Predicted UV-C Sensitivity of Human and Non-human Vertebrate (+) ssRNA Viruses

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Abstract

Epidemic and pandemic infectious diseases caused by RNA viruses constitute a significant hazard to human and animal health. Disinfection is an essential aspect of infection prevention and control measures. In this study, we estimated UV-C sensitivity of 83 human and veterinary pathogenic (+) ssRNA viruses by developed pyrimidine dinucleotide frequency-based genomic model. The data showed that the avian infectious bronchitis virus (genus: γ-coronavirus) with an estimated D_{90} value of 17.8 J/m^2 was highly UV sensitive, whereas Salivirus NG-J1 (genus: salivirus) with a D_{90} value of 346.4 J/m^2 was highly UV resistant. Overall, the trend of UV-C sensitivity of (+) ssRNA virus families followed as Coronaviridae < Flaviviridae < Togadoviridae < Arteriviridae, Matonaviridae, Astroviridae < Caciviridae < Picornaviridae < Nodaviridae < Herpeviridae. The results revealed that the enveloped viral families (Coronaviridae, Flaviviridae, Togadoviridae Arteriviridae, and Matonaviridae) are more UV-C sensitive than other non-enveloped families. Further validation of the model estimated UV sensitivity with literature available experimental data showed good agreement of predicted values. The estimates presented here could make it possible to reasonably predict UV-C disinfection efficiency of human and veterinary pathogenic viruses, which need specific biosafety requirements and/or difficult to cultivate in lab conditions.

Introduction

Ten virus families whose members are pathogenic to humans and animals possess positive-sense (+) single-stranded (ss) RNA genomes. The families Astroviridae, Caliciviridae, Picornaviridae, Nodaviridae and Hepeviridae are characterized by non-enveloped, whereas other families Coronaviridae, Flaviviridae, Togaviridae, Arteriviridae and Matonaviridae have enveloped capsids (https://viralzone.expasy.org/294). The spread and persistence of these pathogenic viruses in diverse environments, such as hospitals, residential, public areas, pet care facilities, animal sheds, animal husbandry, etc., emphasize developing efficient decontamination processes to control epidemic and pandemic outbreaks (Cozad and Jones, 2003). Conventional chemical decontamination procedures are time-consuming, labor and resource-intensive, prone to high degrees of human error, and not applicable to air disinfection (McGinn et al., 2020). Alternative physical disinfection methods, such as germicidal ultraviolet light treatment, have gained importance due to their potential to disinfect air (Reed, 2010) and overwhelm the limitations mentioned above (McGinn et al., 2020).

The germicidal ultraviolet light disinfection method uses UV-C light to disinfect microorganisms by damaging the nucleic acids, causing them to be unable to replicate and alters vital cellular functions (Patras et al., 2020). It is well known that the disinfection level of microorganisms by UV-C light depends on their UV susceptibility, defined as D90 or D10 (dose for 90% inactivation or 10% survival) expressed as J/m2 or mJ/cm2 (Patras et al., 2020). UV-C sensitivity of a wide range of microorganisms has been reported, including vegetative and spore forms of bacteria, yeast, fungi, protozoa, algae, and viruses (Malayeri et al., 2016; Gopisetty et al., 2019; Pendyala et al., 2019, 2020a, 2021). However, the UV-C sensitivity data for many (> 80 %) human and animal pathogenic viruses is not available due to the prerequisite for biosafety level

(BSL)-3 containment and the need for specifically trained skilled labor and cultivation limitations in the laboratory environment (Pendyala et al., 2020b). Acquiring the knowledge of UV susceptibility of target viruses is essential to deliver sufficient doses for efficient decontamination of the environment.

