Supplementary Information
A Computational Spatial Whole-Cell Model for Hepatitis B Viral Infection and Drug Interactions

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Table S1. Diffusion coefficients of species involved in the reactions

Species	Diffusion coeff.	Compartment	Reference
$capsid_{DNA}$	7.4×10^{-12}	Cytoplasm/ER	[1]
$capsid_{DNA}$	16×10^{-12}	NPC	[1]
$capsid_{empty}$	7.4×10^{-12}	Cytoplasm/ER	[1]
$capsid_{empty}$	16×10^{-12}	NPC	[1]
$capsid_{RNA}$	7.4×10^{-12}	Cytoplasm/ER	[1]
$capsid_{RNA}$	16×10^{-12}	NPC	[1]
$viral_{pol}$	22×10^{-12}	Cytoplasm	Equals to L (assumption)
RNA_{pol}	22×10^{-12}	Nucleus	Equals to $viral_{pol}$ (assumption)
$cccDNA.RNA_{pol}$	22×10^{-12}	Nucleus	Equals to $viral_{pol}$ (assumption)
rcDNA	0.07×10^{-12}	NPC	[2]
rcDNA	0.61×10^{-12}	Nucleus	[2]
cccDNA	0.61×10^{-12}	Nucleus	[2]
LSmRNA	0.61×10^{-12}	Nucleus	[2]
pgRNA	0.61×10^{-12}	Nucleus	[2]
SmRNA	0.61×10^{-12}	Nucleus	[2]
XmRNA	$0.61\times s10^{-12}$	Nucleus	[2]

preCmRNA	0.61×10^{-12}	Nucleus	[2]
LSmRNA	2.24×10^{-12}	Cytoplasm	[2]
pgRNA	2.24×10^{-12}	Cytoplasm	[2]
SmRNA	2.24×10^{-12}	Cytoplasm	[2]
XmRNA	2.24×10^{-12}	Cytoplasm	[2]
preCmRNA	2.24×10^{-12}	Cytoplasm	[2]
LSmRNA	0.07×10^{-12}	NPC	[2]
pgRNA	0.07×10^{-12}	NPC	[2]
SmRNA	0.07×10^{-12}	NPC	[2]
XmRNA	0.07×10^{-12}	NPC	[2]
preCmRNA	0.07×10^{-12}	NPC	[2]
preC	22×10^{-12}	Cytoplasm	Equals to L (assumption)
S	22×10^{-12}	Cytoplasm/ER	Equals to L (assumption)
M	22×10^{-12}	Cytoplasm/ER	Equals to L (assumption)
L	22×10^{-12}	Cytoplasm/ER	scaled diffusion coefficient of GFP[3] based on [4]
X	22×10^{-12}	Cytoplasm	Equals to L (assumption)
interm	9.7×10^{-12}	Cytoplasm	ref [1] scaled based on [4]
RNP	2.24×10^{-12}	Cytoplasm	Equals to RNAs in cytoplasm
$capsid_{DNA}.L(1,\ldots20)$	22×10^{-12}	ER	Equals to L (assumption)
$capsid_{RNA}.L(1,\ldots20)$	22×10^{-12}	ER	Equals to L (assumption)
$capsid_{empty}.L(1,\ldots20)$	22×10^{-12}	ER	Equals to L (assumption)

