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

Import

general

```
In[•]:= (* imported data all Ca in uM, all times in ms,
        all ampltiudes and Nv in vesicels *)

        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]];
```

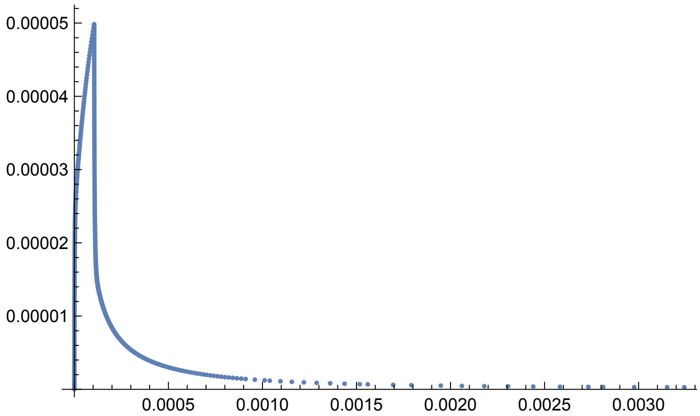
tau2 Deconv

```
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[•]= $3.839313680412683 \times 10^9$

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 = CmToVesConversionFactor * 1.36937*^-14 / rrp(*cannot be 0*)
signalToNoiseRatioC5 = 1.;(*minimum s-to-n-ratio to attempt fitting*)
dtOfDataC5 = (1 / (1000 * samplingOfDataInKHzC5));

samplingOfDataInKHzC10 = 10;
myNoiseC10 = CmToVesConversionFactor * 1.67583*^-14 / rrp(*cannot be 0*)
signalToNoiseRatioC10 = 1.;(*minimum s-to-n-ratio to attempt fitting*)
dtOfDataC10 = (1 / (1000 * samplingOfDataInKHzC10));

samplingOfDataInKHzD = 10;
myNoiseD = 0.367584 / rrp(*cannot be 0*)
signalToNoiseRatioD = 1.;(*minimum s-to-n-ratio to attempt fitting*)
dtOfDataD = (1 / (1000 * samplingOfDataInKHzD));

samplingOfDataInKHzLong = 1;
myNoiseLong = myNoiseC5;(*cannot be 0*)
dtOfDataLong = (1 / (1000 * samplingOfDataInKHzLong));
```

Out[∘]= 0.217071

Out[∘]= 0.265651

Out[∘]= 0.0367584

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

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 = 100000.;
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],
```

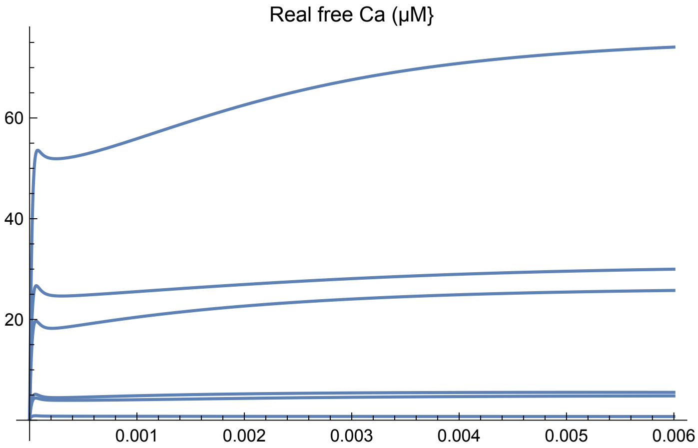
```
    MgPP1'[tt] == kOnMg * Mg[tt] * PP1[tt] - kOffMgPP * MgPP1[tt]

   }
  ;

  (*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]];
 ];
```

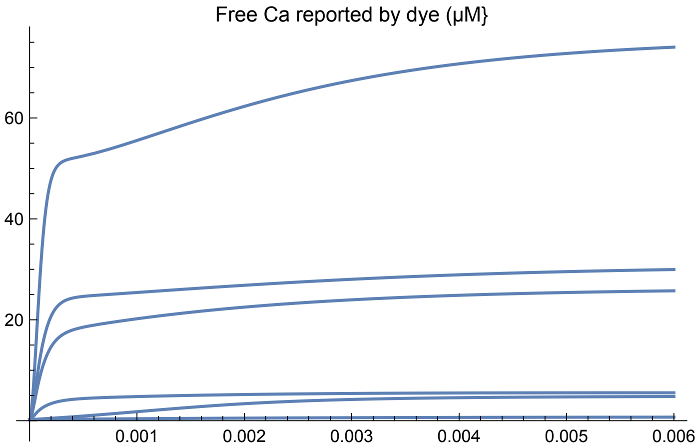
Plot and further processing

```
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 {{}}*)
```

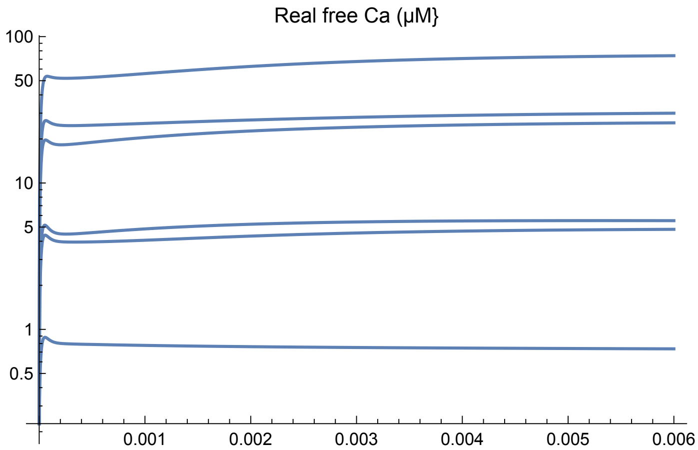
Out[•]=

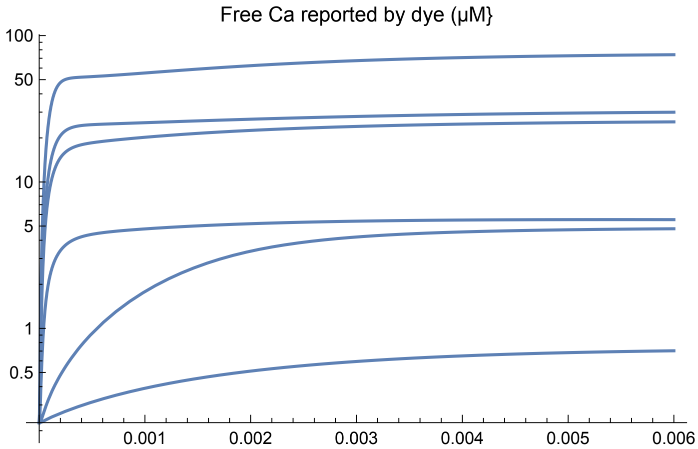

Real free Ca (μM}
60
40
20
0.001
0.002
0.003
0.004
0.005
0.006

Out[•]=


Free Ca reported by dye (μM}
60
40
20
0.001
0.002
0.003
0.004
0.005
0.006

Out[•]=


Real free Ca (μM}
100
50
10
5
1
0.5
0.001
0.002
0.003
0.004
0.005
0.006

Out[ ]=


Out[ ]= $\{7.03073 \times 10^{-7}, 4.79194 \times 10^{-6}, 5.53376 \times 10^{-6}, 0.0000257412, 0.0000299583, 0.0000740312\}$

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

Release scheme and parameters

Define release scheme

In[ ]:=
```
nStates = 7;
mat = Table[0, {nStates}, {nStates}];
```

forward rates

In[•]:=
```
from = 1; (*0 ca bound*)
kk = 5 kon;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;

from = 2;
kk = 4 kon;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;

from = 3;
kk = 3 kon;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;

from = 4;
kk = 2 kon;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;

from = 5; (*4 ca bound*)
kk = kon;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;

from = 6; (*5 ca bound*)
kk = gamma;
mat[[from + 1, from]] += kk; mat[[from, from]] += -kk;
```

backwards rates

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

from = 3;
kk = 2 koff b^1;
mat[[from - 1, from]] += kk; mat[[from, from]] += -kk;

from = 4;
kk = 3 koff b^2;
mat[[from - 1, from]] += kk; mat[[from, from]] += -kk;

from = 5;
kk = 4 koff b^3;
mat[[from - 1, from]] += kk; mat[[from, from]] += -kk;

from = 6; (*5 ca bound*)
kk = 5 koff b^4;
mat[[from - 1, from]] += kk; mat[[from, from]] += -kk;
```

outflux from matrix

In[*]:=
```
mat[[1, 1]] += -kunfill; (* is multiplied by ss1[t] *)
```

influx in matrix

In[*]:=
```
mat[[1, 1]] += (1 / ss1[t]) kfill fillStateSS[t];
(* (1/ss1[t]) is needed to merge the fillState
 Diff Eq. in the matrix format. Note ss1[t] is never 0 *)
```

Matrix

In[*]:=
```
mat // TableForm
```

Out[*]//TableForm=

$-5\,\text{kon} - \text{kunfill} + \frac{\text{kfill fillStateSS}[t]}{\text{ss1}[t]}$	koff	0	0
5 kon	$-\text{koff} - 4\,\text{kon}$	2 b koff	0
0	4 kon	$-2\,\text{b koff} - 3\,\text{kon}$	$3\,b^2\,\text{koff}$
0	0	3 kon	$-3\,b^2\,\text{koff} - 2\,\text{kc}$
0	0	0	2 kon
0	0	0	0
0	0	0	0

Parameters of release scheme

```
In[•]:= linInterpol[x_, a_, b_] := a + x * (b - a);

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 = 3.0;
konScheme = linInterpol[sitePlugging[t],
   caFunc[t] Sqrt[affinityFactor] tempFact 1.*^8,
   0.1 caFunc[t] Sqrt[affinityFactor] tempFact 1.*^8
  ];(*M^-1 s^-1*)

koffScheme = linInterpol[sitePlugging[t],
   (1/Sqrt[affinityFactor]) tempFact 15 000,
   0.4 (1/Sqrt[affinityFactor]) tempFact 15 000
  ];(*s^-1*)
gammaScheme = tempFact 6000;(*s^-1*)
bScheme = 0.25;

KdPrim = 2.*^-6;
kprimScheme  = 2.5 + 60. (caFunc[t] / (KdPrim + caFunc[t]));
kunprimScheme = 2.5 + 60. (caRest / (KdPrim + caRest));

KdFill = 2.*^-6;
kfillScheme =  100 + 800. (caFunc[t] / (KdFill + caFunc[t]));
kunfillScheme = 100 + 800. (caRest / (KdFill + caRest));


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

   kprim → kprimScheme ,
   kunprim → kunprimScheme ,

   kfill → kfillScheme ,
   kunfill → kunfillScheme

    (*
   kbasal→ kbasalScheme  ,
   kunfill→ kunfillScheme
   *)
  };
```

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

In[•]:=
```
siteClearanceTau = 0.04;
```

Initial occupancy

In[•]:=
```
(*test initial equilibrium occupancy*)
caFunc[t_] := caTmp;
fillStateSSInitial = kprimScheme / kunprimScheme;
ss0Initial = fillStateSSInitial * kfillScheme / kunfillScheme;
(ss0Initial /. caTmp → 180*^-9)
(ss0Initial /. caTmp → 50*^-9)
(ss0Initial /. caTmp → 30*^-9)
(ss0Initial /. caTmp → 180*^-9) / (ss0Initial /. caTmp → 30*^-9)
(*test initial *)
Plot[kprimScheme / kunprimScheme, {caTmp, 0, 300*^-9}]
Plot[kfillScheme / kunfillScheme, {caTmp, 0, 300*^-9}]
LogLinearPlot[{kprimScheme / kunprimScheme, kfillScheme / kunfillScheme},
 {caTmp, .1*^-9, 30*^-6}, PlotRange → All]
Plot[{kprimScheme / kunprimScheme, kfillScheme / kunfillScheme},
 {caTmp, .1*^-9, 1*^-6}, PlotRange → All]
```

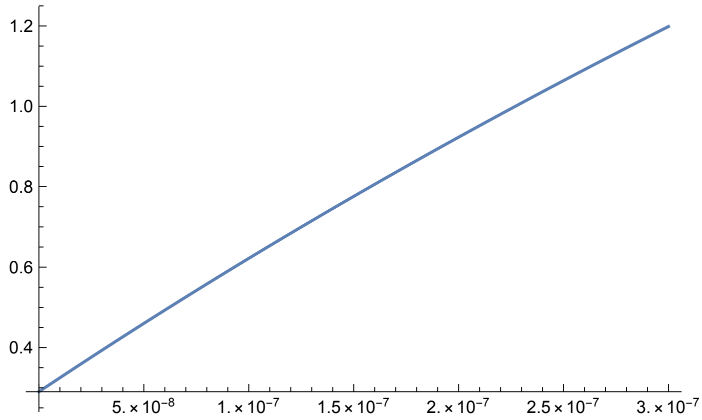
Out[•]= 0.791348

Out[•]= 0.302831

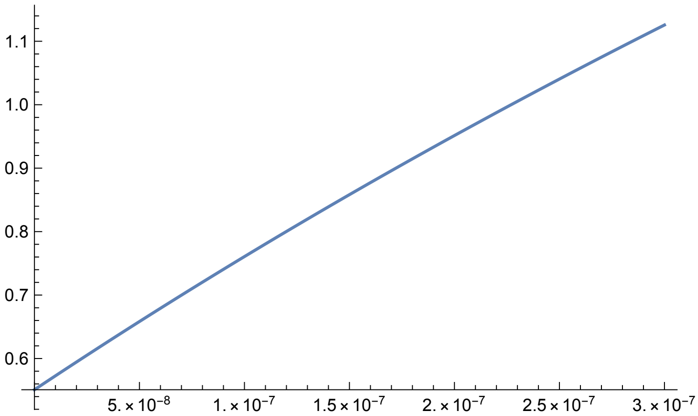
Out[•]= 0.242117

Out[•]= 3.26845

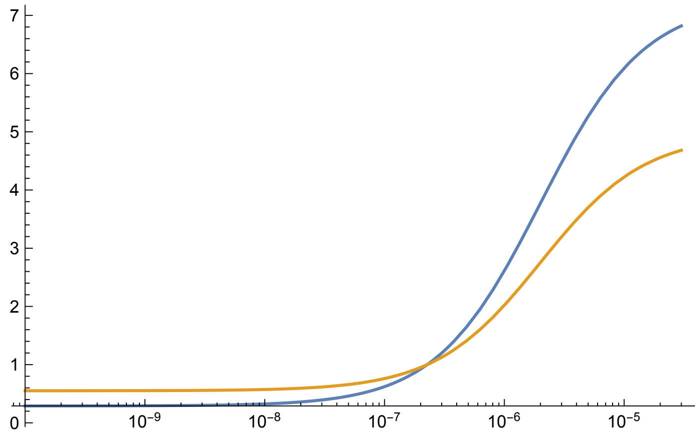
Out[•]=



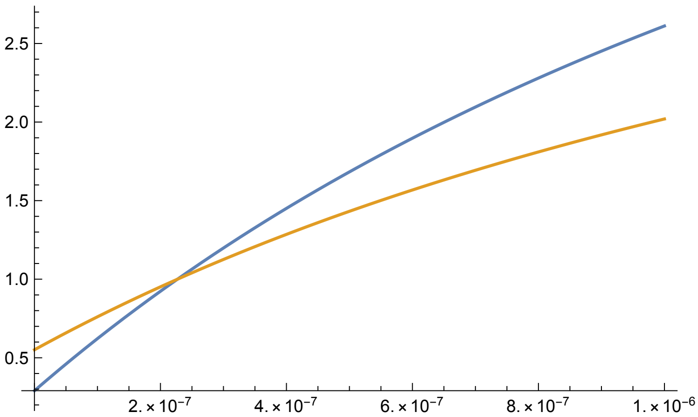
Out[∘]=


1.1
1.0
0.9
0.8
0.7
0.6
5. × 10^-8
1. × 10^-7
1.5 × 10^-7
2. × 10^-7
2.5 × 10^-7
3. × 10^-7

Out[∘]=


7
6
5
4
3
2
1
0
10^-9
10^-8
10^-7
10^-6
10^-5

Out[∘]=


2.5
2.0
1.5
1.0
0.5
2. × 10^-7
4. × 10^-7
6. × 10^-7
8. × 10^-7
1. × 10^-6

```
In[•]:= (*calualte initial equilibrium occupancy*)
        caFunc[t_] := caRest;
        kprimScheme
        kunprimScheme
        fillStateSSInitial = kprimScheme / kunprimScheme
        kfillScheme
        kunfillScheme
        ss0Initial = fillStateSSInitial * kfillScheme / kunfillScheme
Out[•]= 8.61585
Out[•]= 8.61585
Out[•]= 1.
Out[•]= 181.545
Out[•]= 181.545
Out[•]= 1.
In[•]:= caRest
Out[•]= 2.27 × 10^-7
```

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], ss5[t], ss6[t], ss7[t]};
        eq = {ss'[t] == (mat /. repl).ss[t],
            ss[0] == {ss0Initial, 0., 0., 0., 0., 0., 0.},
            (fillStateSS'[t] == kprim - kunprim fillStateSS[t] -
                kfill fillStateSS[t] + kunfill ss1[t]) /. repl,
            fillStateSS[0] == fillStateSSInitial,
            sitePlugging'[t] ==
             (1 - sitePlugging[t]) ss7'[t] - siteClearanceTau sitePlugging[t],
            sitePlugging[0] == 0
           };
```

Print diff eq.

In[•]:= mat

```
Out[•]= {{-5 kon - kunfill + kfill fillStateSS[t]/ss1[t], koff, 0, 0, 0, 0, 0},
  {5 kon, -koff - 4 kon, 2 b koff, 0, 0, 0, 0},
  {0, 4 kon, -2 b koff - 3 kon, 3 b^2 koff, 0, 0, 0},
  {0, 0, 3 kon, -3 b^2 koff - 2 kon, 4 b^3 koff, 0, 0},
  {0, 0, 0, 2 kon, -4 b^3 koff - kon, 5 b^4 koff, 0},
  {0, 0, 0, 0, kon, -gamma - 5 b^4 koff, 0}, {0, 0, 0, 0, 0, gamma, 0}}
```

In[•]:= repl

```
Out[•]= {kon → 5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t],
  koff → 25 572.7 - 15 343.6 sitePlugging[t], gamma → 17 717.3,
  b → 0.25, kprim → 2.5 + 60. caFunc[t]/(2. × 10^-6 + caFunc[t]), kunprim → 8.61585,
  kfill → 100 + 800. caFunc[t]/(2. × 10^-6 + caFunc[t]), kunfill → 181.545}
```

In[•]:= mat /. repl

