IMAGING TECHNIQUES FOR STUDYING VIRUS-CELL INTERACTIONS: A REVIEW OF CURRENT METHODS AND CHALLENGES

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МЕТОДЫ ВИЗУАЛИЗАЦИИ ДЛЯ ИЗУЧЕНИЯ ВЗАИМОДЕЙСТВИЙ ВИРУС-КЛЕТКА: ОБЗОР СОВРЕМЕННЫХ МЕТОДОВ И ПРОБЛЕМ

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Abstract

Knowledge of virus-host cell interactions is central to the formulation of antiviral therapies and vaccines. Because of their nanoscale size and dynamic nature, viruses are inherently difficult objects to investigate. Virus characterization, such as imaging viral structures, intracellular viral trafficking, and infection molecular mechanisms, has relied heavily on sophisticated imaging approaches. Classical light microscopy imaging, such as fluorescence and super-resolution microscopy, provides information on viral entry, replication, and protein localization within living cells. Electron microscopy (EM) techniques, such as Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), and Cryo-Electron Microscopy (Cryo-EM), provide high-resolution structural information on the viruses and their replication compartments [53]. Advances in correlative imaging techniques, which include light and electron microscopy, have improved our ability to study virus-induced cellular changes in three dimensions. But in comparison to the earlier developments, it remains challenging in virus imaging: a compromise between resolution and sample preparation, restrictions in labeling methods, the challenge in imaging rapid virus-host interactions, and biosafety limitations for highly pathogenic viruses [10]. Solutions to these types of issues will be provided with the newer techniques such as AI-powered imaging analysis, nanotechnology-based imaging probes, and cryo-electron tomography. This review covers the present imaging methods in virology, their utilities and limitations, as well as future prospects, with an emphasis on microscopy to discern the interaction of viruses with cells [51].

Резюме

Знание взаимодействия вируса и клетки-хозяина имеет решающее значение для разработки противовирусных терапий и вакцин. Из-за своего наномасштабного размера и динамической природы вирусы являются сложными объектами для исследования. Характеризация вирусов при помощи визуализация вирусных структур, внутриклеточного вирусного трафика и молекулярных механизмов инфекции, в значительной степени опиралась на сложные технологические подходы. Классическая световая микроскопия, такая как флуоресцентная микроскопия и микроскопия сверхвысокого разрешения, предоставляет информацию о проникновении вируса, репликации и локализации белка в живых клетках. Методы электронной микроскопии (ЭМ), такие как просвечивающая электронная микроскопия (ПЭМ), сканирующая электронная микроскопия (СЭМ) и криоэлектронная микроскопия (крио-ЭМ), предоставляют структурные данные высокого разрешения о вирусах и их репликационных компартментах [53]. Достижения в области корреляционных методов визуализации, которые включают световую и электронную микроскопию, улучшили возможность изучать вызванные вирусом клеточные изменения в трех измерениях. Но по сравнению с более ранними разработками, визуализация вирусов остается сложной из-за компромисса между разрешением и подготовкой образцов, ограничений в методах маркировки, проблемы визуализации быстрых взаимодействий вируса с хозяином и ограничения биологической безопасности для высокопатогенных вирусов [10]. Решения таких проблем будут предоставлены с помощью новых методов, таких как анализ изображений на основе ИИ, зондов для визуализации на основе нанотехнологий и криоэлектронной томографии. В настоящем обзоре рассматриваются современные методы визуализации в вирусологии, их

применимость и ограничения, а также будущие перспективы с акцентом на микроскопию для распознавания взаимодействия вирусов с клетками [51].

Ключевые слова: молекулярные механизмы, просвечивающая электронная микроскопия, вирус, методы визуализации, криоэлектронная томография, микроорганизмы.

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1 **Introduction**

Viruses are obligate intracellular parasites requiring host cells to multiply. Understanding how viruses communicate with their host cells—isolate, multiply, form, and exit is very essential for the development of antiviral drugs and vaccines. As viruses on the move are detectable only with the aid of advanced imaging techniques due to their nanometer-scale and dynamic character, the techniques permit researchers to trace viral structures, track virus mobility inside cells, and determine the molecular mechanism of virus-cell interaction [8].