Our earlier study developed and validated a genome-sequence-based mathematical model (r^2 = 0.90) to predict the UV sensitivity and identify potential SARS-CoV-2 and human norovirus surrogates (Pendyala et al., 2020b). This model was developed based on the pyrimidine dinucleotides frequency (PyNNF) of genome sequence, that effects the formation of pyrimidine dimers and 6-4 photoproducts and thereby UV susceptibility. The objective of the study was to estimate the UV-C sensitivity of 83 human and veterinary pathogenic viruses, belongs to all the families of (+) ssRNA viruses (Coronaviridae, Flaviviridae, Togadoviridae, Arteriviridae, Matonaviridae, Astroviridae, Caciviridae, Picornaviridae, Nodaviridae, Herpeviridae) by using developed pyrimidine dinucleotide frequency based mathematical model. Further validation of the model-predicted data by comparison with literature available experimental data.

Materials and Methods

Collection and determination of genomic parameters; genome size, and calculation of pyrimidine dinucleotide frequency value (PyNNFV)

We collected the genomic sequence of (+) ssRNA viruses belonging to families of *Flaviviridae, Picornaviridae, Arteriviridae, Coronaviridae, Togaviridae, Retroviridae, Astroviridae, Calciviridae, Nodaviridae, Hepeviridae,* and *Matonaviridae*. The size and nucleotide sequences of genomes used in this study were directly obtained from the available NCBI genome database (Table 1-5). A novel R code was developed to count the PyNNs by the exclusive method (each pyrimidine considered in one PyNN combination only) in the order of TT > TC > CT > CC and

considered 100% probability when PyNN are flanked by pyrimidine on both sides and 50% probability for PyNN flanked by purine on either side. Further PyNNFV values were calculated by the following equation (Pendyala et al., 2020b).

$$\text{PyNNFV} = \frac{(\text{TT }\%)\,(\text{TC }\%)\,(\text{CT }\%)\,(\text{CC }\%)}{\text{Genome bp}} \qquad \text{Eqn 1}$$

Estimation of UV-C sensitivity (D_{90}) values

Calculated PyNNF values were used to estimate the UV-C sensitivity of viruses using the reported linear regression model with $r^2 = 0.90$ (Eqn 2) from our previous study (Pendyala et al., 2020b).

$$y = (19984 \times x) + 10.409 \qquad \text{Eqn 2}$$

Results and discussion

Table 1-5 depicts the selected viruses of various families of (+) ssRNA pathogenic viruses, and genus, host, diseases caused, NCBI GenBank ID, genome size, and estimated PyNNFV and D_{90} values. The genome size values ranged from 4528 bp to 30033 bp, and PyNNFV varied from 0.000371 to 0.016812. Graphical representation of data shows the estimated D_{90} values of different virus families were in the order of Coronaviridae < Flaviviridae < Togadoviridae < Arteriviridae, Matonaviridae, Astroviridae < Caciviridae < Picornaviridae < Nodaviridae < Hepeviridae (Figure 1). The results revealed that the enveloped virus families (Coronaviridae, Flaviviridae, Togadoviridae Arteriviridae and Matonaviridae) are more UV-C sensitive than other non-enveloped families.

Elucidation of the variability of calculated UV-C sensitivity (D_{90}) at the genus level

Flaviviridae. The estimated UV-C sensitivity of different genera of the flaviviridae family was shown in Table 1. The data shows the genus pestivirus had higher UV-C sensitivity with D_{90} of

26.3 J/m^2 than flavivirus (29.1 - 40.7 J/m^2), pegivirus (90.8 J/m^2), and hepacivirus (107.5 - 110 J/m^2).

Picornaviridae. Table 2 shows the predicted UV-C sensitivity of various genera of the picornaviviridae family. Bluegill picornavirus belongs to limnipivirus, was predicted to be highly UV sensitive with D_{90} of 33.2 J/m^2, whereas salivirus NG-J1 was highly UV resistant (346.4 J/m^2). The results revealed that the D_{90} values of major genus enterovirus and genera of hepatovirus, tremovirus, sapelovirus, avihepatovirus, avisvirus, and cosavirus was in the range of 47.9 – 88 J/m^2. Medium UV sensitivity (100.9 – 125.7 J/m^2) was observed with genera teschovirus, erbovirus, rosavirus, dicipivirus, and cardiovirus. Suboptimal UV resistance with D_{90} 171.9 to 267.7 J/m^2 was noticed with genera megrivirus, sicinivirus, kobuvirus, and sakobuvirus.