```
Out[•]= {{-181.545 - 5 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]) +
   ((100 + 800. caFunc[t]/(2.×10^-6+caFunc[t])) fillStateSS[t])/ss1[t],
  25 572.7 - 15 343.6 sitePlugging[t], 0, 0, 0, 0, 0},
 {5 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]),
  -25 572.7 + 15 343.6 sitePlugging[t] -
   4 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]),
  0.5 (25 572.7 - 15 343.6 sitePlugging[t]), 0, 0, 0, 0},
 {0, 4 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]),
  -0.5 (25 572.7 - 15 343.6 sitePlugging[t]) -
   3 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]),
  0.1875 (25 572.7 - 15 343.6 sitePlugging[t]), 0, 0, 0},
 {0, 0, 3 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]),
  -0.1875 (25 572.7 - 15 343.6 sitePlugging[t]) -
   2 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]),
  0.0625 (25 572.7 - 15 343.6 sitePlugging[t]), 0, 0},
 {0, 0, 0, 2 (5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t]),
  -5.11454 × 10^8 caFunc[t] - 0.0625 (25 572.7 - 15 343.6 sitePlugging[t]) +
   4.60309 × 10^8 caFunc[t] × sitePlugging[t],
  0.0195313 (25 572.7 - 15 343.6 sitePlugging[t]), 0},
 {0, 0, 0, 0, 5.11454 × 10^8 caFunc[t] - 4.60309 × 10^8 caFunc[t] × sitePlugging[t],
  -17 717.3 - 0.0195313 (25 572.7 - 15 343.6 sitePlugging[t]), 0},
 {0, 0, 0, 0, 0, 17 717.3, 0}}
```

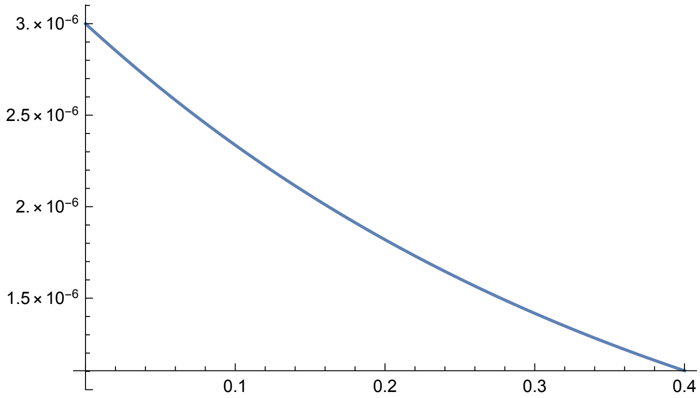
In[•]:= **eq**

```
Out[•]= {{ss1′[t], ss2′[t], ss3′[t], ss4′[t], ss5′[t], ss6′[t], ss7′[t]} ==
  {(-181.545 - 5 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]) +
        ((100 + 800. caFunc[t]/(2.×10^-6+caFunc[t])) fillStateSS[t])/ss1[t]) ss1[t] +
     (25572.7 - 15343.6 sitePlugging[t]) ss2[t],
    5 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]) ss1[t] +
     (-25572.7 + 15343.6 sitePlugging[t] -
        4 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]))
      ss2[t] + 0.5 (25572.7 - 15343.6 sitePlugging[t]) ss3[t],
    4 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]) ss2[t] +
     (-0.5 (25572.7 - 15343.6 sitePlugging[t]) -
        3 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]))
      ss3[t] + 0.1875 (25572.7 - 15343.6 sitePlugging[t]) ss4[t],
    3 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]) ss3[t] +
     (-0.1875 (25572.7 - 15343.6 sitePlugging[t]) -
        2 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]))
      ss4[t] + 0.0625 (25572.7 - 15343.6 sitePlugging[t]) ss5[t],
    2 (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]) ss4[t] +
     (-5.11454×10^8 caFunc[t] - 0.0625 (25572.7 - 15343.6 sitePlugging[t]) +
        4.60309×10^8 caFunc[t] × sitePlugging[t]) ss5[t] +
     0.0195313 (25572.7 - 15343.6 sitePlugging[t]) ss6[t],
    (5.11454×10^8 caFunc[t] - 4.60309×10^8 caFunc[t] × sitePlugging[t]) ss5[t] +
     (-17717.3 - 0.0195313 (25572.7 - 15343.6 sitePlugging[t])) ss6[t],
    17717.3 ss6[t]}, {ss1[0], ss2[0], ss3[0], ss4[0], ss5[0],
    ss6[0], ss7[0]} == {1., 0., 0., 0., 0., 0., 0.},
  fillStateSS′[t] == 2.5 + 60. caFunc[t]/(2.×10^-6 + caFunc[t]) - 8.61585 fillStateSS[t] -
    (100 + 800. caFunc[t]/(2.×10^-6 + caFunc[t])) fillStateSS[t] + 181.545 ss1[t],
  fillStateSS[0] == 1., sitePlugging′[t] ==
   -0.04 sitePlugging[t] + (1 - sitePlugging[t]) ss7′[t],
  sitePlugging[0] == 0}
```

Solve all states

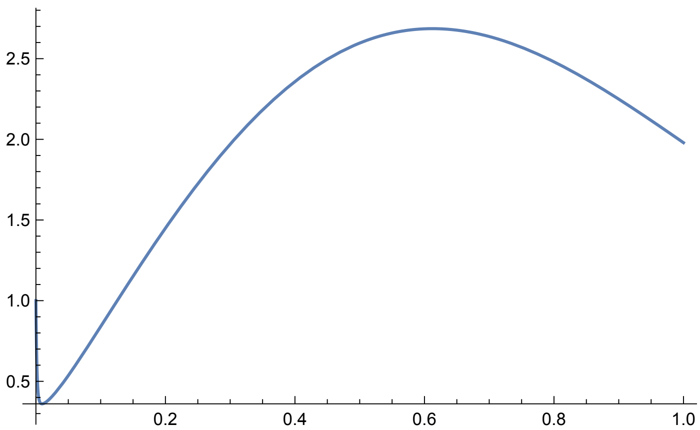
In[•]:=
```
caFunc[t_] := 3*^-6 * Exp[-t / tauOfDecayOfUncagedCa];;
Plot[caFunc[t], {t, 0, 0.4}, PlotRange → All]
```

Out[•]=

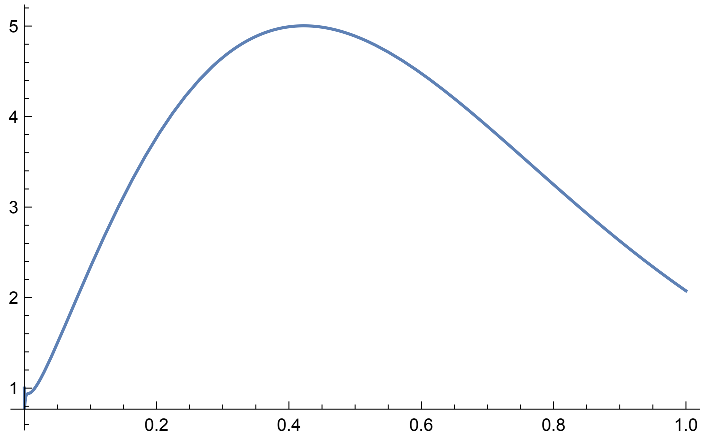


In[•]:=
```
myNDSolveResults = NDSolve[eq,
    {fillStateSS, ss1, ss2, ss3, ss4, ss5, ss6, ss7, sitePlugging}, {t, 0, 10.}];
tEndForPlot = 1.;
Plot[(fillStateSS[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss1[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss2[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss3[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss4[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss5[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss6[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(ss7[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
Plot[(sitePlugging[t] /. myNDSolveResults), {t, 0, tEndForPlot}, PlotRange → All]
```

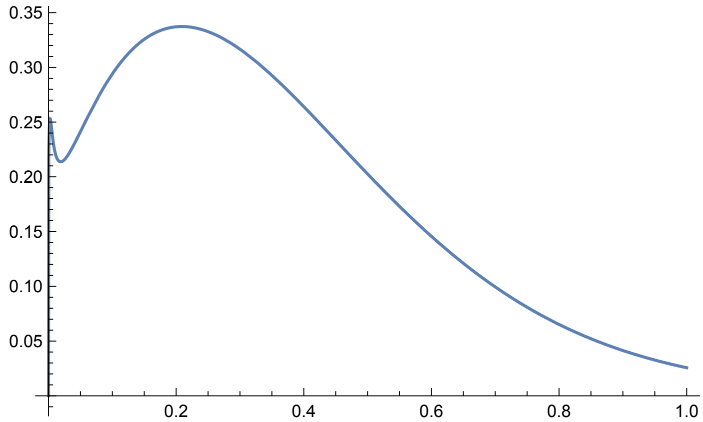
Out[•]=



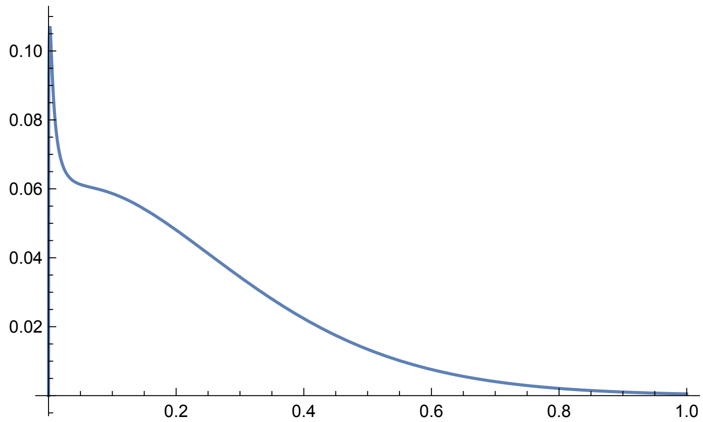
Out[•]=



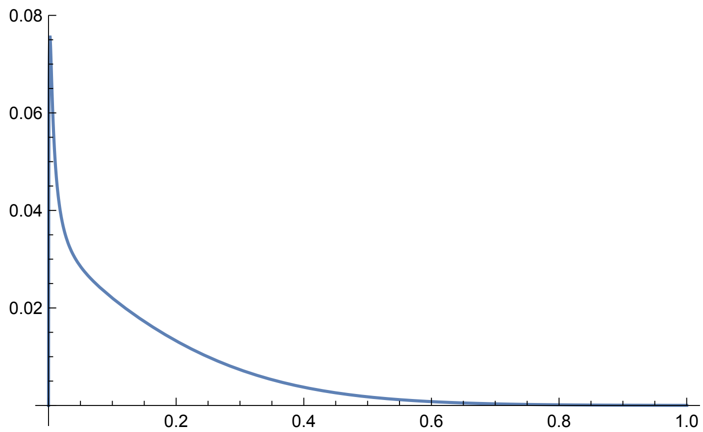
Out[•]=



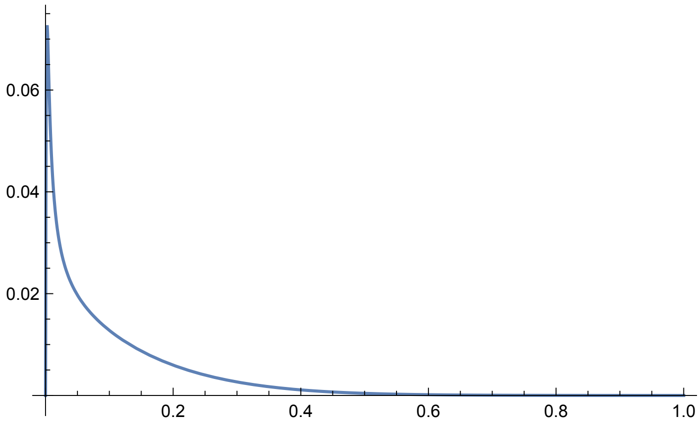
Out[•]=



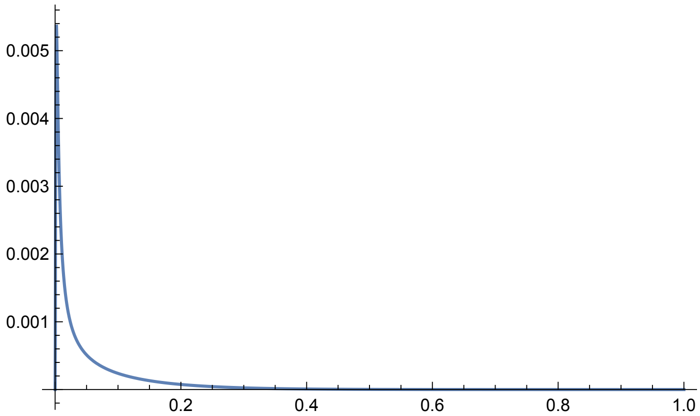
Out[•]=



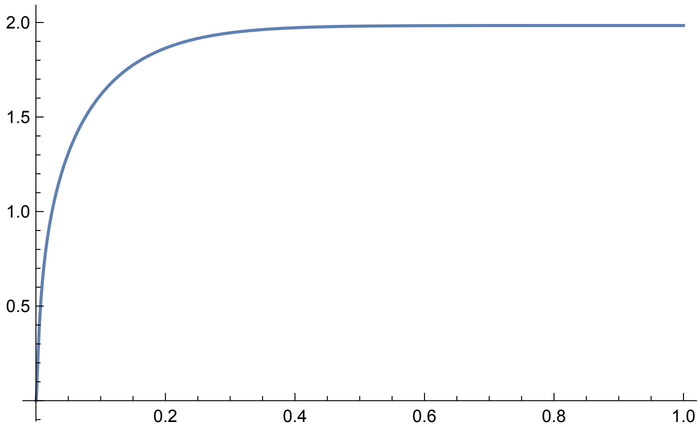
Out[ ]=



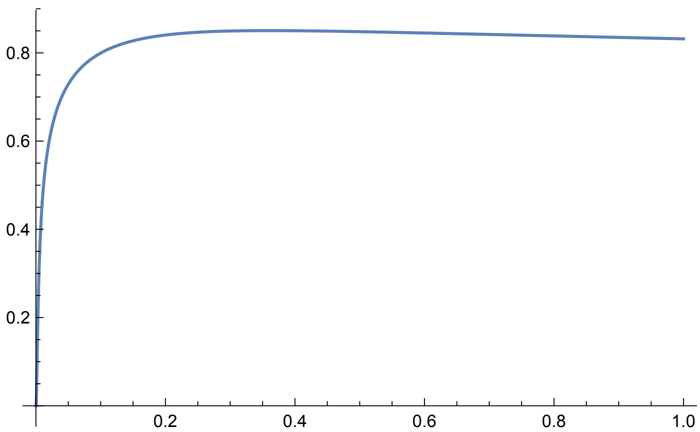
Out[ ]=



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, ss7, {t, 0, 0.4}];
(* plot results: *)
fused[t_] := ss7[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
  several times and do the fitting and than 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 imporve(=decrease) by >10%*)
 (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 imporve(=decrease) by >10%*)
 (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
   and do the fitting several times and then 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)
```

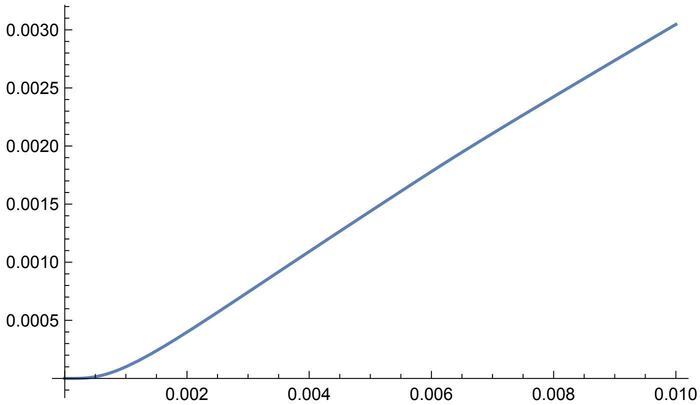
```
    &&
    (*relative amplitude of 1st component should be < 95% *)
    (((amp1 /. fitResultBi)) [[1]] < 0.95)
   ,
   (*take bi*)
   Print["take bi"];
   simParamNoiseD[[12, noiseN]] = simParamNoiseD[[7, noiseN]];
   (*delay*)
   simParamNoiseD[[13, noiseN]] = simParamNoiseD[[8, noiseN]];
   (*amp*)
   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"];
];
```

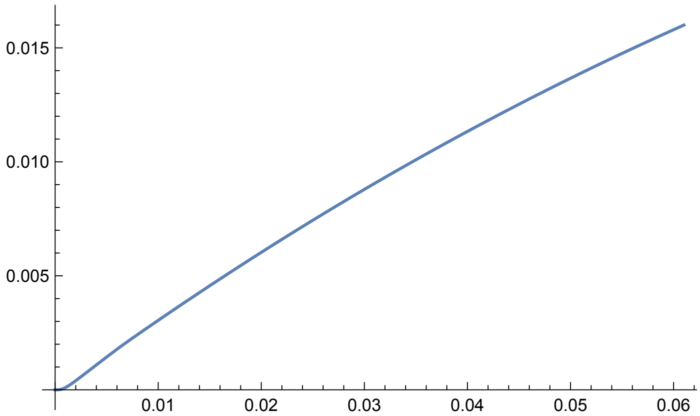
```
noiseN = noiseRepeats; (*fit parameter of last noisetrace*)
Print["Mono: chi2 = ", simParamNoiseD[[2, noiseN]],
 "     d = ", simParamNoiseD[[2, noiseN]], "     a = ",
 simParamNoiseD[[4, noiseN]], "     t = ", 1/simParamNoiseD[[5, noiseN]]];
Print["Bi: ratio chi2Mono/chi2Bi = ", simParamNoiseD[[6, 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 --



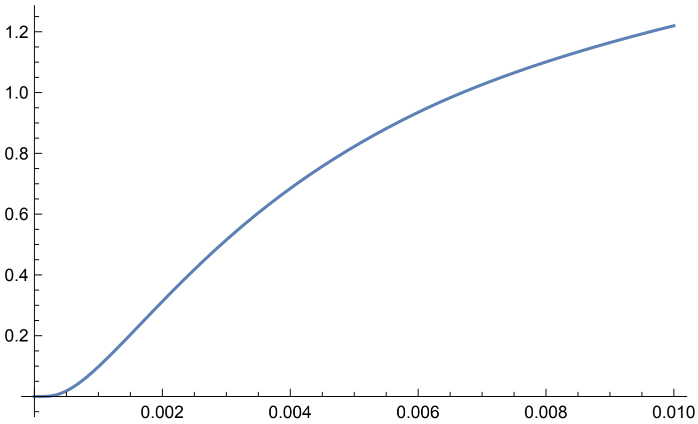


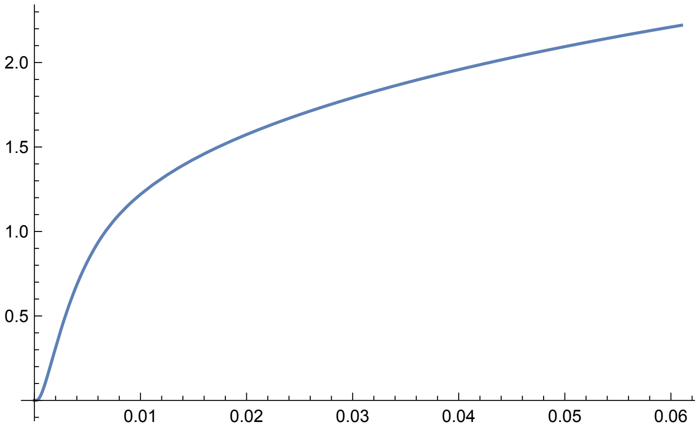
-- C5

-- C10

-- D

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





-- C5

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

take mono

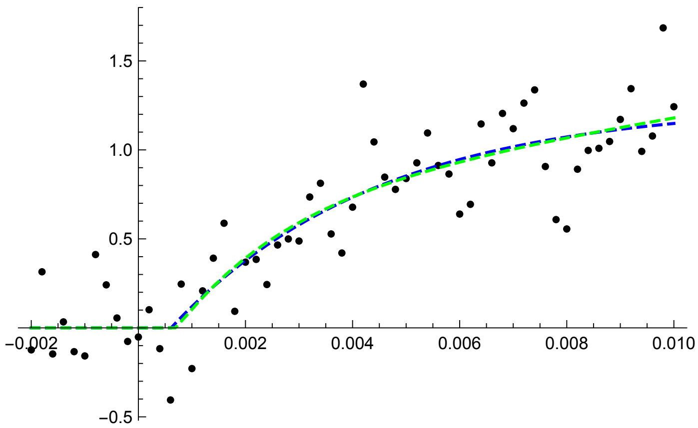
··· NonlinearModelFit: Failed to converge to the requested accuracy or precision within 100 iterations.

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 = 2.96481 d = 2.96481 a = 1.26086 t = 0.0038824

Bi: ratio chi2Mono/chi2Bi = 1.00554 d = 0.000716352 a = 21.5738 a1 = 0.736358 t1 =0.00217229 t2 = 0.421949

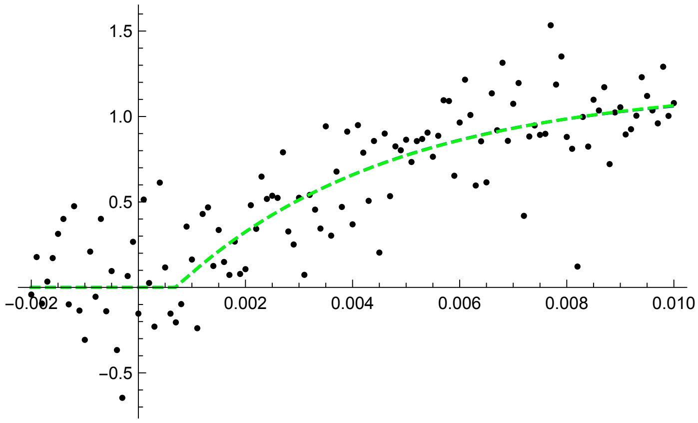
••• Quantile: Argument {} should be a non−empty list.

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

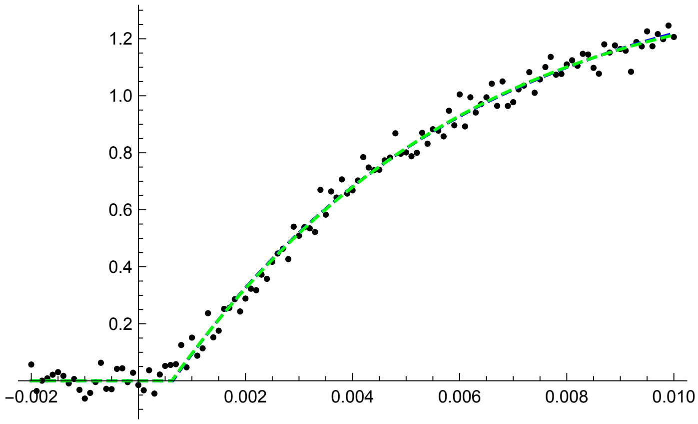
••• Quantile: Argument {} should be a non−empty list.

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

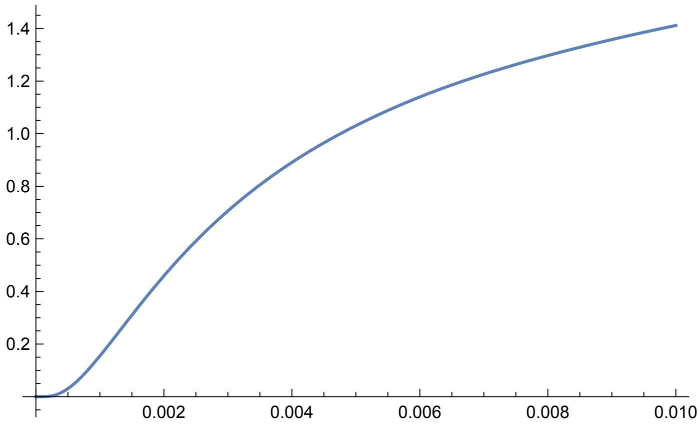
```
--------------------------------------------------------------------------- C10