In the last decades, microscopy has transformed the field of virology, providing unparalled information on the viral life cycle. Electron microscopy had been the force that changed the field with its arrival in the early decades of the 20th century and the provision of the first viral particle images [24]. Light microscopy, electron microscopy, and correlative imaging methods, in turn, are still under continuous development since then, allowing researchers to visualize viruses more vividly and even in real-time. In the current years, the use of super-resolution microscopy, cryo-electron tomography, and single-molecule imaging has become instrumental in elucidating fine-scale molecular mechanisms of virus infection [9].

Despite these advances, virus imaging remains challenging. Most viral mechanisms are in the nanometre range, which is below the resolution limit of standard light microscopy. Moreover, the imaging of live viruses inside infected cells requires techniques that balance resolution, speed, and sample minimization damage. This review shall detail current imaging methods utilized in virology, their usage, their strengths, and their weaknesses, as well as the future direction of viral imaging.

While there are variations, all viruses adhere to basic steps: entry into host cells, replication of the genome, assembly of new virions, and their subsequent release. Techniques such as confocal microscopy, imaging flow cytometry, and cryo-electron microscopy are routinely utilized in virology to visualize and investigate such interactions between host cells and viruses. [29]

2. Virus-Cell Interactions: A Detailed Overview

Viruses are obligate intracellular parasites that depend entirely on the host cells for their growth and survival. Virus-cell interactions include several steps, each necessary for the completion of the viral life cycle: attachment and entry, penetration and uncoating, replication and gene expression, virus assembly and maturation, and virion release and spread. Each step has some molecular mechanisms that vary with the type of virus, structural make-up, and the host cell it infects [37].

2.1 Attachment and Entry: The First Step in Viral Infection

Infection begins with attachment through interactions between viral surface proteins and specific receptors on a cell membrane. Binding specificity defines tropism and host range for a virus. HIV binds on CD4 receptors, and the influenza virus bind on sialic acid residues. Certain viruses also require additional co-receptors. HIV, for example, requires CCR5 or CXCR4 as a co-receptor with CD4. Efficiency at infection also relies on number and density of viral receptors on a cell surface, as increased receptor density increases virus attachment possibilities [39].

Entry mechanisms vary: enveloped viruses use membrane fusion or receptor-mediated endocytosis; non-enveloped viruses use pore formation or endocytosis. [3].

2.2 Penetration and Uncoating: Delivering the Viral Genome

Upon infection of the cellular host, the virus must release its genome for replication through a process called uncoating. Uncoating occurs via membrane fusion or through endocytic vesicles. Non-enveloped viruses cause endosomal damage to deliver their genome into cytoplasm. Low endosomal pH can trigger a conformational shift in viral proteins for penetration through the membrane. [20].

2.3 Replication and Gene Expression: Hijacking the Host Machinery

After uncoating, the viral genome must be replicated and transcribed to generate viral proteins. Replication is different based on the nature of the viral genome, which can be DNA or RNA, single-stranded or double-stranded, positive-sense or negative-sense. DNA viruses replicate in the nucleus using host or viral DNA polymerases to replicate new genomes. RNA viruses, however, usually

59 replicate in the cytoplasm, as they require RNA-dependent RNA polymerases
60 (RdRp) to replicate new RNA strands. This enzyme is not present in host cells, and
61 therefore RNA viruses must encode it in the genome.

62 Positive-sense RNA viruses, can be translated as soon as they are in the
63 cytoplasm, while negative-sense RNA viruses, must form complementary positive-
64 sense RNA before they can be translated. Retroviruses, use a unique strategy in
65 which reverse transcriptase (RT) copies their RNA genome into DNA, which then
66 becomes integrated into the host genome, allowing long-term replication and
67 persistence [37].

68 Viral protein translation is another process that has been maximized by viruses
69 for successful replication. Certain viruses produce a single large polyprotein, which
70 is subsequently cleaved into functional proteins, while others use processes like
71 alternative splicing, ribosomal frame-shifting, and leaky scanning to produce more
72 than one protein from a single mRNA transcript. Most viruses repress host cell
73 protein synthesis to promote their gene expression.