Arteriviridae and Coronaviridae. The families arteriviridae and coronaviridae are assigned to the order Nidovirales. The data show the coronaviridae family viruses were more UV sensitive (D_{90} 17.8 – 28.1 J/m^2) than arteriviridae viruses (D_{90} 58.8 – 81.2 J/m^2) (Table 3). In coronaviridae, genus γ-coronavirus was noticed to be more UV sensitive (D_{90} 17.8 J/m^2) and β-coronavirus (MERS coronavirus) was more UV resistant (D_{90} 28.1 J/m^2). The λ-arterivirus and δ-arterivirus were identified as more UV sensitive and UV resistant genera in arteriviridae.

Togadoviridae and Matonaviridae. In this family, the genus alphavirus includes mosquito-borne human and veterinary pathogenic viruses. The model predicted UV D_{90} values were between 20.9 – 40.9 J/m^2, minimum with O'nyong-nyong virus and maximum with Venezuelan equine encephalitis virus (Table 4). Rubella virus belongs to the genus rubivirus, and family matonaviridae had predicted D_{90} value of 65.5 J/m^2.

Calciviridae. The estimated D_{90} of calciviridae family ranged from 65.7 – 98.6 J/m^2, and the genera lagovirus and nebovirus predicted with minimum and maximum D_{90} values (Table 5). The

model predicted D_{90} values of human norovirus (HNoV) groups GI, GII and GIV were 69.1, 89.0, and 77.6 J/m^2, respectively.

Nodaviridae. This family viruses comprised of are pathogenic to fish, comprised of two genera: α-nodavirus and β-nodavirus. The D_{90} data show the high resistance to UV (D_{90} varies from 118.4 – 156.9 J/m^2), α-nodavirus more sensitive than β-nodavirus (Table 5).

Astroviridae. The estimated UV sensitivity of two genera, mamastrovirus and avastrovirus were 58.5 and 59.3 J/m^2, respectively (Table 5).

Hepeviridae. Hepatitis E virus belongs to genus hepevirus had predicted D_{90} value of 247.2 J/m^2, while other genus piscihepevirus (causes disease in fish) with lower D_{90} of 133.3 J/m^2 (Table 5).

Though the developed genomic sequence-based parameter (PyNNFV) model may be sufficient to estimate UV-C susceptibility of viruses in many scenarios, the generation of more experimental data at specific regions (where the model does not have enough empirical data) is required to improve the accuracy of our predicted D_{90} values. In conclusion, our model predicted D90 values could be helpful to develop an efficient UV-C treatment process to achieve the target disinfection level of specific (+) ssRNA viruses where experimental UV-C sensitivity data is not available or feasible.

Note: There are no conflicts to declare

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Figure legends

Figure 1: Predicted UV_{254} D_{90} values of (+) ssRNA vertebrate virus families

Table 1: Genomic model predicted UV-C (254 nm) sensitivity (D_{90}) of Flaviviridae family viruses.