take mono

take mono

take mono
```

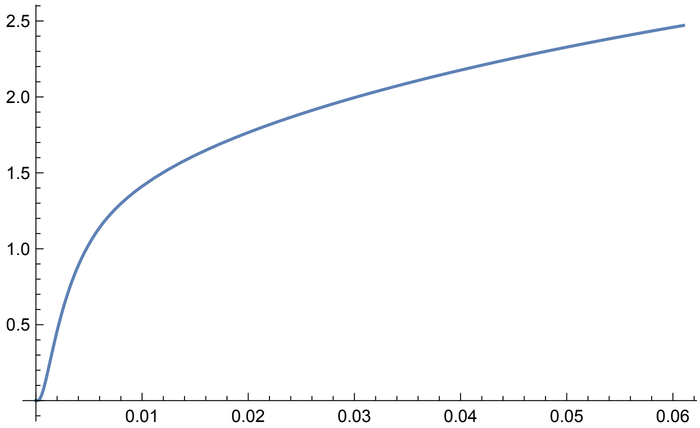



```
Mono: chi2 = 7.08688      d = 7.08688      a = 1.17872      t = 0.00403296

Bi: ratio chi2Mono/chi2Bi = 0.999794      d = 0.0007      a =
 1.44509      a1 = 1.12956      t1 =0.00391193      t2 = 0.070724

--------------------------------------------------------------------------- D

take mono

take mono

take mono
```




```
Mono: chi2 = 0.158654      d = 0.158654      a = 1.49144      t = 0.00550646

Bi: ratio chi2Mono/chi2Bi = 1.01159      d = 0.000623127      a =
 0.86273      a1 = 2.87366      t1 =0.00768285      t2 = 0.0181125

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

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



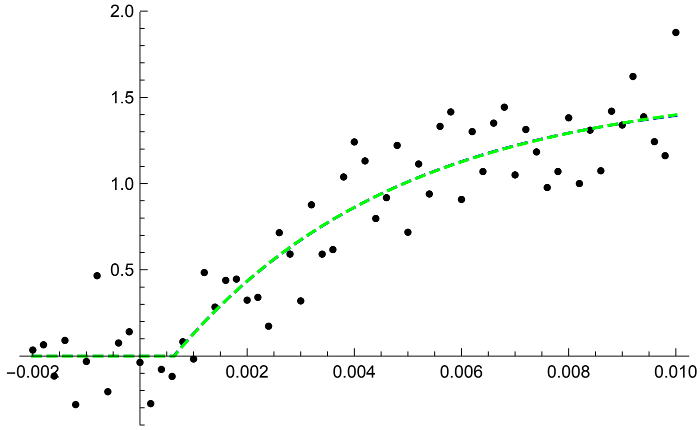


C5

take mono

take mono

take mono



Mono: chi2 = 2.46192   d = 2.46192   a = 1.5634   t = 0.00420158

Bi: ratio chi2Mono/chi2Bi = 1.00006   d = 0.000641544

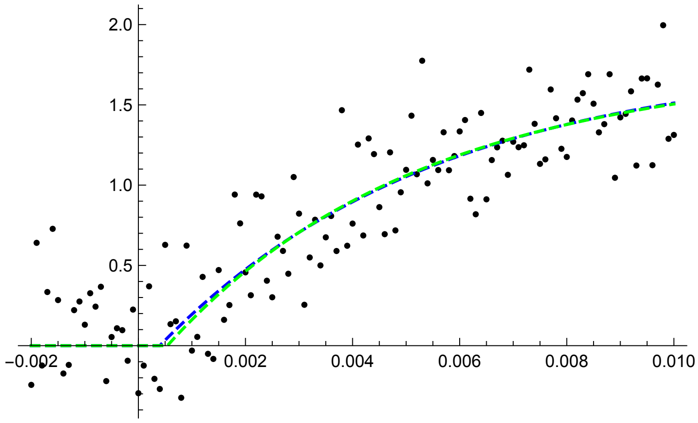
a = 4.70221   a1 = 1.44954   t1 =0.0039355   t2 = 0.360279

C10

take mono

take mono

take mono



Mono: chi2 = 8.52092 d = 8.52092 a = 1.79507 t = 0.0052043

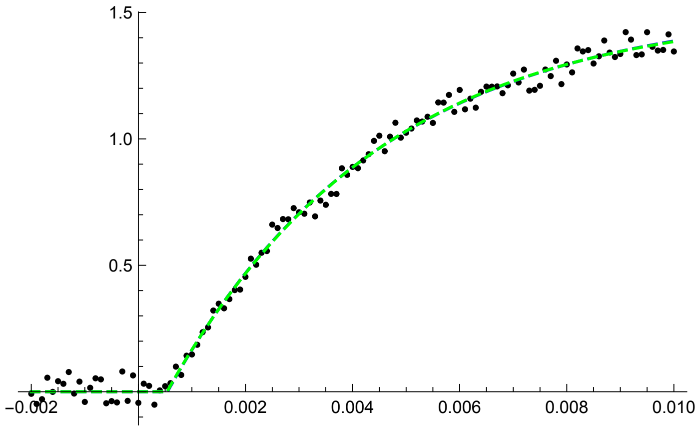
Bi: ratio chi2Mono/chi2Bi = 0.99677 d = 0.000541875 a = 1.82858 a1 = 1.33796 t1 =0.00416516 t2 = 0.00971541

-- D

take mono

take mono

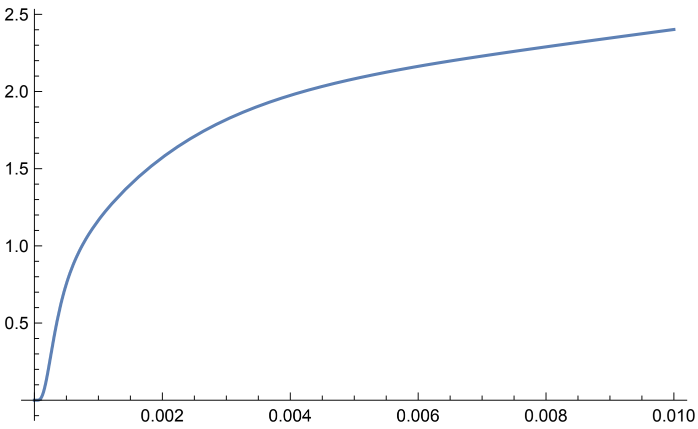
take mono

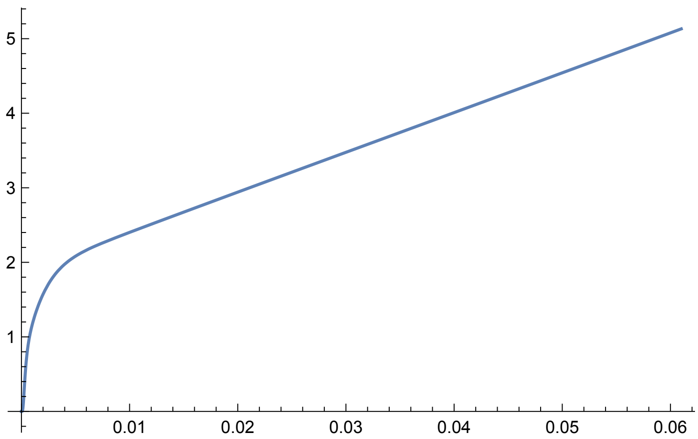


Mono: chi2 = 0.150791 d = 0.150791 a = 1.52878 t = 0.00397755

Bi: ratio chi2Mono/chi2Bi = 1.00064 d = 0.000535539 a = 1.481 a1 = 1.94351 t1 =0.00439514 t2 = 0.00743034

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



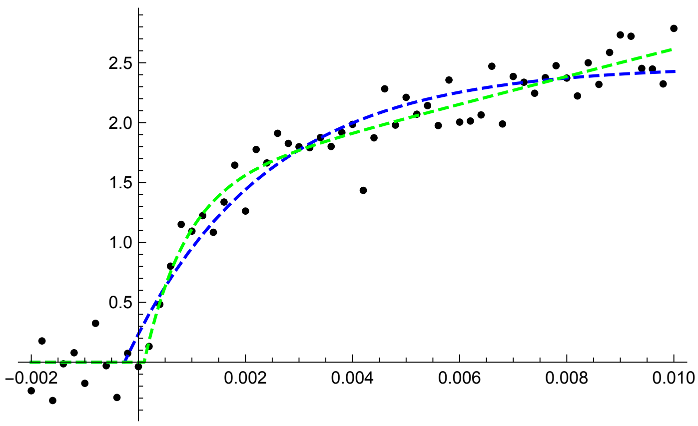


--- C5

take bi

take bi

take bi



Mono: chi2 = 2.32801   d = 2.32801   a = 2.47382   t = 0.00258321

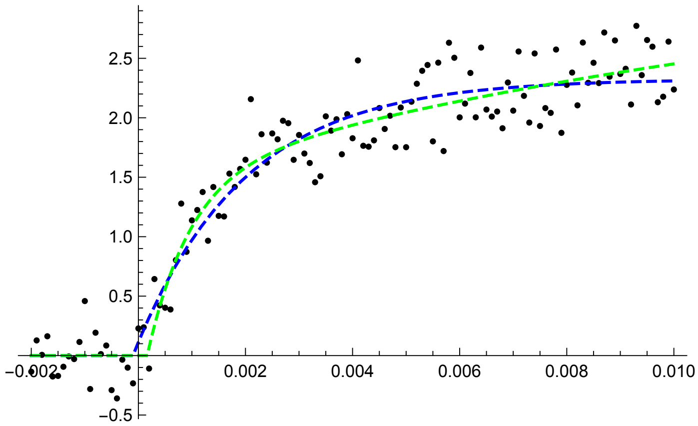
Bi: ratio chi2Mono/chi2Bi = 1.35302   d = 0.000108022   a = 23.5084   a1 = 1.45666   t1 =0.000763861   t2 = 0.183317

--- C10

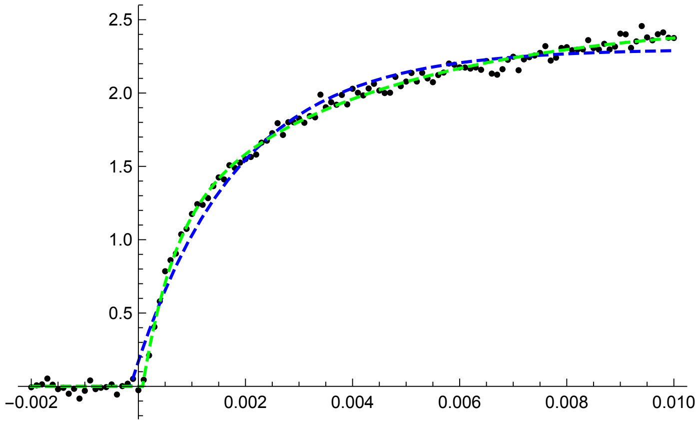
take bi

take bi

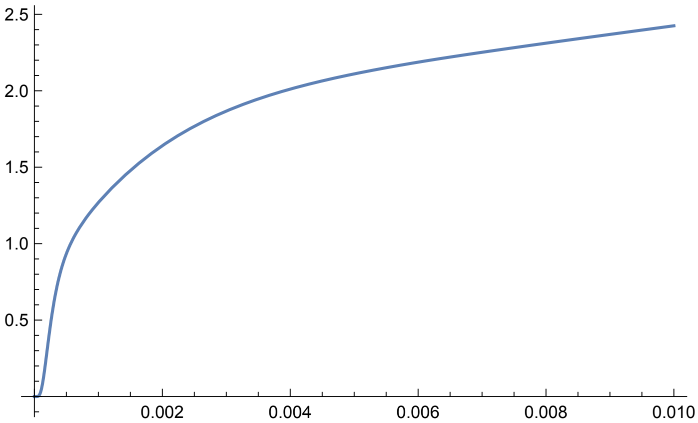
take bi

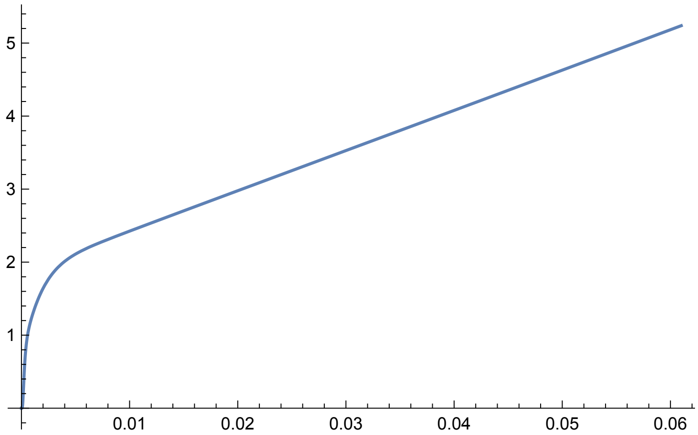



```
Mono: chi2 = 6.84202      d = 6.84202      a = 2.32614      t = 0.00202853

Bi: ratio chi2Mono/chi2Bi = 1.0904      d = 0.00016458      a =
 3.45458      a1 = 1.50402      t1 =0.000799165      t2 = 0.0147441

--------------------------------------------------------------------------- D

take bi

take bi

take bi
```




```
Mono: chi2 = 0.623135      d = 0.623135      a = 2.3009      t = 0.00192783

Bi: ratio chi2Mono/chi2Bi = 3.66281      d = 0.0000793084      a =
 2.50245      a1 = 1.10304      t1 =0.000577102      t2 = 0.00413312

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

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

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



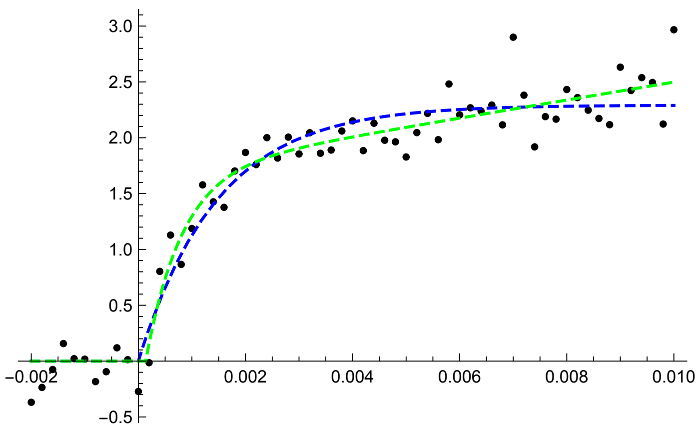


-- C5

take bi

take bi

take bi



Mono: chi2 = 2.81045   d = 2.81045   a = 2.29184   t = 0.00147492

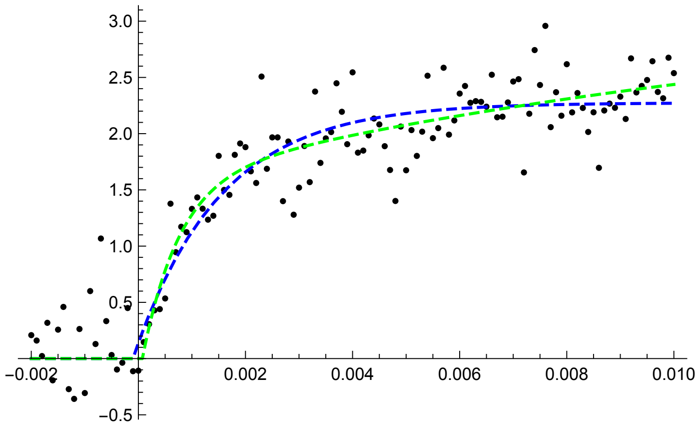
Bi: ratio chi2Mono/chi2Bi = 1.25971   d = 0.000136624   a = 20.7439   a1 = 1.69265   t1 =0.000671877   t2 = 0.228367

-- C10

take mono

take bi

take bi



Mono: chi2 = 10.4883 d = 10.4883 a = 2.2743 t = 0.00160435

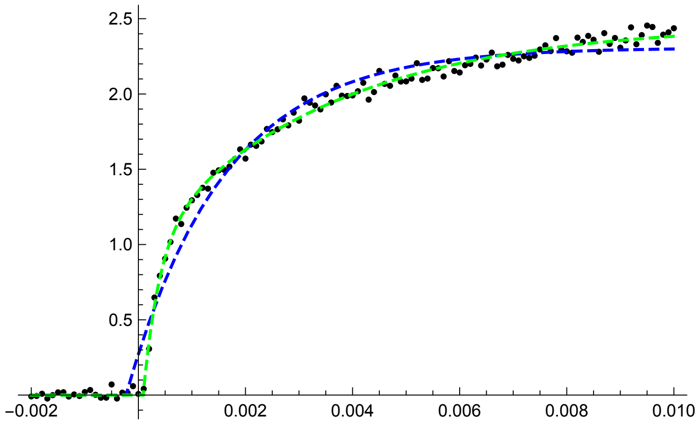
Bi: ratio chi2Mono/chi2Bi = 1.09923 d = 0.0000747615 a = 3.29227 a1 = 1.57775 t1 =0.000681779 t2 = 0.0142666

-- D

take bi

take bi

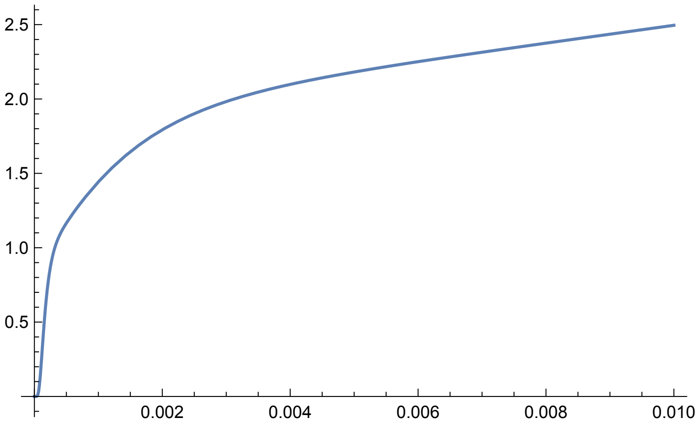
take bi

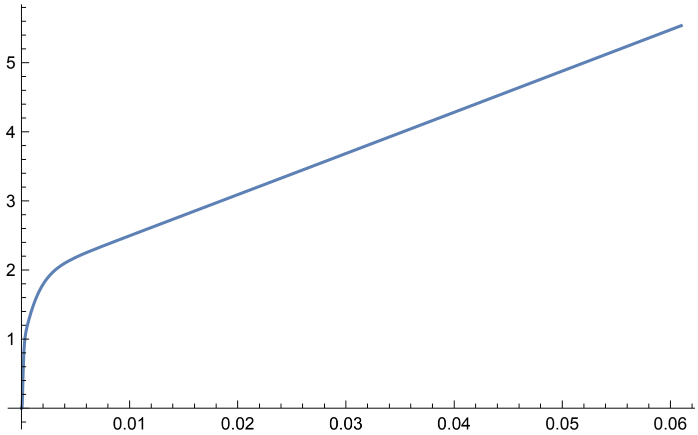


Mono: chi2 = 0.91061 d = 0.91061 a = 2.30711 t = 0.00181864

Bi: ratio chi2Mono/chi2Bi = 4.79737 d = 0.0000900976 a = 2.46542 a1 = 1.0158 t1 =0.000302678 t2 = 0.00344934

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






