% Leggett model was published as a mass-transfer model (units of ug/day). In this publication, the model parameters were set up as fractional mass per day transfer coefficients. Whenever it was necessary to compare model predictions to biological data, Leggett reported additional volume estimates applied to the model to make those comparisons. In this supplement, OEHHA first provides the adjustments, based on additional information, that were incorporated into the updated (adjusted) core model for the purpose of comparing model predictions to biological data. Specifically, predictions from the adjusted core model were compared to bone, plasma and urine data. In addition, an estimate of RBC volume was needed to simplify Leggett’s module addressing nonlinear kinetics in blood.

% General physiologic parameters (Hematocrit, body weight, initial BLL, breathing rate)
HCT = 0.3822 % assumed for estimating RBC volume in saturation module (values between 35% and 45% used in simulations)
X(3) = 0.5/3 %set for initializing purposes only %lead mass transferred to RBC compartment(ug)
% Weight
BW = 73.5(6.1)(4.1)%body weight kg(leggett and Williams 1991)
WBONE = 29*(BW/1.21) % marrow-free bone weight (g) O'flaherty 1991, Brown et al 1997, O'flaherty 2000
tABLEGROWTH = (62.45-35)/years of age-related bone loss in Nie retired lead-workers
CAGELOSS = (62.45-35)/%cfb = 1.5% conversion ratio ashed bone+protein/bone ash alone (similar to estimates in Fleming et al 1999)
TAGELOSS = 0.01*years after absorption
TGBONE = 0.00695*CAGELOSS; %
% Components of the exposure model
PbAv = 0.5% ug/m3 workplace air concentration
PbAl = 0.5% ug/m3 workplace air concentration over a second interval of exposure
BR = 26/breathing rate for workers M3/day
ITC = 0.3% inhalation transfer factor accounting for the deposition and gut absorption of inhaled particles
TADJ = 0.2283*62/256565/adjustment for work time
%uptake from ingestion sources (and uptake from ambient air sources) uptake
% intake=absorption
J = 1.7611/uptake from background sources (after absorption)
J2 = 0.464/uptake from background sources after employment ends (step adjustment for drop in lead content from background sources after 40 years)
Tuptake1 = PbA*I*ITC*TADJ/uptake from workplace sources
Tuptake2 = PbA*I*ITC*TADJ/uptake from workplace sources
% timing commands (pre-exposure time, exposure time (1,2), post-exposure time)
strike = 0*yr; % number of days from start of workplace exposure to the strike
expos2 = 4*yr; %number of days from start of employment to second workplace exposure or the strike
expos = 40*yr; % number of days from start of employment to second workplace exposure or the strike; strikeref = 0*yr; %number of days from the end of employment to bone measurement
Simtime = (BBinit+expos)+expos2+strike+retire; %
tau = floor(Simtime); %computes simulation time in days
Ctime = 0; % cumulative time variable
% Cumulative blood volume at 62 years
volume = 0.74%*bloodvol = 54.2;
% RBC volume= bloodvol*HCT; % RBC volume(ug/dL) RBC assuming HCT of 38%
plasmavol = bloodvol*0.55 % assuming HCT of 45% OR bloodvol*(1-HCT)
urinevol = BW/24*1000; %urine output liters per day
% hematocrit-adjusted urine clearance of 0.015, 0.02 and 0.03 based on a hematocrit of 42% would be 0.0175, 0.023 and 0.035 based on a hematocrit of 36%. OEHHA’s urine clearance value of 0.032 based on a hematocrit of 45% would be reduced by about 20% to a value of 0.027 per blood volume (closer to that assumed by Leggett 1993).
% Concentrations
RBCCd = X(3)/RBCv; %lead concentration ug/dL in RBCs (Leggett 1993 page 609)
Sat = 270*(73/BW)*0.0382/(HCT); %lead saturation concentration ug/dL in RBCs (Leggett 1993 page 609) the value of 270 ug/dL RBC (O'flaherty et al 1996)
% and changes with changes in body weight and HCT
Thresh = 0%lead threshold concentration ug/dL in RBCs(Leggett 1993 page 609)
BLLbeg = 1*bloodvol*0.025; %set for initializing purposes only; BLL
bllinit = BLLbeg/bloodvol; %full blood lead level (ug/dL) in whole blood
% Initialize constants and vectors
%initialize proportionate distribution of 1 ug/dL of initial blood lead as measured in adulthood
plasmapd = 0.0000;
evlp = 0.0000;
rbcp = 0.0279;
plasmabp = 0.0000;
csarp = 0.0010;
carp = 0.0207;
cnep = 0.5833;
tsurfp = 0.0012;
texp = 0.0259;
texp = 0.2367;
Ltv1p = 0.0093;
Ltv2p = 0.0339;
spop = 0.0007;
\[ st1p = 0.0117; \]
\[ st2p = 0.0405; \]
\[ brp = 0.0025; \]
\[ othkidp = 0.0017; \]
\[ smintp = 0.0001; \]
\[ urpathp = 0.0023; \]
\[ uLip = 0.0002; \]
\[ LLip = 0.0004; \]