Virus	Genus	Host	Disease	NCBI #	Genome (bp)	PyNNFV	D_{90} (J/m^2)
Bovine viral diarrhea virus 1	Pestivirus	Mammals	Hemorrhagic syndromes, abortion, fatal mucosal disease	NC_001461.1	12573	0.000793	26.3
Usutu virus	Flavivirus	Human, birds, mosquitoes	Encephalitis	NC_006551.1	11066	0.001518	40.7
Murray Valley encephalitis virus	Flavivirus	Human, mosquitoes	Encephalitis	NC_000943.1	11014	0.001139	33.2
Japanese encephalitis virus	Flavivirus	Human, horses, birds, mosquitoes	Encephalitis	NC_001437.1	10976	0.001262	35.6
West Nile virus	Flavivirus	Human, birds, ticks, mosquitoes	Encephalitis	NC_001563.2	10962	0.001374	37.9
Langat virus	Flavivirus	Human, ticks	Encephalitis	NC_003690.1	10943	0.001078	31.9
Saint Louis encephalitis virus	Flavivirus	Human, birds, mosquitoes	Encephalitis	NC_007580.2	10940	0.001004	30.5
Louping ill virus	Flavivirus	Human, mammals, ticks	Encephalitis	NC_001809.1	10871	0.001117	32.7
Tick-borne encephalitis virus	Flavivirus	Humans, small rrodents, ticks	Encephalitis	DQ401140.3	11097	0.001141	33.2
Yellow fever virus	Flavivirus	Human, monkeys, mosquitoes	Hemorrhagic fever	NC_002031.1	10862	0.001489	40.2
Powassan virus	Flavivirus	Human, ticks	Encephalitis	NC_003687.1	10839	0.001205	34.5
Zika virus	Flavivirus	Human, monkeys, mosquitoes	Fever, joint pain, rash	NC_012532.1	10794	0.001194	34.3
Dengue virus 1	Flavivirus	Human, mosquitoes	Hemorrhagic fever	NC_001477.1	10735	0.001015	30.7
Dengue virus 2	Flavivirus	Human, mosquitoes	Hemorrhagic fever	NC_001474.2	10723	0.000935	29.1
Hepatitis C virus 2	Hepacivirus	Human	Hepatitis	NC_009823.1	9711	0.004857	107.5
Hepatitis C virus 1	Hepacivirus	Human	Hepatitis	NC_004102.1	9646	0.004986	110.0
GB virus C/Hepatitis G virus	Pegivirus	Human	None	NC_001710.1	9392	0.004022	90.8

Table 2: Genomic model predicted UV-C (254 nm) sensitivity (D_{90}) of Picornaviridae family viruses.

Virus	Genus	Host	Disease	NCBI #	Genome (bp)	PyNNFV	D_{90} (J/m^2)
Sicinivirus 1	Sicinivirus	Chicken, birds	-	NC_023861.1	9276	0.010280	215.8
Turkey hepatitis virus	Megrivirus	Turkey	Hepatitis	NC_021201.1	9075	0.008082	171.9
Rosavirus 2	Rosavirus	Human	-	NC_024070.1	8931	0.005468	119.7
Equine rhinitis B virus 1	Erbovirus	Horse	-	NC_003983.1	8828	0.004771	105.7
Canine picodicistrovirus	Dicipivirus	Dog	-	NC_021178.1	8785	0.005690	124.1
Aichi virus	Kobuvirus	Human	Gastroenteritis	NC_001918.1	8251	0.012327	256.7
Bluegill picornavirus	Limnipivirus	Fish	-	NC_018506.1	8050	0.001090	32.2
Salivirus NG-J1	Salivirus	Human	Gastroenteritis	NC_012957.1	7982	0.016812	346.4
Encephalomyocarditis virus	Cardiovirus	Human, mouse, rat, pig	Encephalitis	NC_001479.1	7835	0.005768	125.7
Human cosavirus	Cosavirus	Human	-	NC_023984.1	7802	0.003883	88.0
Duck hepatitis A virus	Avihepato virus	Ducks and geese	Fatal hepatitis	NC_008250.2	7711	0.003003	70.4
Feline sakobuvirus A	Sakobuvirus	Cat	-	NC_022802.1	7507	0.012626	262.7
Porcine sapelovirus 1	Sapelovirus	Pig	-	NC_003987.1	7491	0.002167	53.7
Hepatitis A virus	Hepatoviruus	Human	Hepatitis	KP879217.1	7476	0.002093	52.2 (51)
Poliovirus	Enterovirus	Human	Poliomyelitis	NC_002058.3	7440	0.002626	62.9 (73)
Coxsackievirus	Enterovirus	Human	Meningitis, myo-carditis, paralysis	KX595291.1	7410	0.003138	73.1 (79)
Turkey avisivirus	Avisivirus	Turkey	-	KC614703.1	7373	0.003120	72.8
Human enterovirus 68	Enterovirus	Human	Diarrhea, neurological disorder	NC_038308.1	7367	0.001877	47.9
Human parecho virus	Enterovirus	Human	Common cold	NC_001897.1	7348	0.002096	52.5 (73)
Human rhinovirus 14	Enterovirus	Human	Respiratoty	NC_001490.1	7212	0.002110	52.6
Porcine teschovirus 1	Teschovirus	Pig	Teschen disease	NC_003985.1	7117	0.004529	100.9
Human rhinovirus C	Enterovirus	Human	Respiratoty	NC_009996.1	7099	0.002872	67.8
AEV	Tremovirus	Birds	Reduced hatching. Tremors and/or ataxia.	NC_003990.1	7055	0.002126	52.9
Swine pasivirus 1	Pasivirus	Pig	-	NC_018226.1	6916	0.003108	72.5