```
--------------------------------------------------------------------------- C5
```

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.

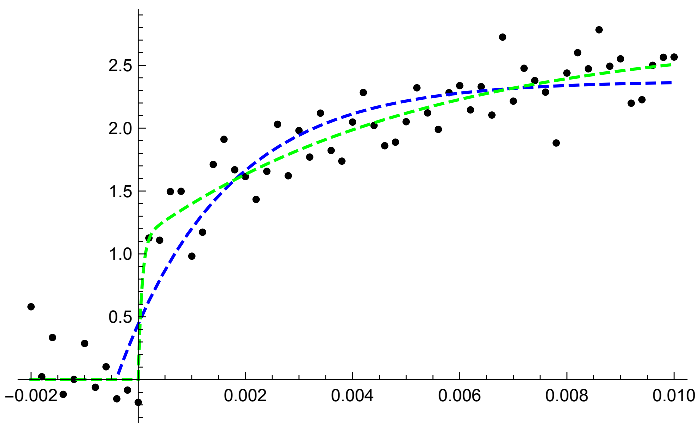
General: Exp[−736.49] is too small to represent as a normalized machine number; precision may be lost.

General: Exp[−793.04] is too small to represent as a normalized machine number; precision may be lost.

General: Exp[−849.59] is too small to represent as a normalized machine number; precision may be lost.

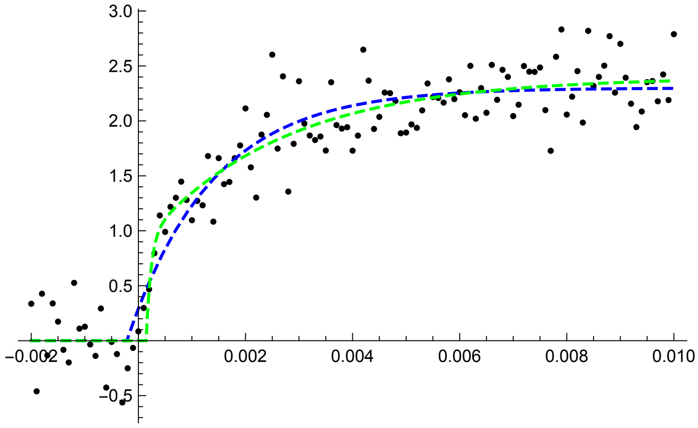
General: Further output of General::munfl will be suppressed during this calculation.

```
take mono
take bi
take bi
```

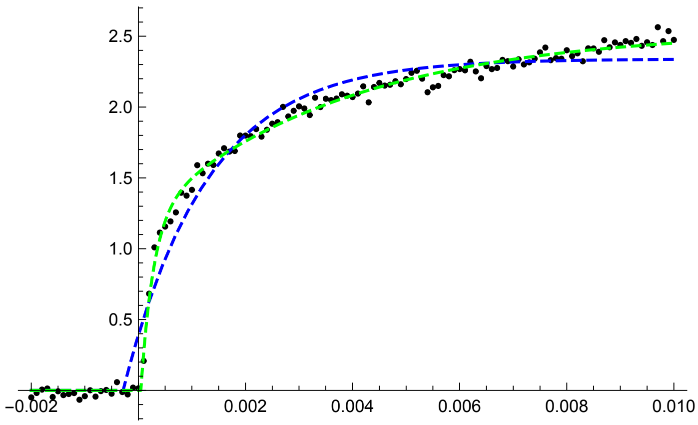



```
Mono: chi2 = 4.01756      d = 4.01756      a = 2.37426      t = 0.00199883
```

```
Bi: ratio chi2Mono/chi2Bi = 1.58562     d = -8.24866×10^-17     a =
 2.75155     a1 = 1.11654     t1 =0.000069318     t2 = 0.00526753
--------------------------------------------------------------------------- C10
take bi
take mono
take bi
```




```
Mono: chi2 = 8.52843     d = 8.52843     a = 2.29944     t = 0.00158323
Bi: ratio chi2Mono/chi2Bi = 1.07682     d = 0.000145139     a =
 2.39724     a1 = 0.936027     t1 =0.0000897784     t2 = 0.00259214
--------------------------------------------------------------------------- D
take bi
take bi
take bi
```




```
Mono: chi2 = 1.41395     d = 1.41395     a = 2.33924     t = 0.00155065
Bi: ratio chi2Mono/chi2Bi = 5.74032     d = 0.0000457876     a =
 2.54393     a1 = 1.22128     t1 =0.000236239     t2 = 0.00374787
```

Plots

In[∘]:=
```
caFact = 1*^6;
```

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

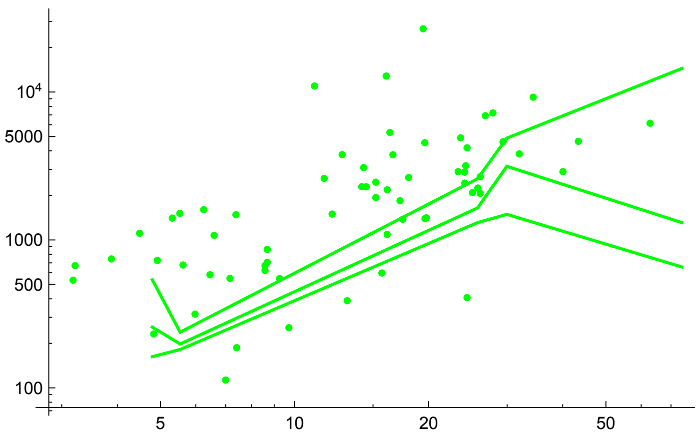
release rate 1/tau1 (merge of mono 1/tau and bi 1/tau1)

```
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"];
         ];
```

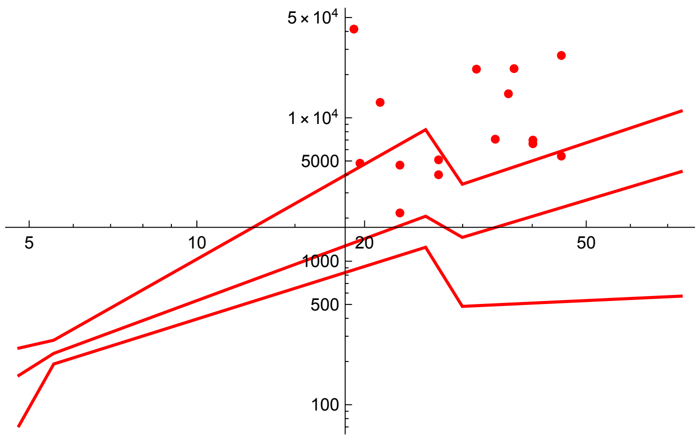
Out[•]=



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"];
 ];
```

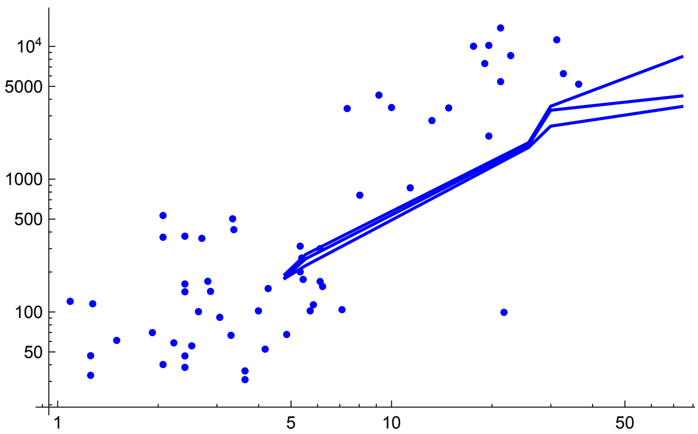
Out[∘]=



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"];
 ];
```

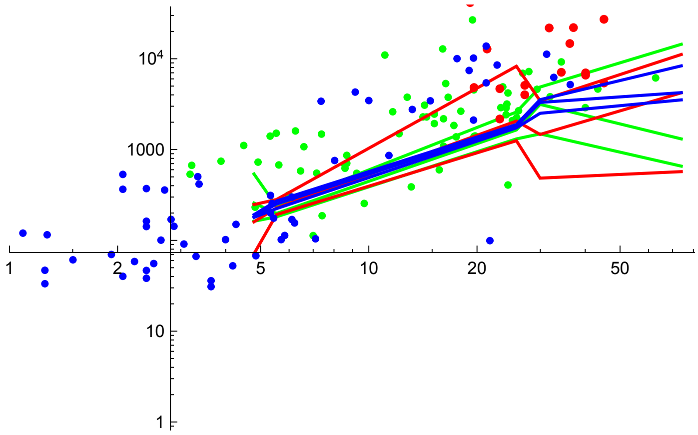
Out[◦]=



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
```

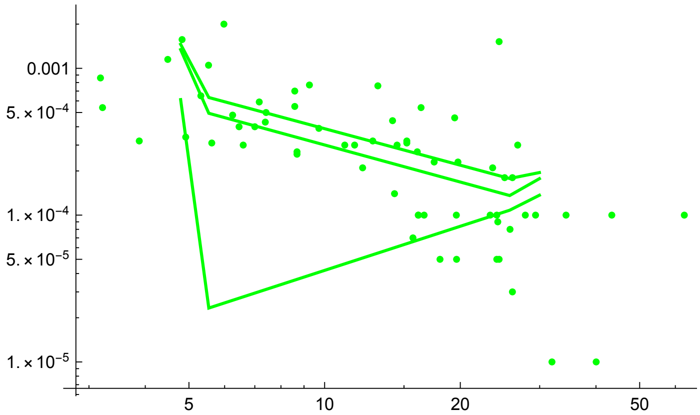
Out[∘]//TableForm=

0.703073	
4.79194	0.00134142
5.53376	0.00049394
25.7412	0.000135972
29.9583	0.000177138
74.0312	-0.000147837

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"];
 ];
```

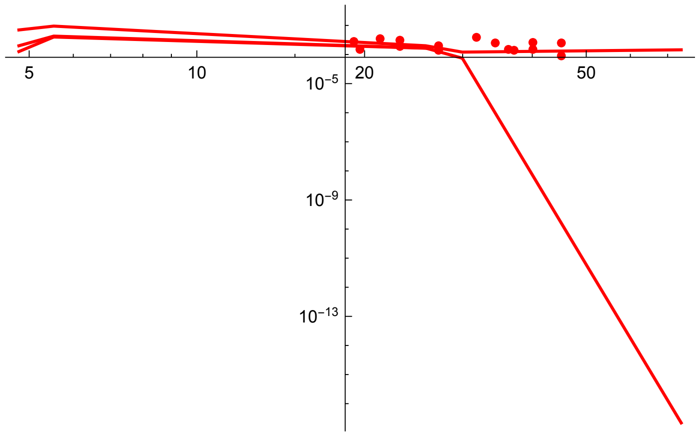
Out[∘]=



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"];
 ];
```

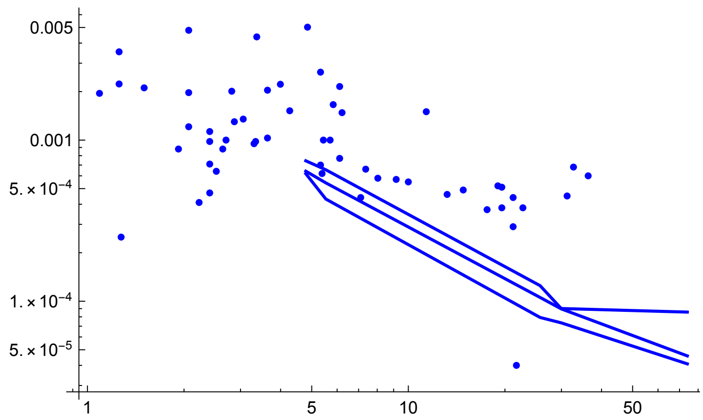
Out[∘]=



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"];
 ];
```

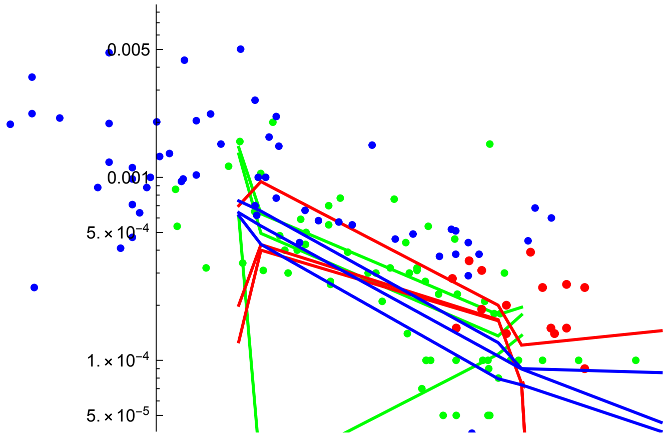
Out[•]=



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];
```

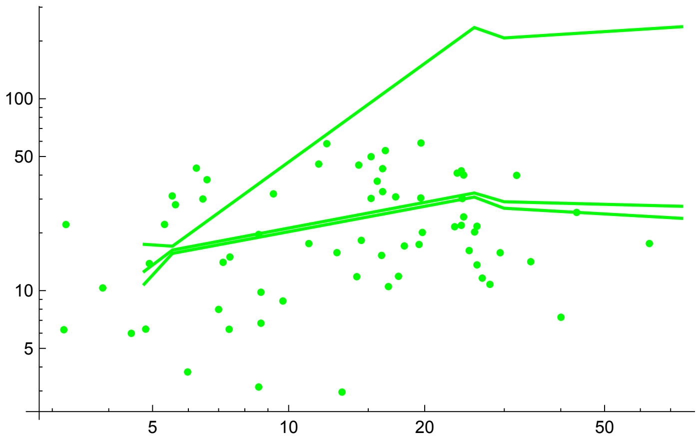
amp (merge of mono amp and bi amp)

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 ]
```

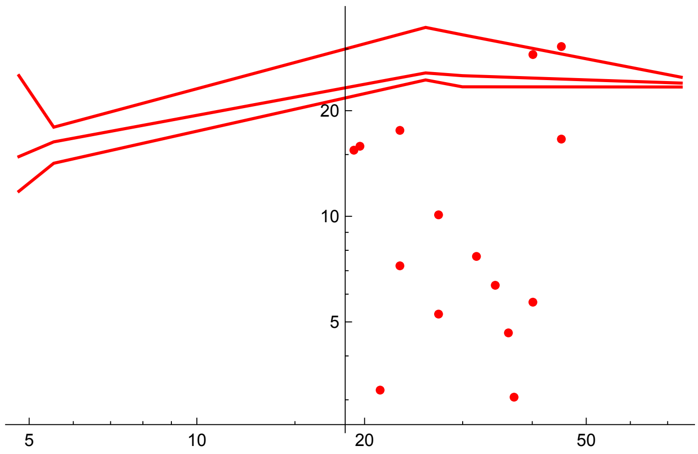
Out[◦]=



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 ]
```