% initial body burden based on pre-employment blood lead level
BBurden = [plasmaDp evfp rbcplasmDp csurfp cexp csurfp texp csurfp Liv1p Liv2p st0p st1p st2p brp othkidp smintp urpathp uLip LLip]';
Xinit = BBurden*(bllinit*bloodvol/sum(BBurden(1:4)) - BBurden(2));

% CONSTANTS

% BLOOD AND EXTRAVASCULAR FLUID
Krbcpd = 0.1390/day; % transfer rate from RBCs to Plasma
Kevfpd = 333.3/day; % transfer rate from EVF to Plasma
Kpbpd = 0.1390/day; % transfer rate from Plasma-B to Plasma-D

% BONE
Kcspd = 0.50/day; % transfer rate from Cort surf to Plasma
Ktspd = 0.50/day; % transfer rate from Trab surf to Plasma
Kcsev = 0.50/day; % transfer rate from Cort surf to Exch vol
Ktsev = 0.50/day; % transfer rate from Trab surf to Exch vol
Kcnev = 0.00462/day; % transfer rate from Cort Exch vol to Nonexch vol
Ktnev = 0.00462/day; % transfer rate from Trab Exch vol to Nonexch vol
Kcevnev = Cexch*0.00462/day; % transfer rate from Cort Exch vol to Nonexch vol
Ktnevpd = Tboneadj*0.000493/day; % transfer rate from Trab nonexch vol to Plasma-D

% LIVER TRANSFER
Kliv1pd = 0.0312/day; % transfer rate from Liver 1 to Plasma-D
Kliv12v = 0.00693/day; % transfer rate from Liver 1 to Liver 2
Kliv2pd = 0.00190/day; % transfer rate from Liver 2 to Plasma-D

% GI TRACT TRANSFER
STOM = 1.0/day; % ingested; deposition fraction of ingested amount
Kliv1si = 0.0312/day; % transfer rate from Liver 1 to Small intestine
Kliv1si18 = 1.059/day; % transfer rate from small intestine to plasma-D
Kliv1si20 = (6.0)/day; % transfer rate from small intestine to upper lower intestine
Kliv1si21 = 1.85/day; % transfer rate from upper lower intestine to lower lower intestine

% KIDNEY/URINE PATH TRANSFER
Kurpurb = 0.1390/day; % transfer rate from Urinary path to Urinary bladder
Kcurpurb = 0.00893/day; % transfer rate from Urinary path to Upper lower intestine

% TISSUE TRANSFER
KS0pd = 2.079/day; % transfer rate from ST0 to Plasma-D
Kst1pd = 0.00416/day; % transfer rate from ST1 to Plasma-D
Kst1excr = 0.00277/day; % transfer rate from ST1 to Excreta
Kst2pd = 0.00038/day; % transfer rate from ST2 to Plasma-D

% BRAIN TRANSFER
Kbrpd = 0.00095/day; % transfer rate from Brain to Plasma-D

% DERIVED AND CONDITIONAL ADJUSTMENTS (URINE, BLOOD)