Notes: D_{90} in parenthesis refers literature experimental values (Pendyala et al., 2020); AEV – Avian encephalomyelitis virus)

Table 3: Genomic model predicted UV-C (254 nm) sensitivity (D_{90}) of Arteriviridae and Coronaviridae family viruses.

Virus	**Genus**	**Host**	**Disease**	**NCBI #**	**Genome (bp)**	**PyNNFV**	**D_{90} (J/m^2)**
Equine arteritis virus	α-arterivirus	Horse	vascular lesions, fever, edema, abortion	NC_002532.2	12704	0.003112	72.6
Lelystad virus	β-arterivirus	Pig	Abortions and respiratory disease	M96262.2	15111	0.003014	70.6
Simian hemorrhagic fever virus	δ-arterivirus	Monkey	Fever, edema, dehydration, hemorrhages, death (almost 100%)	NC_003092.2	15717	0.003541	81.2
Forest pouched giant rat arterivirus	λ-arterivirus	Rat	-	NC_026439.1	14953	0.002423	58.8
Wobbly possum disease virus	κ-arterivirus	Brushtail possum	-	NC_026811.2	12917	0.002640	63.2
Human coronavirus 229E	α-coronavirus	Human	Respiratoty	NC_002645.1	27317	0.000489	20.2
SARS coronavirus 1	β-coronavirus	Human, bats, palm civet	Respiratoty	NC_004718.3	29751	0.000674	23.9
SARS coronavirus 2	β-coronavirus	Human, bats, pangolin?	Covid-19	MT192772.1	29891	0.000555	21.5
MERS coronavirus	β-coronavirus	Human, Tomb bat	Respiratoty	MH734115.1	30033	0.000883	28.1
Thrush coronavirus HKU12-600	δ-coronavirus	grey-backed Thrush	Respiratory	NC_011549.1	26396	0.000690	24.2
Avian infectious bronchitis virus	γ-coronavirus	Chicken and turkey	Respiratoty	NC_001451.1	27608	0.000371	17.8
White bream virus (Toro virinae (subfamily)	Bafinivirus	Fish	Hemorrhagic liver with necrotic areas, splenomegaly, enteritis	NC_008516.1	26660	0.000954	29.5
Breda virus (Toro-virinae (subfamily)	Torovirus,	Human, cattle, pig, horse	Gastroenteritis	NC_007447.1	28475	0.000517	20.7

Table 4: Genomic model predicted UV-C (254 nm) sensitivity (D_{90}) of Togaviridaeae and Matonaviridae family viruses.