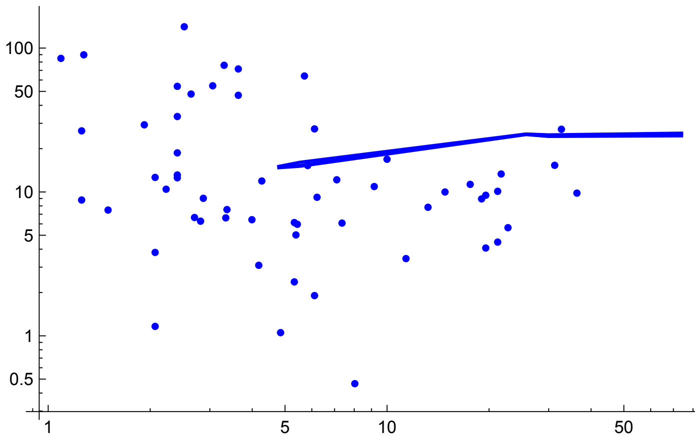
Out[•]=



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 ]
```

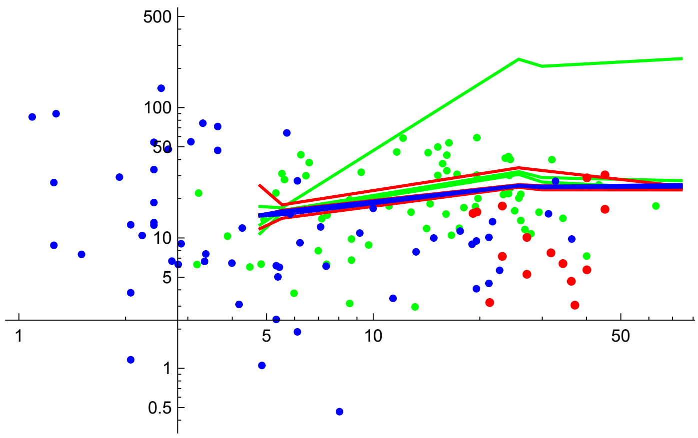
Out[•]=



C5 and C10 and D

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

Out[•]=



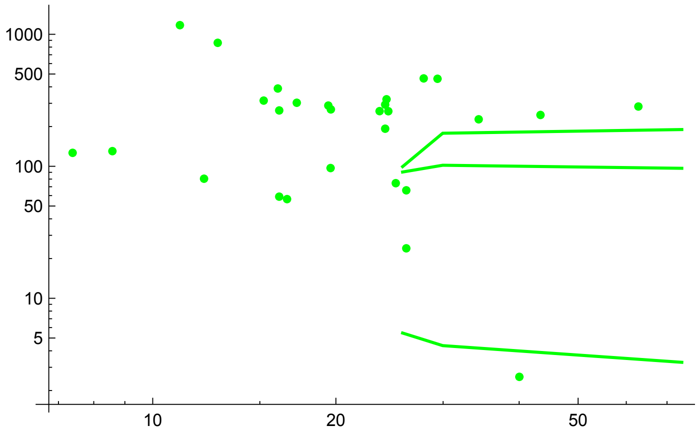
release rate 1/tau2 of bi fits (if bi is justified)

In[•]:=
```
simParam = 16;
```

C5

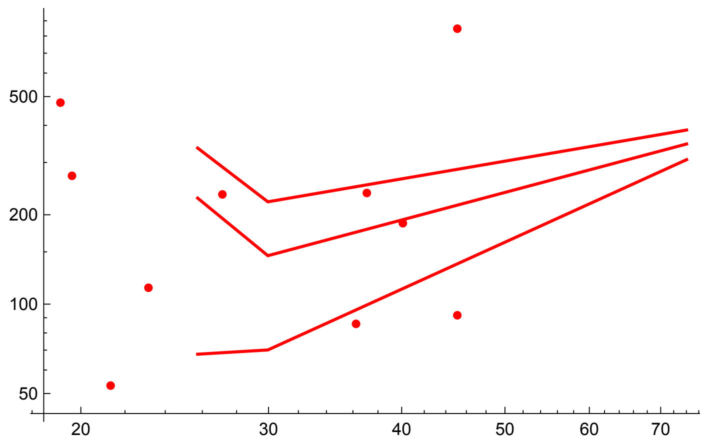
In[∘]:=
```
gr1a = ListLogLogPlot[
   Transpose[{dataT2C5Ca, dataT2C5RelRate}], PlotStyle → {colorA}];
gr2a = ListLogLogPlot[Transpose[{caFact simCaList,
      simParamMedianC5[[simParam, All]]}],
   PlotStyle → {colorA}, Joined → True, PlotRange → All];
gr3a = ListLogLogPlot[Transpose[{caFact simCaList,
      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

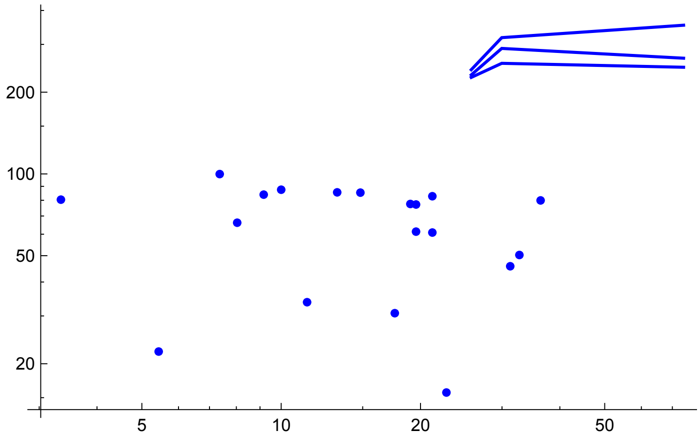
In[•]:=
```
gr1b = ListLogLogPlot[
   Transpose[{dataT2C10Ca, dataT2C10RelRate}], PlotStyle → {colorB}];
gr2b = ListLogLogPlot[Transpose[{caFact simCaList,
     simParamMedianC10[[simParam, All]]}],
   PlotStyle → { colorB}, Joined → True, PlotRange → All];
gr3b = ListLogLogPlot[Transpose[{caFact simCaList,
     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"];
 ];
```

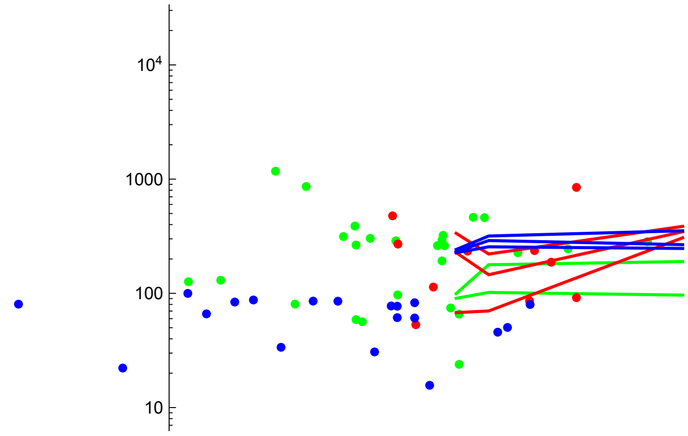
Out[•]=



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];
```

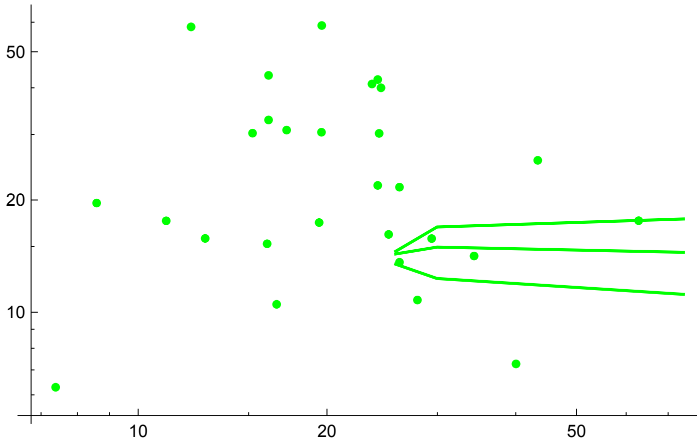
amp1 of bi fits (if bi is justified)

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 ]
```

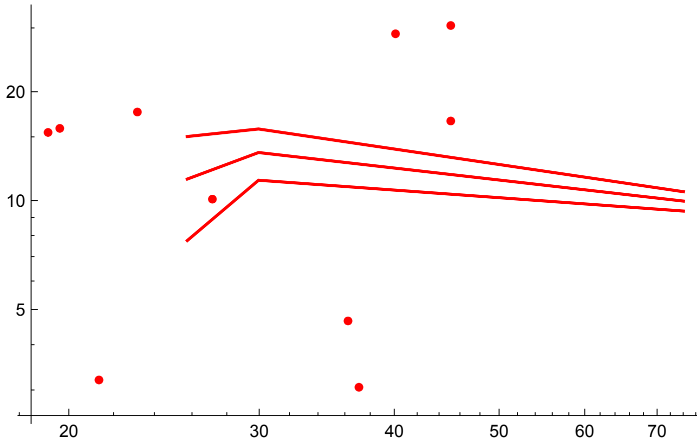
Out[•]=



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 ]
```

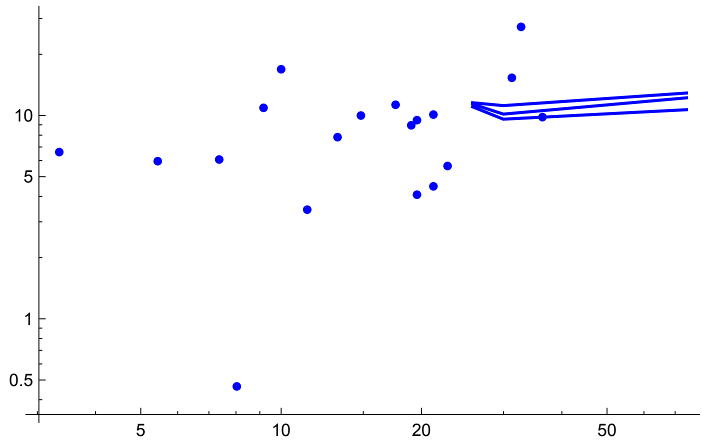
Out[∘]=



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 ]
```

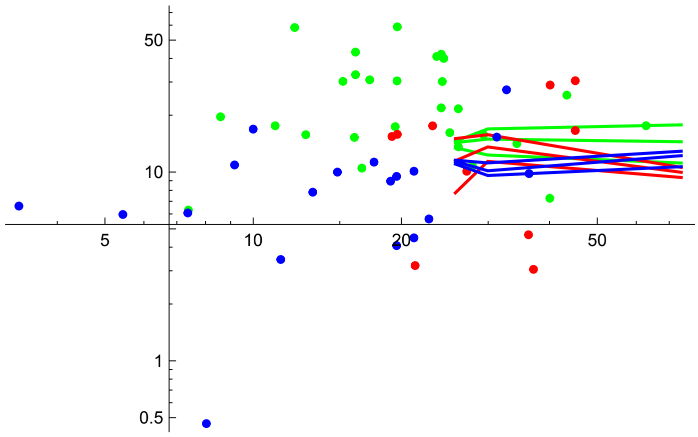
Out[•]=



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[•]=



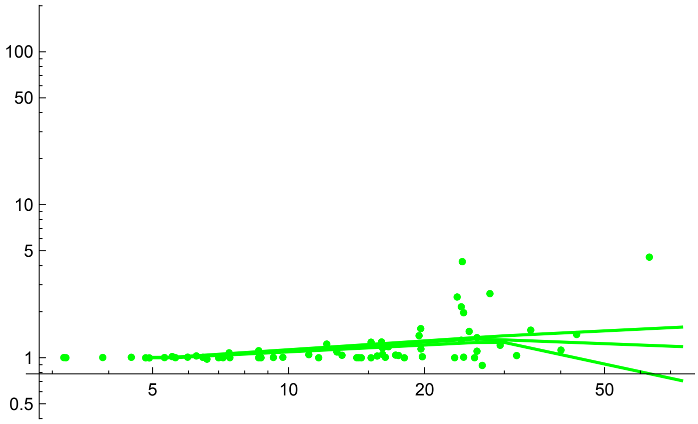
chi2 mono/bi ratio

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"];
 ];
```

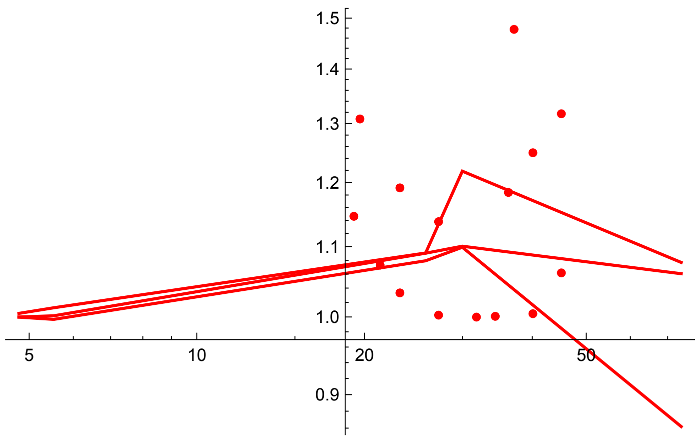
Out[•]=



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"];
 ];
```

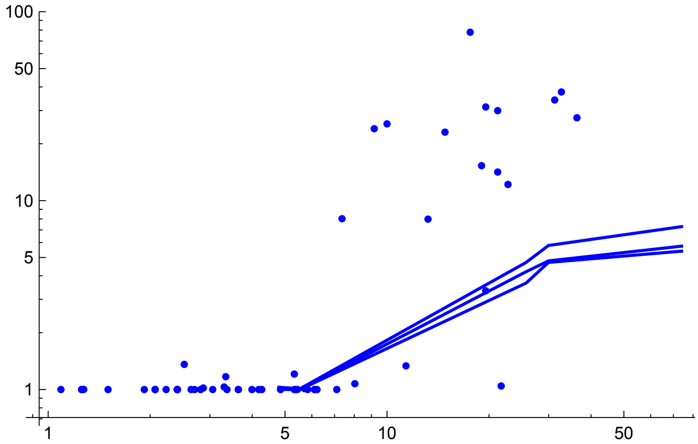
Out[•]=



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"];
 ];
```

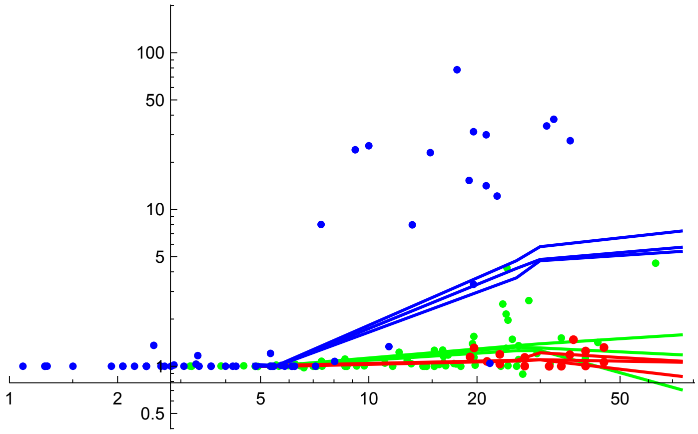
Out[•]=



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];
```

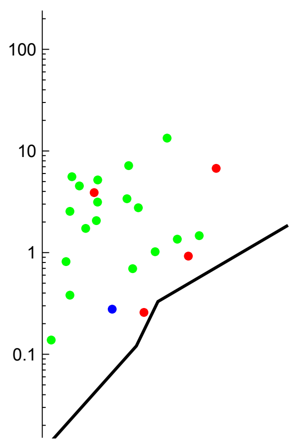
Out[•]=



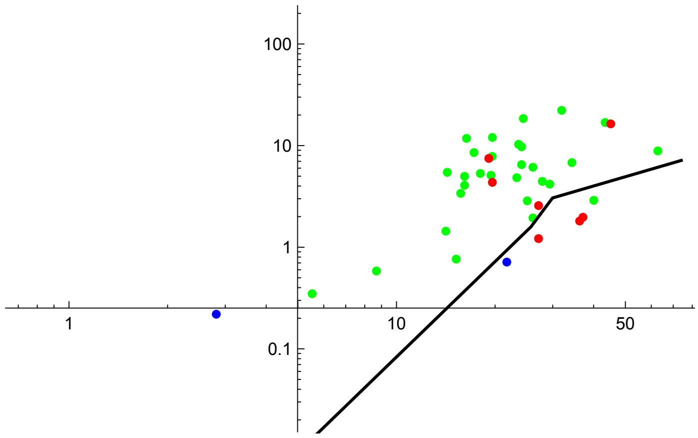
Nv

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;
 ];
```

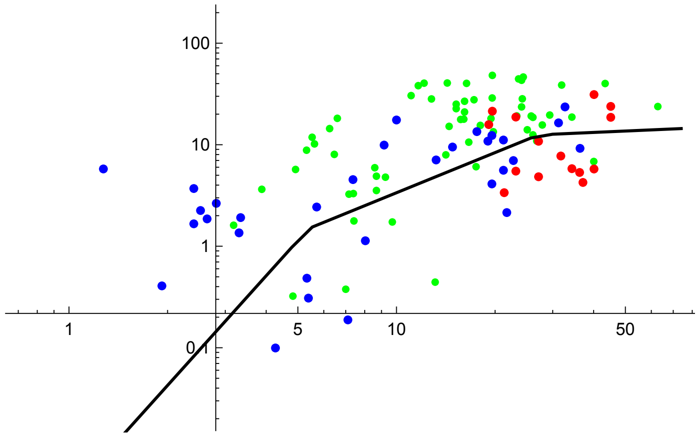
time for Nv (ms) = 0.1



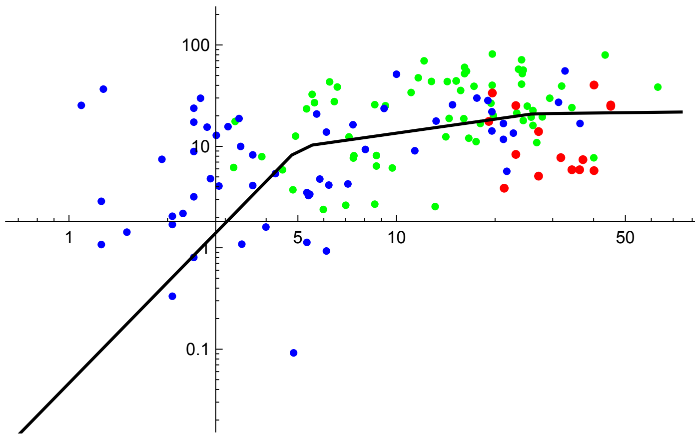
time for Nv (ms) = 0.2



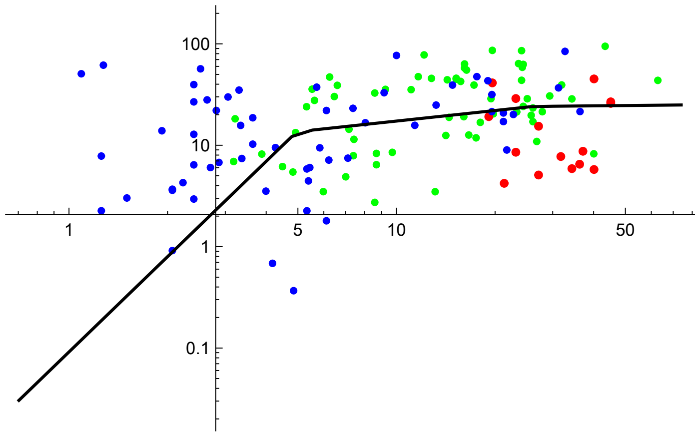
time for Nv (ms) = 1.



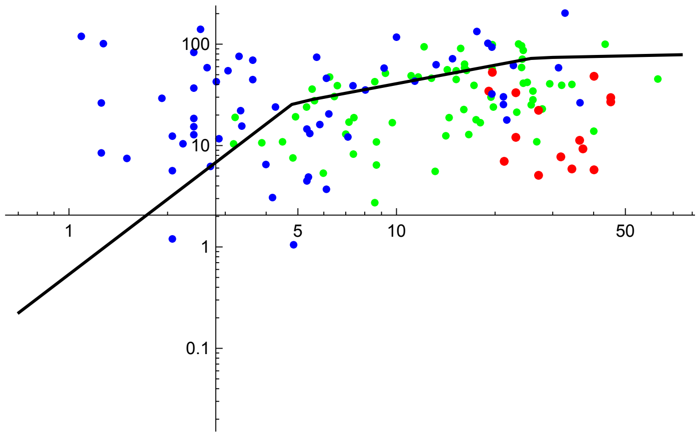
time for Nv (ms) = 5.



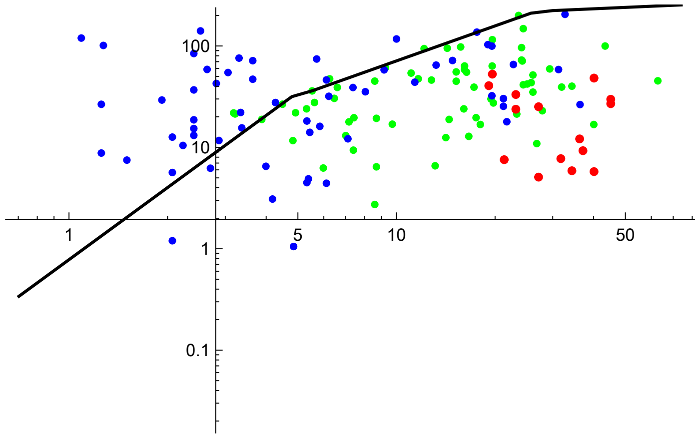
time for Nv (ms) = 10.



time for Nv (ms) = 100.

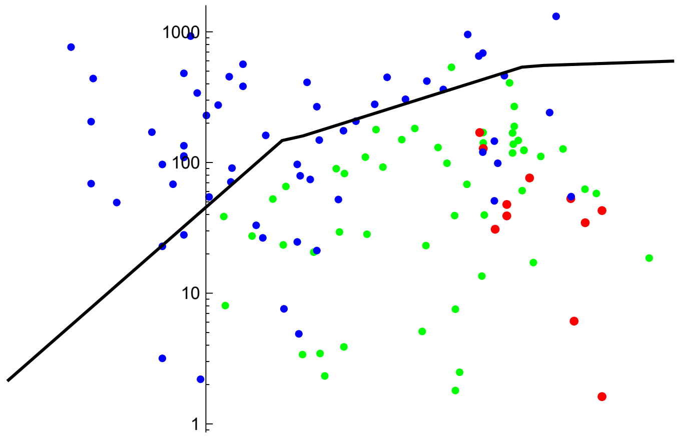


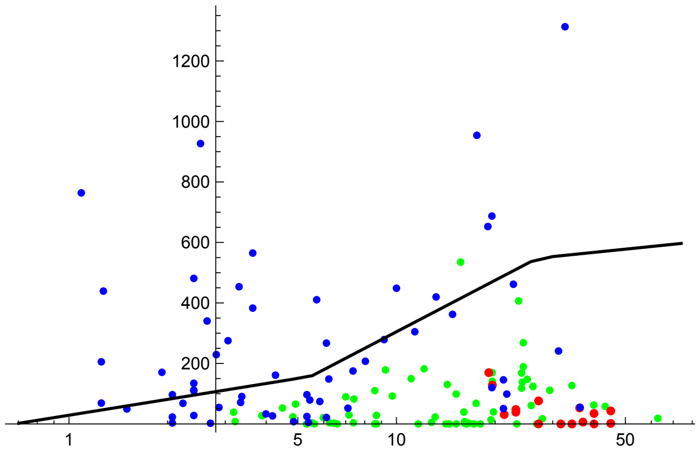
time for Nv (ms) = 400.



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"]
 ];
```