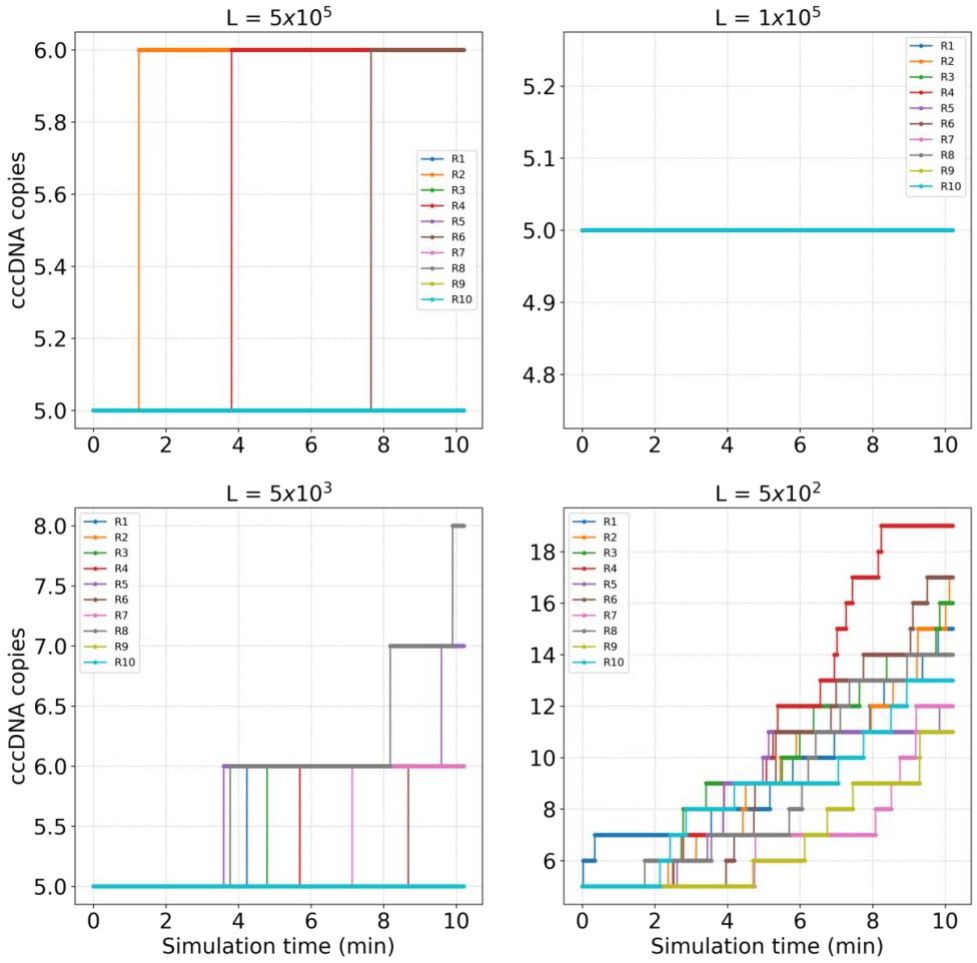

Figure S1. Trajectory of cccDNA copy numbers as a function of simulation time for various L protein abundance for all simulation replicas (R1 to R10). As the copy number of L proteins reduces the dominant pathway switches from secretion to amplification and the cccDNA copy numbers increases. Therefore, for L=5x102 the cccDNA copy number increases such that it reaches an average value of ~ 15 within 10 minutes of simulation time.

Figure S2 shows how the 3D distribution and counts of capsids and cccDNA species change during the simulation time: At the start of a simulation (Figure S2-A), capsids are randomly distributed in the cytoplasm, with 5 cccDNA already present in the nucleus; At the end of the 10 mins of simulation (Figure S2-B), the progress of the infection is shown by an increase in the number of cccDNA. The majority of the mature and empty capsids are bound to the NPCs to be disassembled.

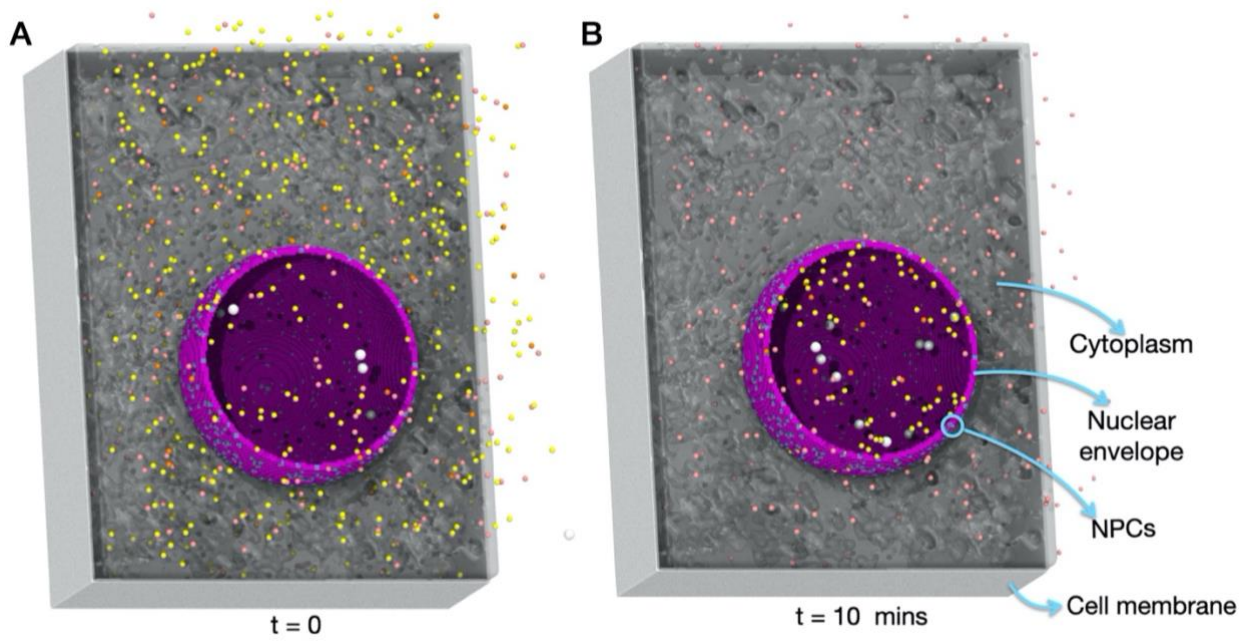

Figure S2: (A) the empty (yellow), RNA-containing (pink) and mature (orange) capsids are randomly distributed in the cytoplasm (shaded grey region), with about 5 cccDNA (white) already present in the nucleus. (B) After 10 mins of simulation, the number of cccDNA increases and some of the capsids are bound to the NPCs before being disassembled.

Table S2. Reactions describing the degradation of different species that were included in the kinetic model

Degradation reactions	Rate	Unit	Compartment
rcDNA → 0	1.60×10^{-7}	s^{-1}	Nucleus
cccDNA→ 0	1.60×10^{-7}	s^{-1}	Nucleus
pgRNA→ 0	3.8×10^{-5}	s^{-1}	Cytoplasm
LSmRNA→ 0	6.4×10^{-5}	s^{-1}	Cytoplasm
SmRNA→ 0	6.4×10^{-5}	s^{-1}	Cytoplasm
XmRNA→ 0	1.9×10^{-4}	s^{-1}	Cytoplasm
preCmRNA→ 0	3.8×10^{-5}	s^{-1}	Cytoplasm
L→ 0	2.9×10^{-4}	s^{-1}	Cytoplasm
M→ 0	2.9×10^{-4}	s^{-1}	Cytoplasm
S→ 0	2.9×10^{-4}	s^{-1}	Cytoplasm
dimer→ 0	2.9×10^{-4}	s^{-1}	Cytoplasm
$viral_{pol}$→ 0	2.9×10^{-4}	s^{-1}	Cytoplasm

References

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