% NEW PLASMA TO RBC SETTINGS
if (RBCCD > Thresh);
SF = 0.24*(1.0 - (RBCCD - Thresh)/(Sat - Thresh))^1.5; % fraction of the initial deposition fraction in RBCs
else
SF = 1.0; %
end
FS = (1 - SF)/(1 - 0.24); % fraction of unbound lead in plasma that is multiplied to the original deposition fraction from plasma-D to other compartments
SFm = SF/0.24; % fraction the original RBC deposition is reduced

% NEW PLASMA TO URINE SETTINGS
Kpdurb = 30.00/day; % transfer rate from plasma-D to Urinary bladder
Kpdurp = 40.00/day; % transfer rate from plasma-D to Urinary path
UCL = 0.25; % urine clearance setting
UC = UCL*SFM*(Kpdurp+Kpdurb)/2000; % urinary path deposition from diffusible plasma (about 2%)
CU = (1-UC)/(1-(Kpdurp+Kpdurb)/2000); %

% INITIAL ADJUSTMENTS OF DEPOSITION OF LEAD FROM PLASMA TO OTHER COMPARTMENTS

% BLOOD AND
Kpdcb = CU*SFM*0.24/day; % transfer rate from plasma-D to Red Blood Cells
Kpdcb = CU*SFM*0.24/day; % transfer rate from plasma-D to Plasma-B

% EVF
Kpdref = CU*SFM*10.000/day; % transfer rate from plasma-D to EVF

% GI TRACT
Kpdf = CU*SFM*12.00/day; % transfer rate from plasma-D to Small intestine

% BONE
Kpdf = CU*SFM*88.96/day; % transfer rate from plasma-D to trab surf
Kpdf = CU*SFM*88.96/day; % transfer rate from plasma-D to trab surf
%LIVER
Kpd1v1 = CU*FS*80.00/day; %80/2000 = transfer rate from plasma-D to liver1

%KIDNEY/URINE
Kpdurb = UCm*FS*30.00/day; %30/2000 = transfer rate from plasma-D to Urinary bladder
Kpdurp = UCm*FS*40.00/day; %40/2000 = transfer rate from plasma-D to Urinary path
Kpdkid = CF*FS*0.40/day; %0.4/2000 = transfer rate from plasma-D to other kidney

%OTHER TISSUE
Kpdst0 = CU*FS*177.5/day; %177.5/2000 = transfer rate from plasma-D to ST0
Kpdst1 = CU*FS*10.00/day; %10/2000 = transfer rate from plasma-D to ST1
Kpdst2 = CU*FS*2.000/day; %2/2000 = transfer rate from plasma-D to ST2

%BRAIN
Kpdr = CU*FS*0.300/day; %0.3/2000 = transfer rate from plasma-D to brain

%SWEAT
Kpdw = CU*FS*7.000/day; %7/2000 = transfer rate from plasma-D to sweat

%CHECK FOR MASS BALANCE
mass_balance = [Kpdevf, Kpdrbc, Kpdpb, Kpdsi, Kpdts, Kpdcs, Kpdb];
MB = sum(mass_balance); % 2000 ug (Leggett 1993)

%DEFINE INPUT AND OUTPUT VECTORS
%INPUT
Q = zeros(tau,1); % %initialize the stimulus amplitude sequence Qk ingested and deposited intake through small intestine
P = zeros(tau,1); % %initialize the stimulus amplitude sequence Pk ingested and deposited intake through small intestine
T = ones(tau,1); % %initialize sample period vector Tk
Time = zeros(tau,1); % %initialize Time axis vector
U = zeros(length(BBurden),1); % %initialize stimulus vector U
X = Xinit; % %initialize initial body burden vector

%OUTPUT
Tissueout = zeros(tau,1);
Bloadout = zeros(tau,1);
Chonout = zeros(tau,1);
Tboneout = zeros(tau,1);
Cboneout = zeros(tau,1);
Bloodout = zeros(tau,1);
Tissueout = zeros(tau,1);

%EQUATIONS AND MATRIX (SET UP AS A CALL SCRIPT)