Nv normalize to the value at 5 ms

In[•]:=
```
timeOfNv
nromPos = 5;
1000 * timeOfNv[[nromPos]]
```

Out[•]= {0.0001, 0.0002, 0.001, 0.005, 0.01, 0.1, 0.4}

Out[•]= 10.

In[•]:=
```
dataT1DNvNorm = Transpose[Transpose[dataT1DNv] / dataT1DNv[[nromPos]]];
dataT1C10NvNorm = Transpose[Transpose[dataT1C10Nv] / dataT1C10Nv[[nromPos]]];
dataT1C5NvNorm = Transpose[Transpose[dataT1C5Nv] / dataT1C5Nv[[nromPos]]];
```

In[•]:=
```
dataT1C5NvNorm // TableForm
```

Out[•]//TableForm=

0.	0.	0.	0.	0.	0.	0.
0.	0.	0.	0.	0.	0.	0.
0.20362	0.265687	0.42823	0.550679	0.804146	0.862111	0.657036
0.719618	0.914034	0.947765	0.995367	0.999983	0.961307	0.985586
1.	1.	1.	1.	1.	1.	1.
1.97523	1.00693	1.44309	1.00001	1.	1.38099	1.17479
1.98885	1.00693	1.64647	1.00001	1.	1.52805	1.34343

In[•]:=
```
simParamNv // TableForm
simParamNvNorm = Transpose[Transpose[simParamNv] / simParamNv[[nromPos]]];
simParamNvNorm // TableForm
```

Out[•]//TableForm=

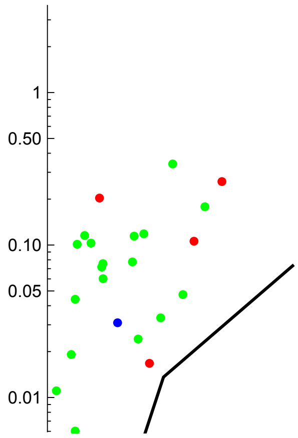
1.15831×10^{-8}	0.0000225289	0.0000470166	0.0120637	0.0330104	0.182311
4.04537×10^{-7}	0.000699228	0.00131308	0.158638	0.305208	0.713778
0.000100151	0.0977688	0.154622	1.16532	1.26874	1.44248
0.00143825	0.822265	1.03048	2.08205	2.11032	2.18122
0.00304654	1.21973	1.41133	2.40188	2.42511	2.49533
0.022522	2.54577	2.84791	7.2319	7.40418	7.86544
0.0339701	3.16342	3.61667	21.0621	22.3219	25.4018

Out[•]//TableForm=

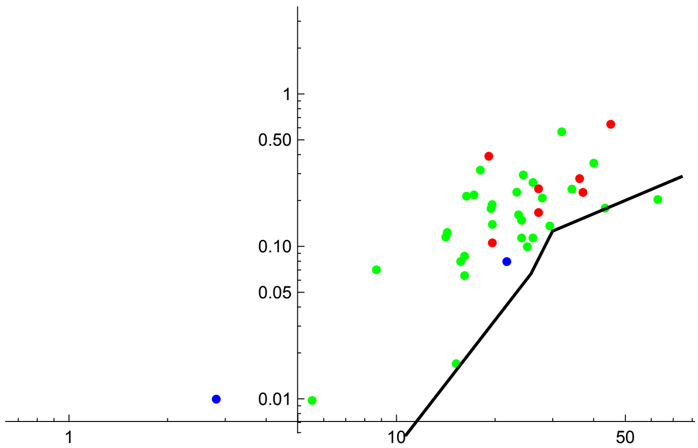
3.80206×10^{-6}	0.0000184704	0.0000333137	0.0050226	0.0136119	0.073061
0.000132786	0.000573263	0.000930384	0.0660475	0.125853	0.286046
0.0328736	0.0801559	0.109558	0.48517	0.523167	0.578071
0.472094	0.674135	0.730146	0.866841	0.870194	0.87412
1.	1.	1.	1.	1.	1.
7.39265	2.08715	2.0179	3.01093	3.05313	3.15207
11.1504	2.59354	2.5626	8.769	9.20447	10.1797

In[*]:=
```
For[NvCount = 1, NvCount ≤ 7, NvCount += 1,
  Print[" time for Nv (ms) = ", 1000 * timeOfNv[[NvCount]]];
  gr1a = ListLogLogPlot[
    Transpose[{dataT1C5Ca, dataT1C5NvNorm[[NvCount]]}], PlotStyle → {colorA}];
  gr1b = ListLogLogPlot[Transpose[{dataT1C10Ca, dataT1C10NvNorm[[NvCount]]}],
    PlotStyle → {colorB}];
  gr1c = ListLogLogPlot[Transpose[{dataT1DCa, dataT1DNvNorm[[NvCount]]}],
    PlotStyle → {colorC}];
  gr2 = ListLogLogPlot[Transpose[{caFact simCaList, simParamNvNorm[[NvCount,
       All]]}], PlotStyle → { Black}, Joined → True, PlotRange → All];
  Show[gr1a, gr1b, gr1c, gr2, PlotRange → {All, {-5, 1}} ] // Print;
 ];
```

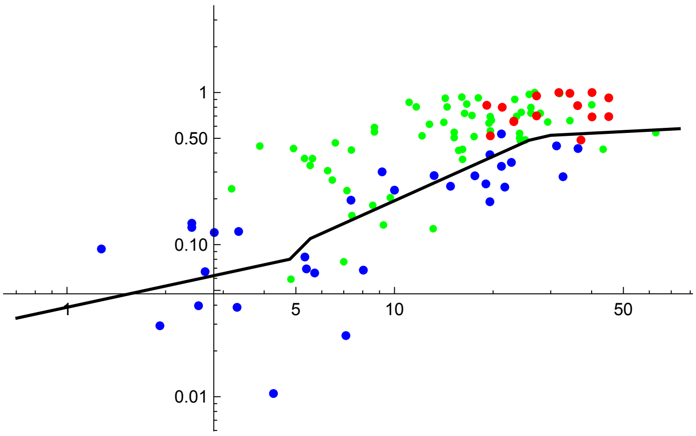
time for Nv (ms) = 0.1



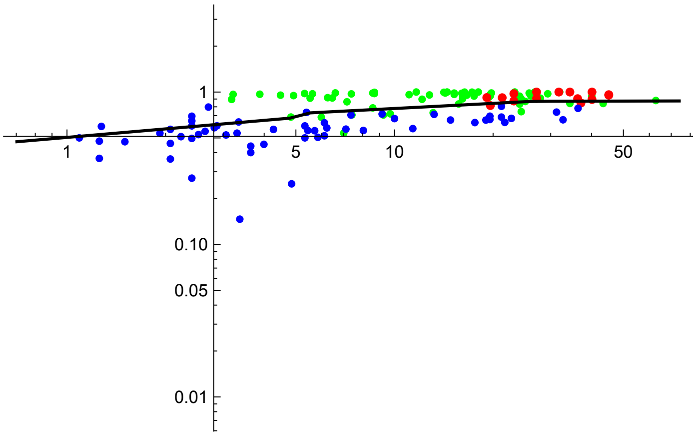
time for Nv (ms) = 0.2



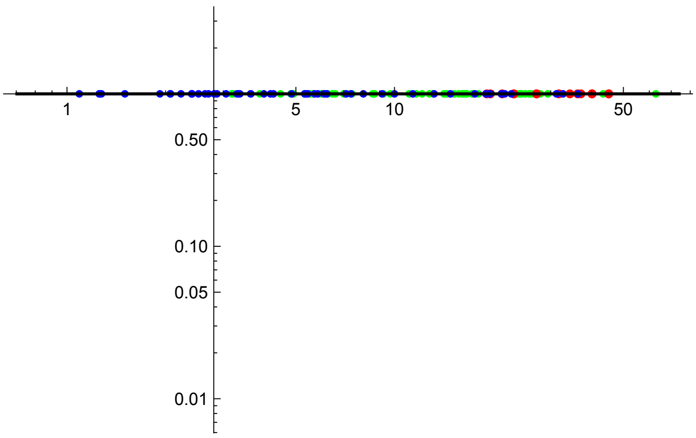
time for Nv (ms) = 1.



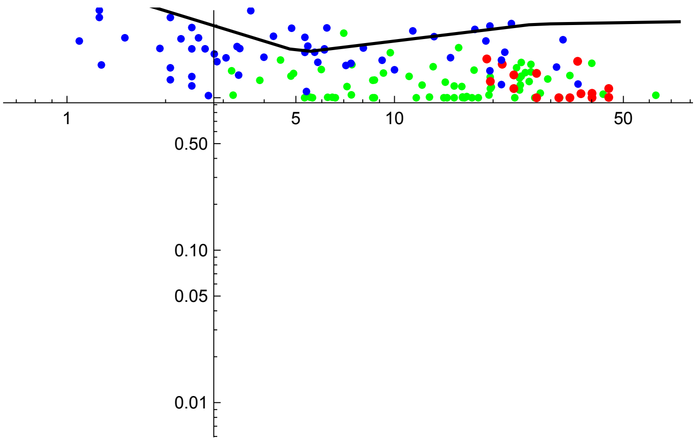
time for Nv (ms) = 5.



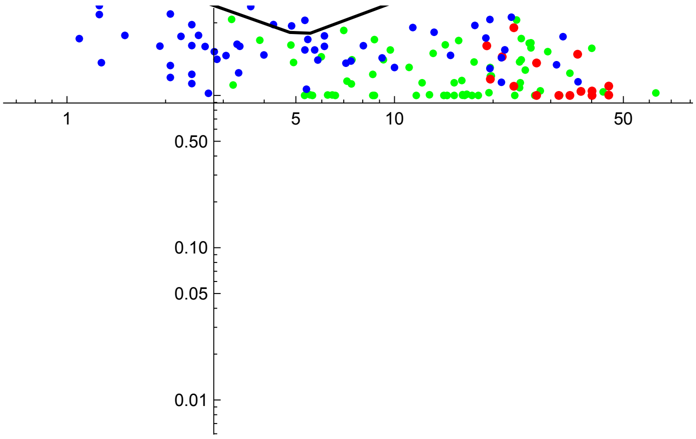
time for Nv (ms) = 10.



time for Nv (ms) = 100.



time for Nv (ms) = 400.



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	2.56849	0.00134142	1.26086	257.573	1.0015	0.00133815
0	2.50124	0.00049394	1.62794	197.853	1.00035	0.000530593
0	2.68527	-0.0002	2.33647	533.976	1.3235	0.000135972
0	3.61673	-0.0000938486	2.26669	678.002	1.30857	0.000177138
0	3.4176	-0.000336771	2.37426	649.489	1.18241	-8.24866×10^{-17}

Out[•]//TableForm=

0	2.51745	0.000612205	1.08074	162.488	1.0013	0.000716352	0
0	2.46192	0.000023287	1.5634	181.755	1.00006	0.00032736	1
0	2.32801	-0.000258229	2.25444	387.116	1.25661	0.000108022	3
0	2.81045	-0.0002	2.21093	636.485	1.25971	0.000136624	2
0	3.22059	-0.000412487	2.31679	500.293	0.708503	-0.000147837	2

Out[•]//TableForm=

0	2.96481	0.00145823	1.74265	538.158	1.00554	0.00150193	21
0	2.74063	0.000632746	1.7046	238.006	1.00713	0.000641544	28
0	2.86931	-0.000103434	2.47382	543.718	1.35302	0.000177605	23
0	3.61708	2.06141×10^{-17}	2.29184	685.279	1.39066	0.000194935	20
0	4.01756	-0.000301624	2.38101	656.787	1.58562	0.000595264	23

C10

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

Out[*]//TableForm=

0	7.71188	0.0002	1.47987	160.138	0.999958	0.0002	2
0	7.8405	0.000429173	1.62998	227.791	1.0016	0.000541875	1
0	8.82845	-0.0001	2.32614	492.968	1.0904	0.000166732	2
0	7.98178	-0.000113113	2.2743	611.729	1.10079	0.0000747615	3
0	8.52843	-0.000353607	2.33671	581.76	1.06048	0.000145139	2

Out[*]//TableForm=

0	7.08688	0.000126294	1.17872	71.2006	0.999794	0.0002
0	7.64974	0.0004	1.41652	192.149	0.99677	0.000360713
0	6.84202	-0.000209557	2.31236	489.208	1.07923	0.00016458
0	7.73302	-0.000542769	2.23329	484.653	1.09923	-0.0000275514
0	7.1172	-0.00040585	2.29944	571.306	0.861835	2.18527×10^{-17}

Out[*]//TableForm=

0	9.16516	0.0007	2.51777	247.957	1.00488	0.0007	2.
0	8.52092	0.000947926	1.79507	281.491	1.01257	0.00106018	36
0	9.75145	-0.0000231327	2.34355	549.149	1.09068	0.0002	3.
0	10.4883	-0.0001	2.3394	623.304	1.21877	0.000121074	35
0	10.3438	-0.000214012	2.34291	631.621	1.07682	0.000530734	2.

D

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

Out[*]//TableForm=

0	0.158654	0.000641456	1.49144	181.605	1.01159	0.000623127	0
0	0.150791	0.000542492	1.52878	251.411	1.00113	0.000535539	1
0	0.657417	-0.000147871	2.3009	523.787	4.20555	0.000105559	2
0	0.887898	-0.000208162	2.29844	561.668	4.79737	0.0000896594	2
0	1.36275	-0.000259953	2.33484	665.864	5.74032	0.0000457876	2

Out[*]//TableForm=

0	0.157877	0.000618486	1.47258	178.885	1.	0.000589261	0
0	0.132567	0.000430563	1.50741	223.687	1.00064	0.000422803	1
0	0.623135	-0.000150779	2.30057	518.718	3.66281	0.0000793084	2
0	0.839884	-0.000228528	2.29565	549.863	4.7089	0.000073433	2
0	1.35841	-0.00028396	2.32779	644.892	5.40133	0.0000408617	2

Out[*]//TableForm=

0	0.171913	0.000743647	1.50705	191.866	1.02839	0.000743647	1
0	0.163033	0.000653992	1.60985	271.131	1.00906	0.000681785	1
0	0.715741	-0.00011199	2.3021	533.414	4.71027	0.000124935	2
0	0.91061	-0.0002	2.30711	564.712	5.79008	0.0000900976	2
0	1.41395	-0.000257475	2.33924	666.878	7.28554	0.0000856202	2

Nv

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

Out[•]//TableForm=

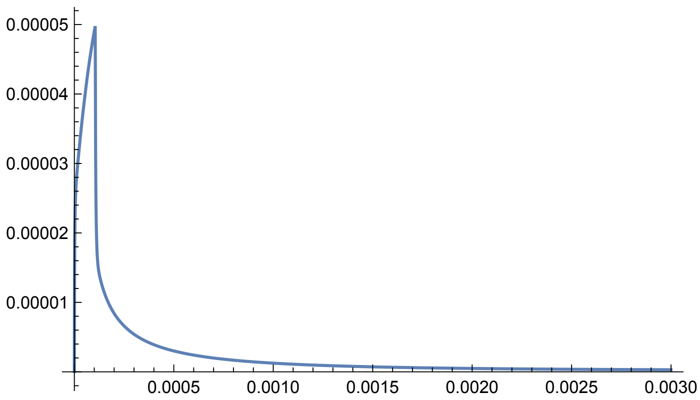
1.15831×10^{-8}	4.04537×10^{-7}	0.000100151	0.00143825	0.00304654	0.02252
0.0000225289	0.000699228	0.0977688	0.822265	1.21973	2.54577
0.0000470166	0.00131308	0.154622	1.03048	1.41133	2.84791
0.0120637	0.158638	1.16532	2.08205	2.40188	7.2319
0.0330104	0.305208	1.26874	2.11032	2.42511	7.40418
0.182311	0.713778	1.44248	2.18122	2.49533	7.86544

