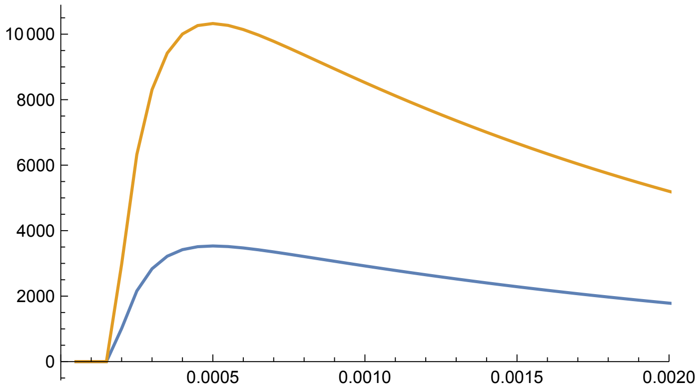
Out[ ]=



In[ ]:=
```
epscLowCaCurrentList = ListConvolve[miniKernelList, epscLowCaList];
epscHighCaCurrentList = ListConvolve[miniKernelList, epscHighCaList];
timeConv = Table[t * dtForConvolve, {t, Length[epscLowCaCurrentList]}];
ListPlot[{Transpose[{timeConv, epscLowCaCurrentList}],
  Transpose[{timeConv, epscHighCaCurrentList}]}, Joined → True, PlotRange → All]
ListPlot[{Transpose[{timeConv, epscLowCaCurrentList}],
  Transpose[{timeConv, epscHighCaCurrentList}]},
 Joined → True, PlotRange → {{0, 0.002}, All}]
maxLow = Max[epscLowCaCurrentList]
maxHigh = Max[epscHighCaCurrentList]
Print["maxHigh/maxLow = ", maxHigh / maxLow];
ListPlot[{Transpose[{timeConv, (1 / maxLow) * epscLowCaCurrentList}],
  Transpose[{timeConv, (1 / maxHigh) * epscHighCaCurrentList}]},
 Joined → True, PlotRange → All]
ListPlot[{Transpose[{timeConv, (1 / maxLow) * epscLowCaCurrentList}],
  Transpose[{timeConv, (1 / maxHigh) * epscHighCaCurrentList}]},
 Joined → True, PlotRange → {{0, 0.002}, All}]
If[exportYes == 1,
  toExport = Transpose[{timeConv, epscLowCaCurrentList, epscHighCaCurrentList,
      (1 / maxLow) * epscLowCaCurrentList, (1 / maxHigh) * epscHighCaCurrentList}];
  Export["plot EPSC - low and high - abs and norm.txt", toExport, "Table"];
 ];
```

Out[ ]=

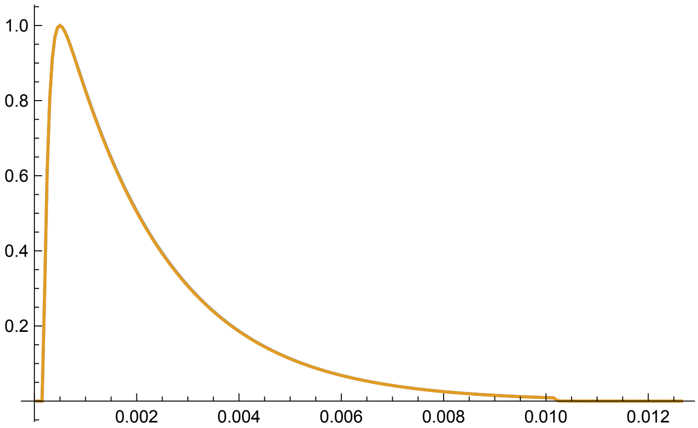


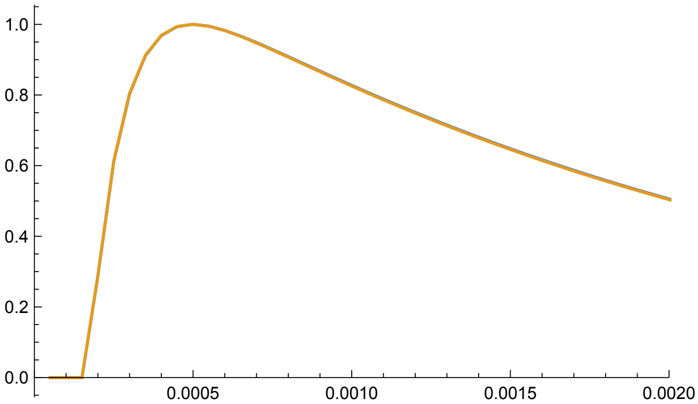
Out[•]=


Out[•]= 3532.14

Out[•]= 10 325.2

maxHigh / maxLow = 2.92322

Out[•]=


Out[•]=


Timing

In[•]:=
```
timeEnd = AbsoluteTime[];
(timeEnd - timeStart) / 60. (* time of calculation in min *)
```

Out[•]= 0.224448