Virus	Genus	Host	Disease	NCBI #	Genome (bp)	PyNNFV	D_{90} (J/m^2)
O'nyong-nyong virus	Alphavirus	Human, mosquitoes	Fever, joint pain	NC_001512.1	11835	0.000930	29.0
Chikungunya virus	Alphavirus	Human, monkeys, mosquitoes	Fever, joint pain	NC_004162.2	11826	0.001108	32.6
Eastern equine encephalitis virus	Alphavirus	Human, birds, mosquitoes	Encephalitis	NC_003899.1	11675	0.001470	39.8
Ross River virus	Alphavirus	Human, mosquitoes, marsupials,	Fever, joint pain	NC_001544.1	11657	0.001187	34.1
Barmah Forest virus	Alphavirus	Human, marsupials, mosquitoes	Fever, joint pain	NC_001786.1	11488	0.001194	34.3
Mayaro virus	Alphavirus	Human, mosquitoes	Fever, joint pain	NC_003417.1	11411	0.001518	40.8
Sindbis virus	Alphavirus	Human, birds, mosquitoes	Pogosta disease, Fever, joint pain	NC_001547.1	11703	0.001486	40.1 (55)
Venezuelan equine encephalitis virus	Alphavirus	Human, rodents, mosquitoes	Fever, joint pain	NC_001449.1	11444	0.001525	40.9 (55)
Western equine encephalitis virus	Alphavirus	Human, vertebrates, mosquitoes	Fever, joint pain	NC_003908.1	11484	0.001512	40.7 (54)
Rubella virus	Rubivirus	Human	Rubella	NC_001545.2	9762	0.002757	65.5

Notes: D_{90} in parenthesis refers literature experimental values (Pendyala et al., 2020)

Table 5: Genomic model predicted UV-C (254 nm) sensitivity (D_{90}) of Astroviridae, Calciviridae, Nodaviridae, and Hepeviridae family viruses.

Virus	Genus	Host	Disease	NCBI #	Genome (bp)	PyNNFV	D_{90} (J/m^2)
Human astrovirus	Mamastro virus	Human, mammals	Gastroenteritis	NC_001943.1	6813	0.002446	59.3
Avastrovirus 1	Avastrovirus	Turkey, birds	Gastroenteritis, liver, or kidney damages	Y15936.2	7003	0.002405	58.5
Human norovirus GI	Norovirus	Human	Gastroenteritis	NC_001959.2	7654	0.002936	69.1
Human norovirus GII	Norovirus	Human	Gastroenteritis	KF712510.1	7509	0.003934	89.0
Human norovirus GIV	Norovirus	Human	Gastroenteritis	JF781268.1	7839	0.003360	77.6
Sapovirus	Sapovirus	Human	Gastroenteritis	NC_006554.1	7476	0.003672	83.8
Rabbit hemorrhagic disease virus-FRG	Lagovirus	Lagomorphs	Necrotizing hepatitis leading to fatal hemorrhages	NC_001543.1	7437	0.002764	65.7
Newbury agent 1 virus	Nebovirus	Bovine	Necrotizing hepatitis	NC_007916.1	7454	0.004414	98.6
Feline calicivirus	Vesivirus	Feline	Conjunctivitis, respiratory disease	NC_001481.2	7683	0.003627	82.9 (60)
Vesicular exanthema of swine virus	Vesivirus	Swine, sea mammals	Respiratory disease	NC_002551.1	8284	0.003508	80.5
Nodamura virus	α-nodavirus	Mammals, fishes	Paralysis and death	AF174533.1, AF174534.1	4540	0.005406	118.4
Striped jack nervous necrosis virus	β-nodavirus	Fish	Viral encephalopathy and retinopathy	NC_003448.1, NC_003449.1	4528	0.007331	156.9
Dragon grouper nervous necrosis virus	β-nodavirus	Fish	Viral nervous necrosis	AY721616.1	4536	0.006953	149.4
Barfin flounder virus	β-nodavirus	Fish	Viral nervous necrosis	EU826137.1	4533	0.006839	147.1
Hepatitis E virus	Hepevirus	Human, pig, monkey, chicken	Hepatitis	NC_001434.1	7176	0.011850	247.2
Cutthroat trout virus	Piscihepevirus	Fish	-	NC_015521.1	7410	0.006150	133.3