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]
```

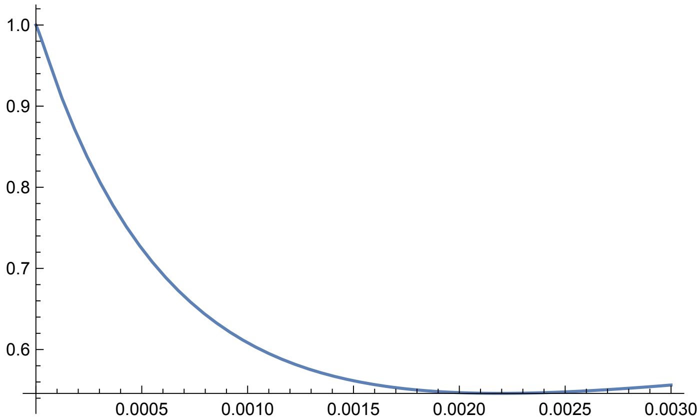
Out[•]=



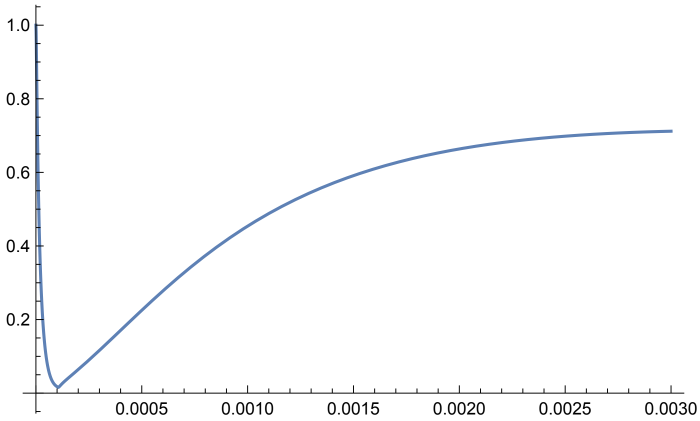
NDSolve

In[•]:=
```
timeStartForPLot = 0.0;
timeEndForPLot = 0.003;
myNDSolveResults = NDSolve[eq,
   {fillStateSS, ss1, ss2, ss3, ss4, ss5, ss6, ss7, sitePlugging}, {t, 0, 0.003}];
Plot[(fillStateSS[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
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]
Plot[(ss5[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss6[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss7[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(sitePlugging[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
```

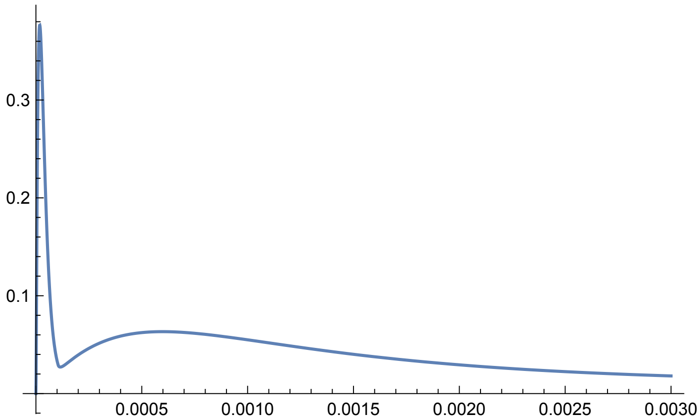
Out[•]=



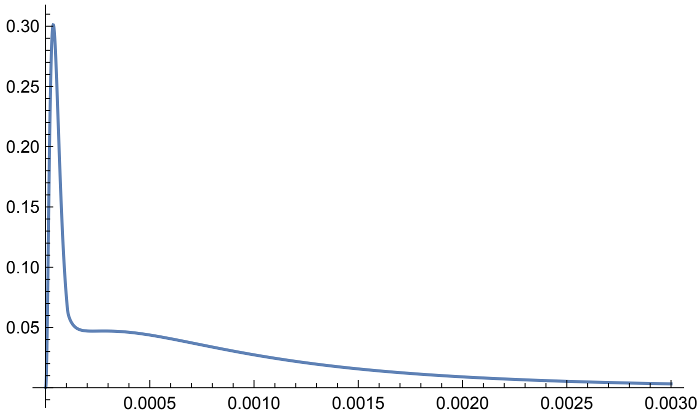
Out[⊛]=



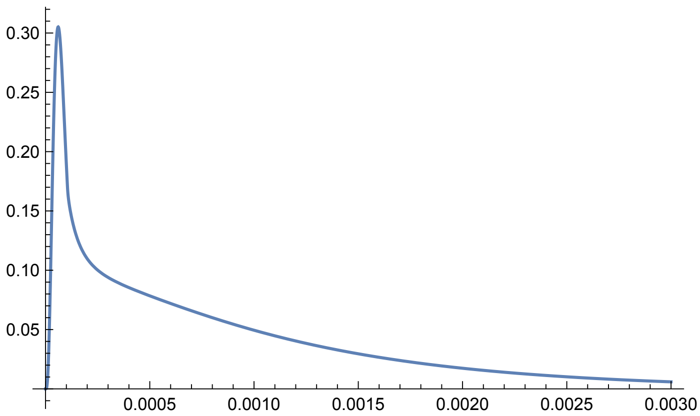
Out[⊛]=



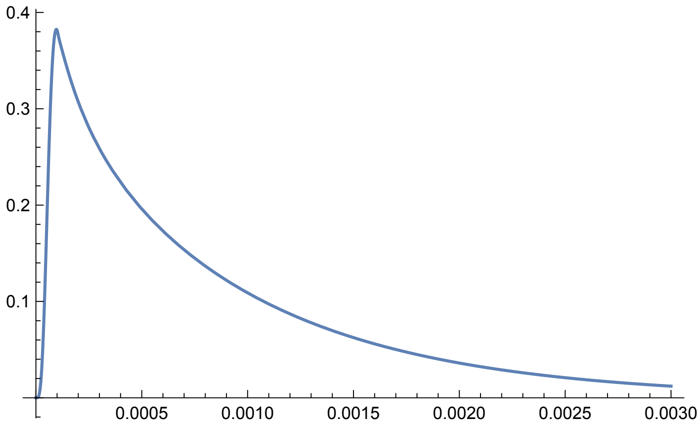
Out[⊛]=



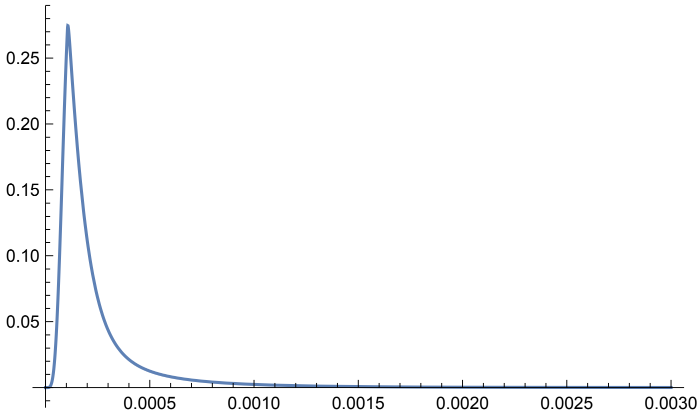
Out[⊛]=



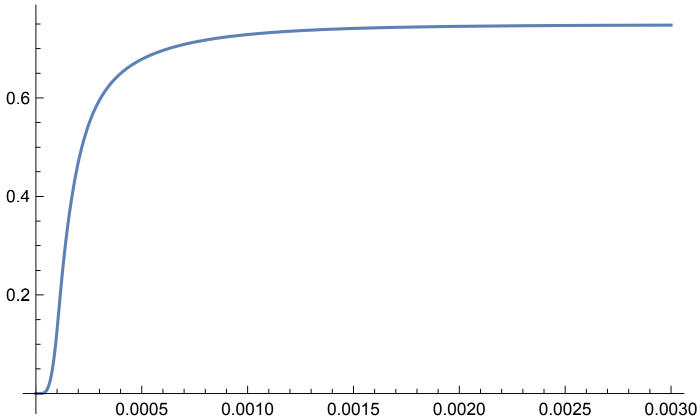
Out[•]=



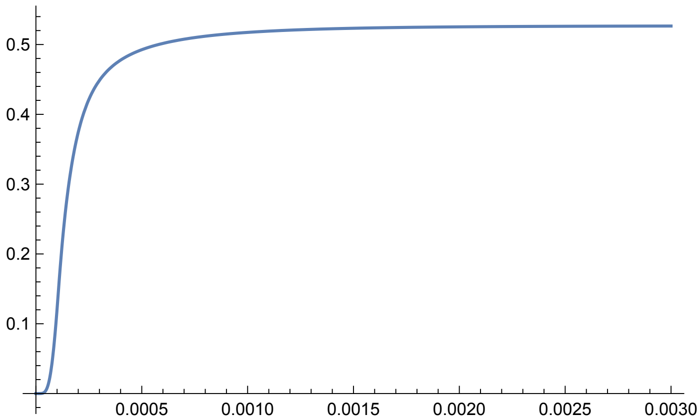
Out[•]=



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
fillStateSSInitial = kprimScheme / kunprimScheme
kfillScheme
kunfillScheme
ss0Initial = fillStateSSInitial * kfillScheme / kunfillScheme
```

Out[•]= 3.3867

Out[•]= 8.61585

Out[•]= 0.393078

Out[•]= 111.823

Out[•]= 181.545

Out[•]= 0.242117

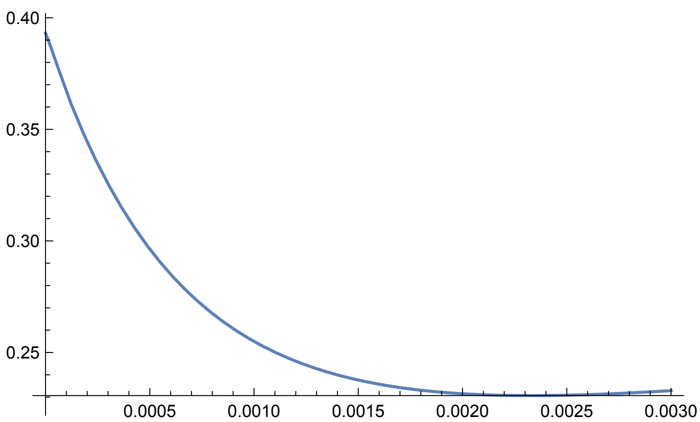
Diff eq.

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], ss5[t], ss6[t], ss7[t]};
eq = {ss'[t] == (mat /. repl).ss[t],
   ss[0] == {ss0Initial, 0., 0., 0., 0., 0., 0.},
   (fillStateSS'[t] == kprim - kunprim fillStateSS[t] -
       kfill fillStateSS[t] + kunfill ss1[t]) /. repl,
   fillStateSS[0] == fillStateSSInitial,
   sitePlugging'[t] ==
    (1 - sitePlugging[t]) ss7'[t] - siteClearanceTau sitePlugging[t],
   sitePlugging[0] == 0
  };
```

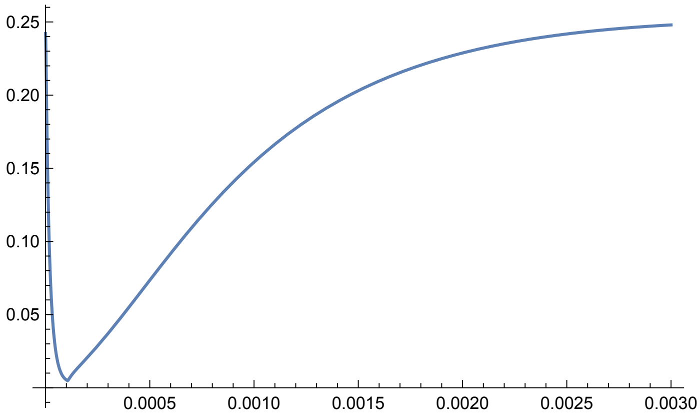
NDSolve

In[•]:=
```
myNDSolveResults = NDSolve[eq,
   {fillStateSS, ss1, ss2, ss3, ss4, ss5, ss6, ss7, sitePlugging}, {t, 0, 0.003}];
Plot[(fillStateSS[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
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]
Plot[(ss5[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss6[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(ss7[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
Plot[(sitePlugging[t] /. myNDSolveResults),
 {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
```

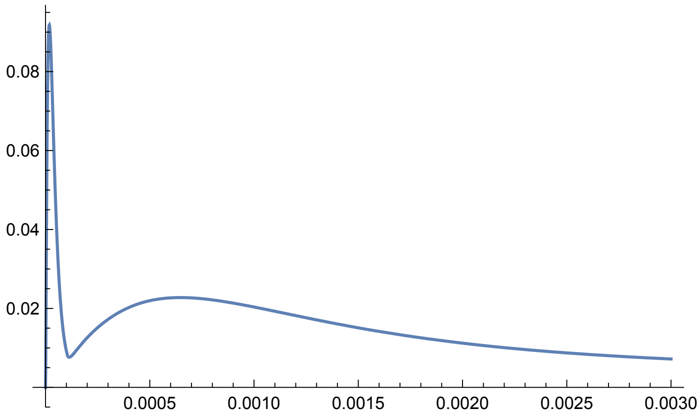
Out[•]=



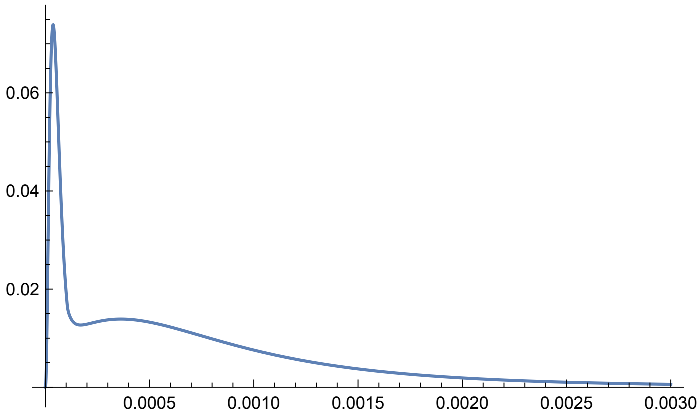
Out[•]=



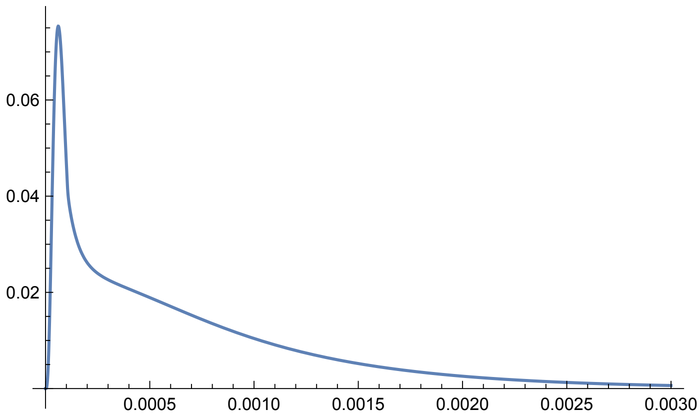
Out[•]=



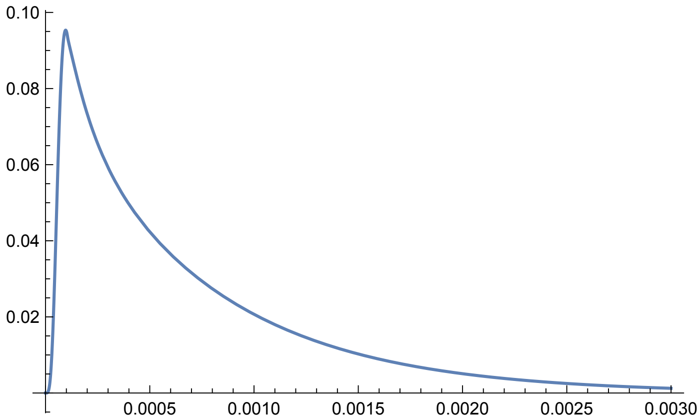
Out[•]=



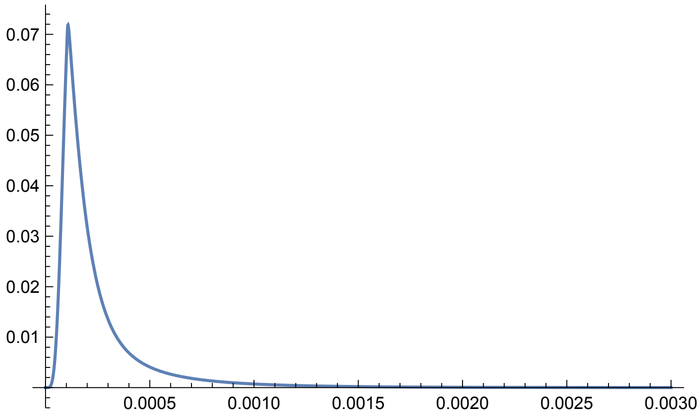
Out[•]=



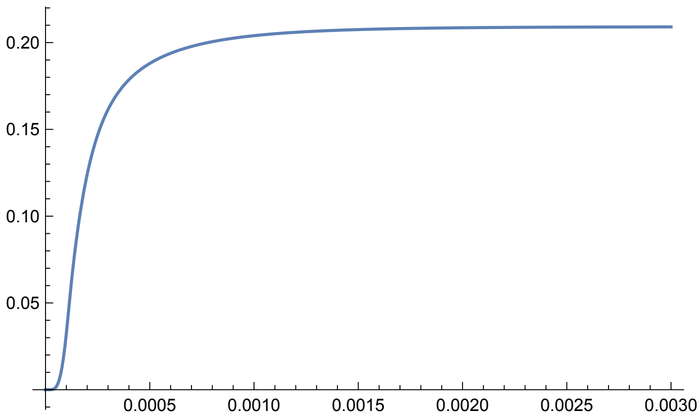
Out[ ]=



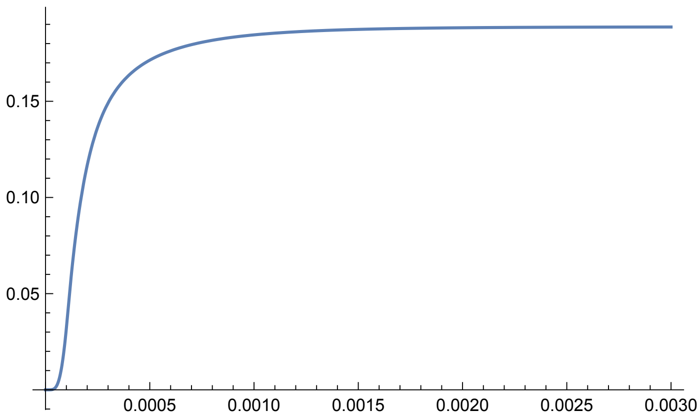
Out[ ]=



Out[ ]=



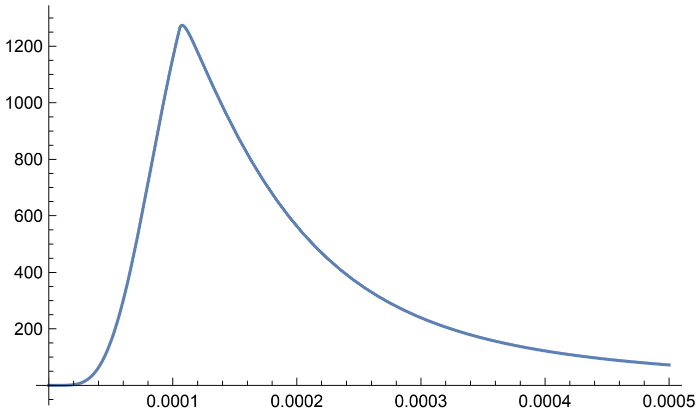
Out[ ]=



Plot EPSC

In[•]:=
```
epscLowCa = D[(ss7[t] /. myNDSolveResults), t];
Plot[(ss7[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
fillStateSSInitial = kprimScheme / kunprimScheme
kfillScheme
kunfillScheme
ss0Initial = fillStateSSInitial * kfillScheme / kunfillScheme
```

Out[•]= 7.45413

Out[•]= 8.61585

Out[•]= 0.865165

Out[•]= 166.055

Out[•]= 181.545

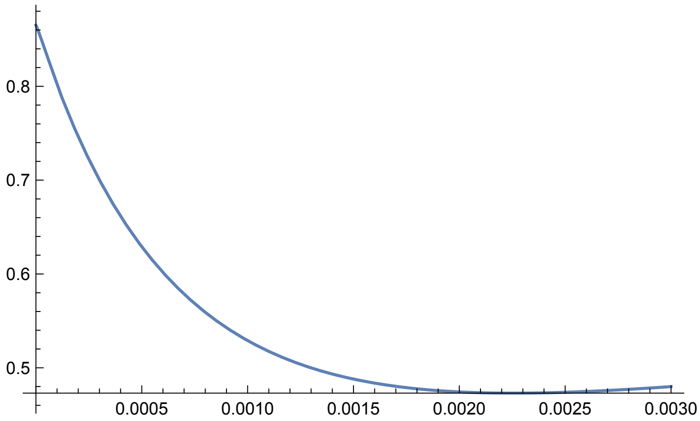
Out[•]= 0.791348

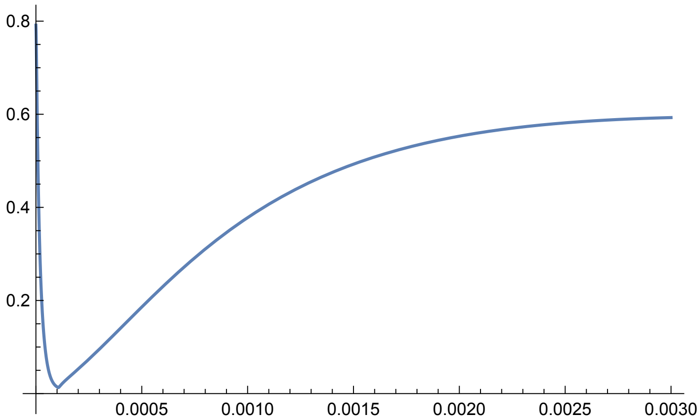
Diff eq.

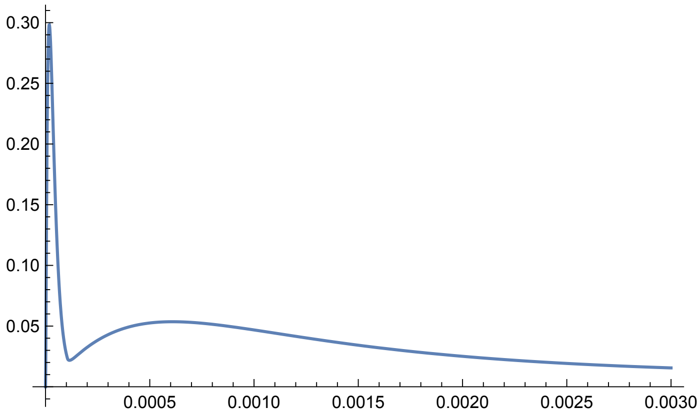
```
In[•]:= Clear[caFunc, eq];(*Clear is needed if the cell is exectued for a 2nd time
         when caFunc is already set to a value or an Interpolationfunction*)
        caFunc[t_] := interpolFunc[t];
        ss[t_] = {ss1[t], ss2[t], ss3[t], ss4[t], ss5[t], ss6[t], ss7[t]};
        eq = {ss'[t] == (mat /. repl).ss[t],
           ss[0] == {ss0Initial, 0., 0., 0., 0., 0., 0.},
           (fillStateSS'[t] == kprim - kunprim fillStateSS[t] -
               kfill fillStateSS[t] + kunfill ss1[t]) /. repl,
           fillStateSS[0] == fillStateSSInitial,
           sitePlugging'[t] ==
            (1 - sitePlugging[t]) ss7'[t] - siteClearanceTau sitePlugging[t],
           sitePlugging[0] == 0
          };
```

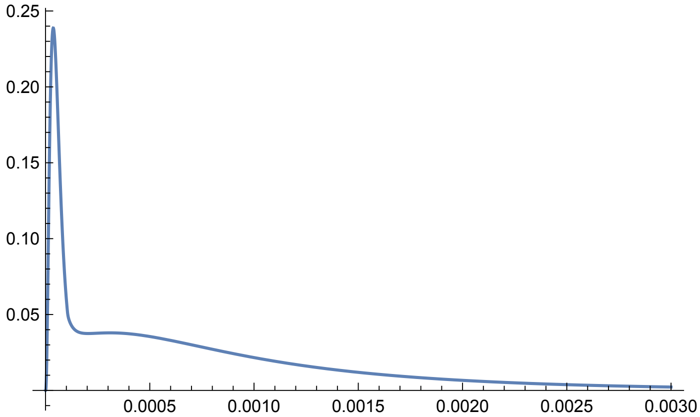
NDSolve