Defining matrix notation for each transfer coefficient just defined

%Define matrix notation for each transfer coefficient just defined
a1_2 = Kevpfd; %333.3/day %transfer rate from EVF to Plasma-D
a1_3 = Khpfpd; %0.1390/day %transfer rate from RBCs to Plasma-D
a1_4 = Khpfpd; %0.1390/day %transfer rate from Plasma-B to Plasma-D
a1_5 = Kscp; %0.5/day %transfer rate from Cort surf to Plasma-D
a1_7 = Kncpvpd; %0.0000822/day %transfer rate from Cort nonexch vol to Plasma-D
a1_8 = Kscp; %0.5/day %transfer rate from Trab surf to Plasma-D
a1_10 = Kncpvpd; %0.004933/day %transfer rate from Trab nonexch vol to Plasma-D
a1_11 = Klv1fpd; %0.013/day %transfer rate from Liver 1 to Plasma-D
a1_12 = Klv2fpd; %0.00196/day %transfer rate from Liver 2 to Plasma-D
a1_13 = Ksfpd; %0.7/day %transfer rate from ST0 to Plasma-D
a1_14 = Ksfpd; %0.04/day %transfer rate from ST1 to Plasma-D
a1_15 = Ksf2pd; %0.00059/day %transfer rate from ST2 to Plasma-D
a1_16 = Ksfpd; %0.00095/day %transfer rate from Brain to Plasma-D
a1_17 = Kscp; %0.01/day %transfer rate from Other kidney to Plasma-D
a1_18 = Kdpfpd; %100/day %transfer rate from plasma-D to EVF
a1_19 = Kdpfpd; %100/day %transfer rate from plasma-D to Red Blood Cells
a1_20 = Kscp; %0.8/2000 = transfer rate from plasma-D to other kidney
a1_21 = Kscp; %0.8/2000 = transfer rate from plasma-D to ST0
a1_22 = Kscp; %0.8/2000 = transfer rate from plasma-D to ST1
a1_23 = Kscp; %0.8/2000 = transfer rate from plasma-D to ST2
a1_24 = Kscp; %0.8/2000 = transfer rate from plasma-D to Small intestine
a1_25 = Kscp; %0.8/2000 = transfer rate from plasma-D to Trab surf
a1_26 = Kscp; %0.8/2000 = transfer rate from plasma-D to Other kidney

%Transfer rates out of each compartment (should be identical to minus side of differential equations)
a1_1 = a1_2 + a1_3 + a1_4 + a1_5 + a1_6 + a1_7 + a1_8 + a1_9; % define rate into each compartment
a2_2 = a1_1; a3_3 = a1_1; a4_4 = a1_1; a5_5 = a1_1; a6_6 = a1_1; a7_7 = a1_1; a8_8 = a1_1; a9_9 = a1_1; a10_10 = a1_1;
% Description of special functions (expm, for, if, else, end, linest, tol)
% User's manual to include the following definitions and examples

plot(Time/yr,Bloodout/bloodvol,'r-';

% %
% %

PHI = expm(A25); % Assume time intervals do not change

% Leggett 1993). proportion of body burden in each of 21 compartments after 25 years of constant exposure (similar to composite tissue values presented in Table 3 of % Leggett 1993). Intake represents amount ingested that enters the small intestine

% Routine for simulations that appear in the lead report 2013

for k = BBinit+1:BBinit+expos+1;% removal from workplace exposure to background
Q(k,1) = J;%inhaled intake;
end

% %
% %

% for k = BBinit+1:BBinit+expos+1;% removal from workplace exposure to background
Q(k,1) = (Tuptake2+J);%inhaled intake

% %
% %

% User's manual to include the following definitions and examples
% Description of special functions (expm, for, if, else, end, linest, tol)
Routine for solving matching problems (ASARCO, Williams, Griffin, Table S-1, Table S-2)
Routines for generating Figure 1, 2, 3, A-1, A-3, A-4, Table A-3
Routine for collecting simulated data
Routine for summarizing simulated data
Routine for importing and exporting data from Excel