Notes: D_{90} in parenthesis refers literature experimental values (Pendyala et al., 2020)

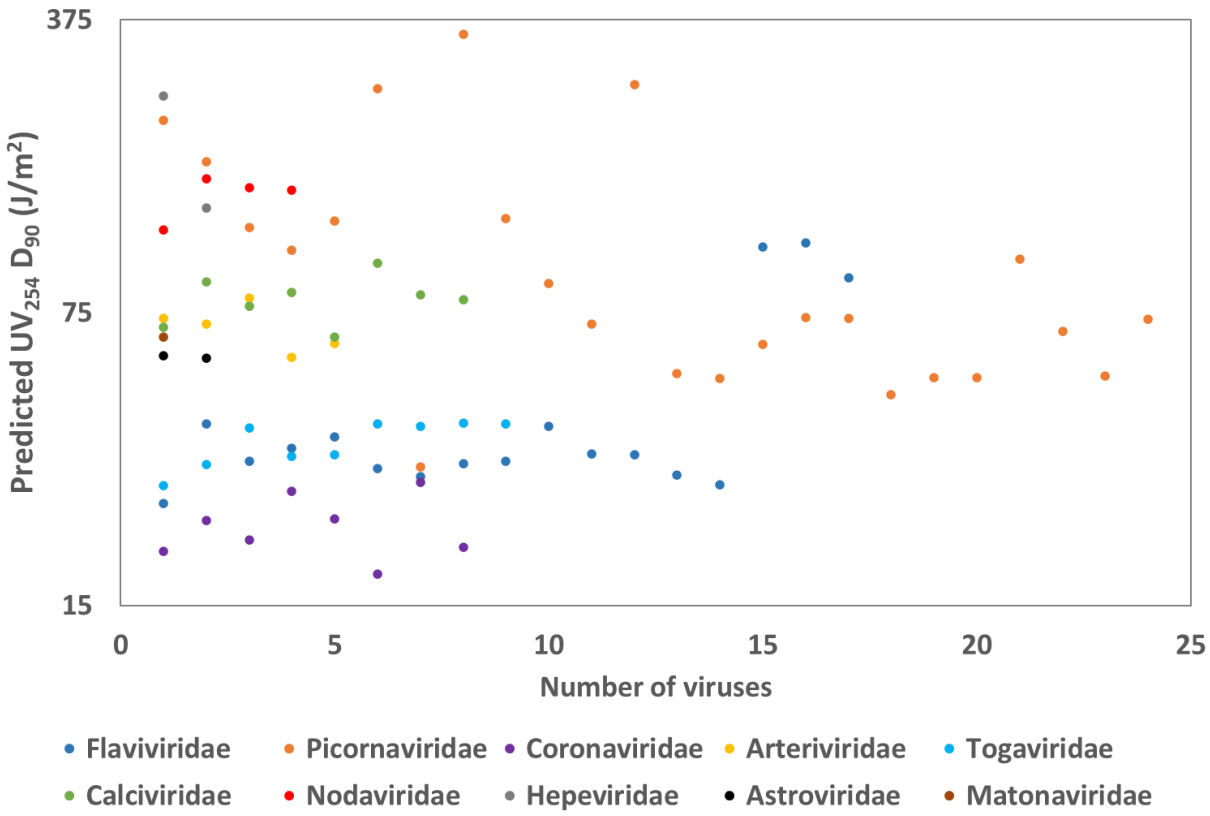

Figure 1: Predicted UV_{254} D_{90} values of (+) ssRNA vertebrate virus families