```
In[•]:= myNDSolveResults = NDSolve[eq,
           {fillStateSS, ss1, ss2, ss3, ss4, ss5, ss6, ss7, sitePlugging}, {t, 0, 0.003}];
        Plot[(fillStateSS[t] /. myNDSolveResults),
         {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
        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]
        Plot[(ss5[t] /. myNDSolveResults),
         {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
        Plot[(ss6[t] /. myNDSolveResults),
         {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
        Plot[(ss7[t] /. myNDSolveResults),
         {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
        Plot[(sitePlugging[t] /. myNDSolveResults),
         {t, timeStartForPLot, timeEndForPLot}, PlotRange → All]
```

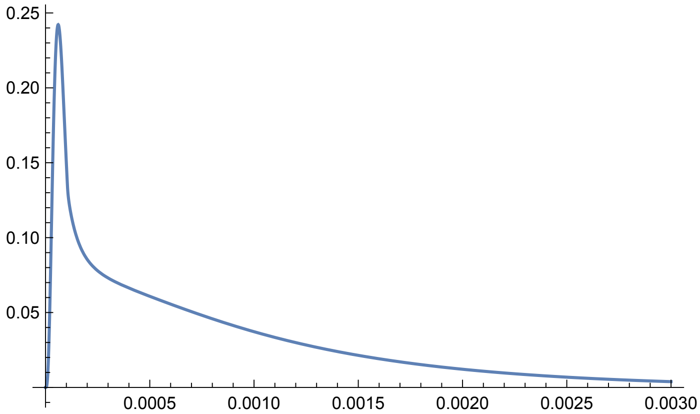
Out[•]=


Out[•]=


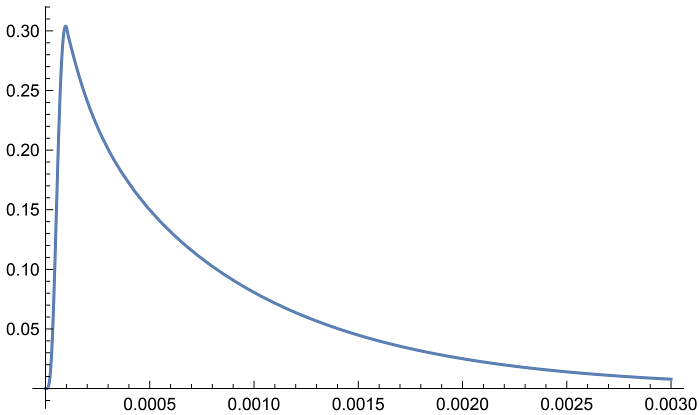
Out[•]=


Out[•]=


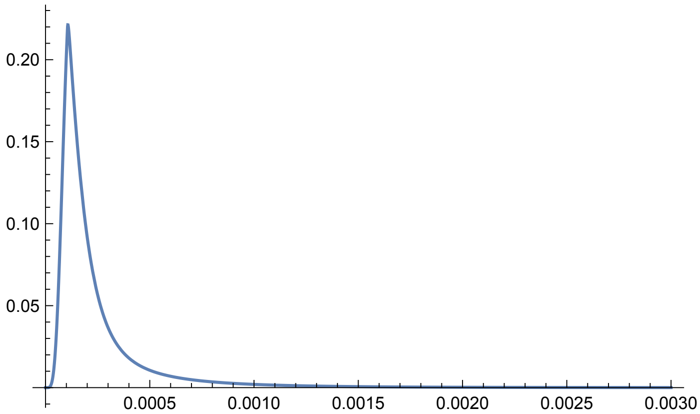
Out[ ]=



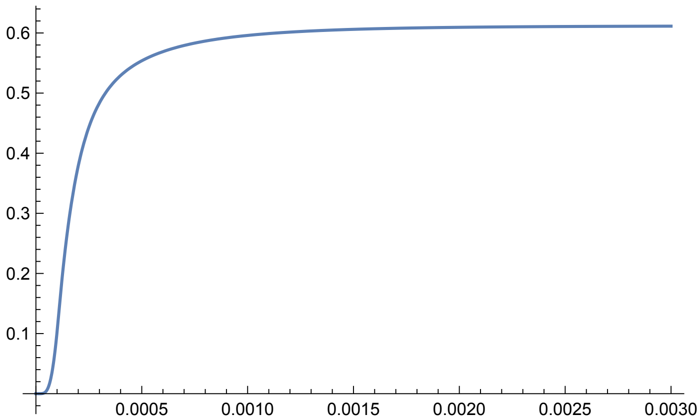
Out[ ]=



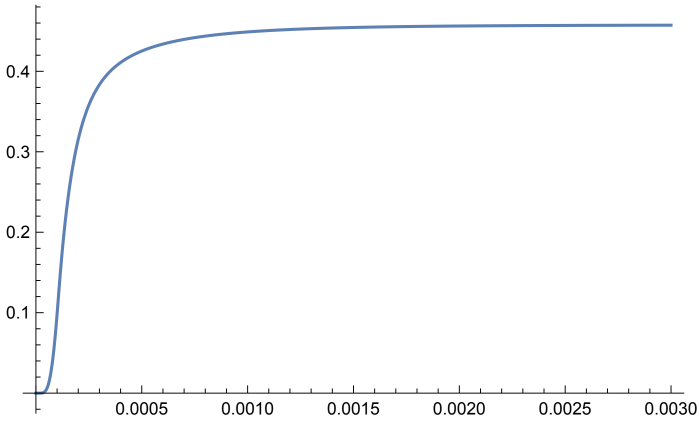
Out[ ]=



Out[ ]=



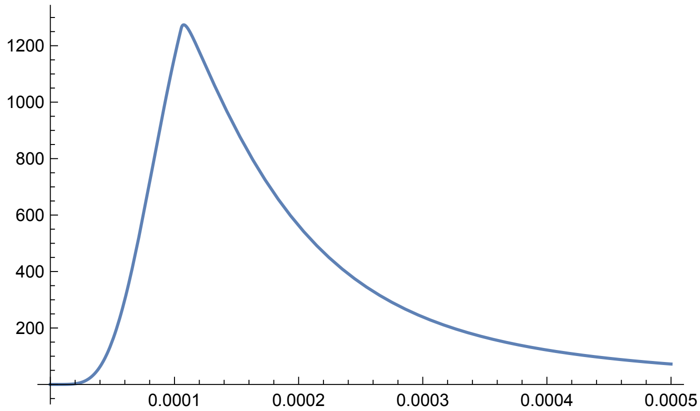
Out[ ]=



Plot EPSC

In[ ]:=
```
epscHighCa = D[(ss7[t] /. myNDSolveResults), t];
Plot[(ss7[t] /. myNDSolveResults), {t, 0, 2*^-3}, PlotRange → All];
Plot[epscLowCa, {t, 0, 0.5*^-3}, PlotRange → All]
```

Out[ ]=

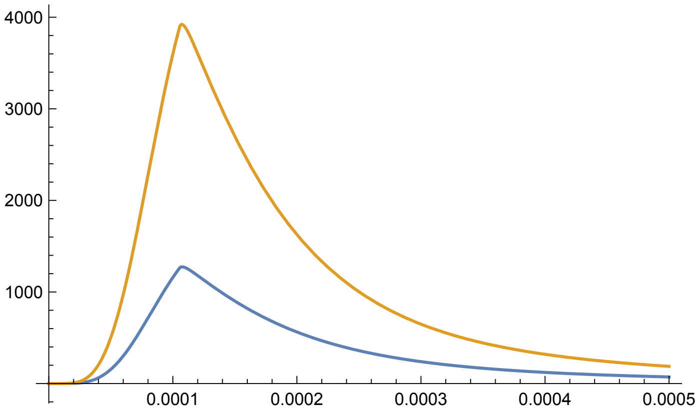


Compare

Plot both release rates

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

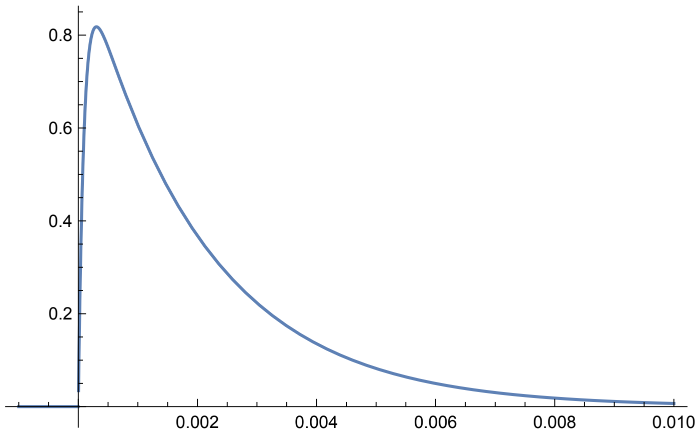
Out[∘]=



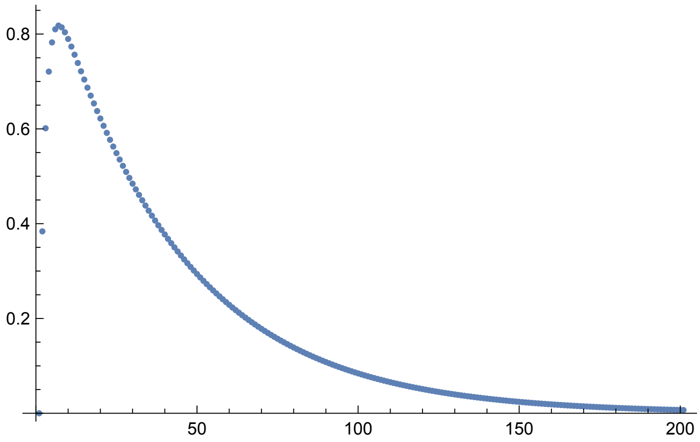
Convolution RelRate => EPSC

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]
```

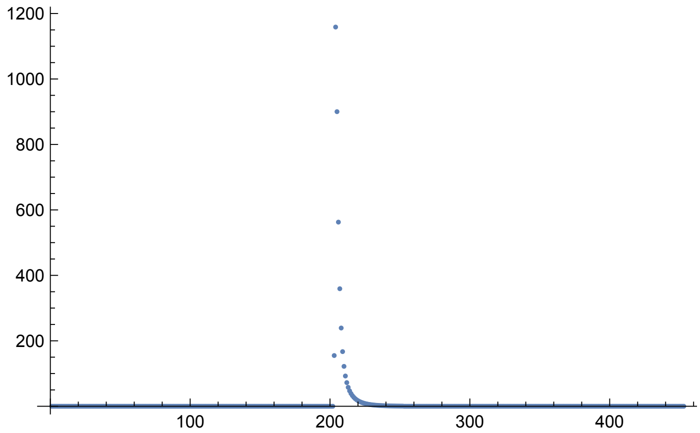
Out[∘]=



Out[∘]=



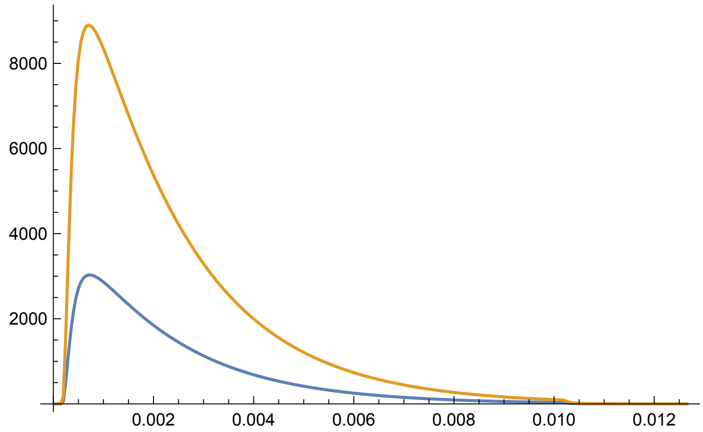
Out[∘]=



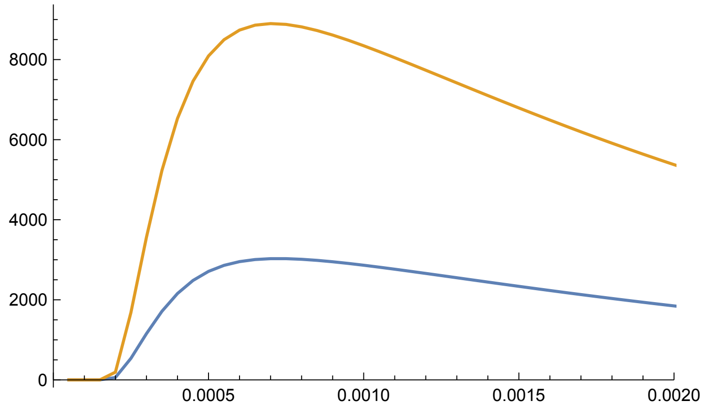
In[∘]:=

```
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[∘]=

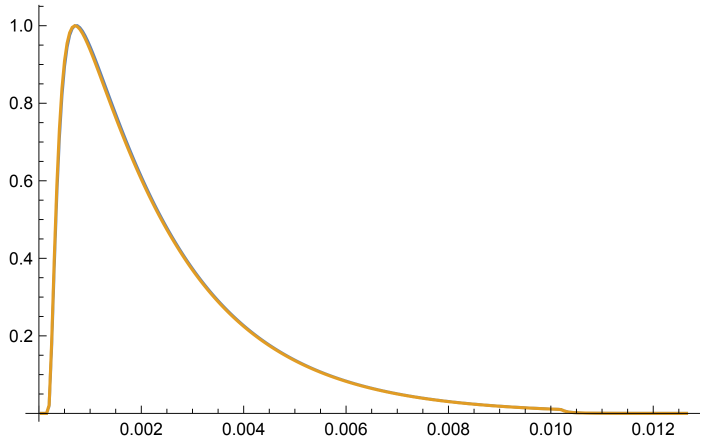


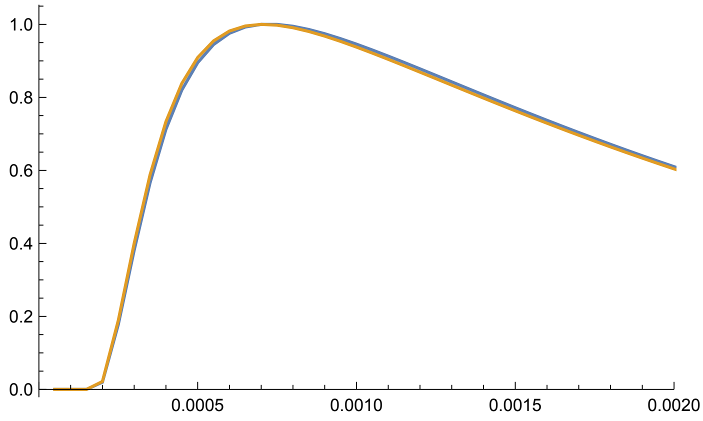
Out[∘]= 3027.59

Out[∘]= 8899.31

maxHigh/maxLow = 2.9394

Out[∘]=



Out[ ]=


Timing

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

Out[ ]= 0.252691