2.4 Virus Assembly and Maturation: Constructing New Virions

75 After replication and protein synthesis, the new viral proteins and genomes
76 must be packaged into mature virions. Virus assembly is a highly organized
77 workflow that occurs in specialized areas of the host cell. Certain viruses, such as
78 herpesviruses and adenoviruses, are assembled within the nucleus, and others, such
79 as coronaviruses and flaviviruses, are assembled within the cytoplasm. Certain
80 viruses, such as HIV, are assembled at the plasma membrane, where they acquire
81 their envelope through budding [20].

82 Maturation is an essential process of viral assembly because some viruses
83 require post-assembly processing to become infectious. HIV virions, for instance,
84 are proteolytically cleaved by viral protease within their Gag polyproteins, allowing
85 infectious particle formation. Prevention of this occurrence is the mode of action of
86 protease inhibitor drugs for antiretroviral therapy.

2.5 Virion Release and Spread: Escaping the Host Cell

The final process in the viral life cycle is the release of new virions to propagate the infection. Non-enveloped viruses exit by lysis, where they burst the plasma membrane and destroy the host cell. Enveloped exit by budding, gaining their envelope from the host cell membrane in the process. Some viruses, such as coronaviruses and Hepatitis B, are released by exocytosis, where virions are enclosed within vesicles and transported to the plasma membrane for secretion [55].

Viruses have developed other mechanisms of spread within the host. Others, like measles virus, induce syncytium formation by inducing infected cells to fuse with neighboring cells and become multinucleated giant cells, facilitating cell-to-cell spread. Others, like Vaccinia virus, use actin-based motility to move from cell to cell without being exposed to the extracellular environment.

3. Why Imaging is Crucial for Studying Virus-Cell Interactions?

Virus-cell interactions are vital to comprehend in virology, as these determine the entire virus life cycle from entry into the host cell, through replication and eventual release. Imaging techniques have become indispensable probes to study such processes, and they offer images of how the viruses infect the host cells, take over the cellular machinery, and spread [56].

Due to the nanoscale dimension of viruses, traditional biochemical and molecular methods fall short in unveiling the structural and dynamic characteristics of viral infection. High-resolution imaging methods, such as Light Microscopy-Based Methods, Electron Microscopy (EM) Methods, Correlative and Multiscale Imaging, and Molecular and Functional Imaging, allow researchers to witness these intricate interactions with unprecedented accuracy. Here, we shall elaborate on each of these techniques in detail, their concepts, uses, and how they have contributed to virus-cell interaction understanding [34].

4. Imaging Techniques for Studying Virus-Cell Interactions

4.1 Light Microscopy

Light microscopy has long been the workhorse of biological studies, allowing researchers to see cell structure and processes with precision. In virology, such approaches serve particular application for the examination of virus-cell interactions, with information on viral entry, replication, assembly, and egress. Visualization of the ability of the virus of investigation actually taking place under real-time conditions of cells has redefined understanding of the mechanism of infection and host-pathogen interactions [47].

Recent advances of light microscopy have collectively enhanced the imaging depth, contrast, and the spatial resolution, allowing researchers to bypass the diffraction limits of conventional optical systems. By using the application of fluorescence labeling and the newer imaging modalities, the viral constituents can be imaged at the molecular level, providing unprecedented insights into their functional dynamics and the structural organization [32]. These procedures capitalize on the principles of light, such as refraction and diffraction, for the generation of high-resolution images of the virus-host interaction, providing critical information for antiviral research as well as for therapeutic discovery.

4.1.1 Super-Resolution Microscopy: STED, STORM, and PALM

Microscopy Super-resolution microscopy techniques have revolutionized cellular imaging by overcoming the diffraction limit of conventional optical microscopy of approximately 200 nm in the lateral plane and 900 nm in the axial plane. Abbe's principle limits conventional fluorescence microscopy such that the minimum resolvable feature is determined by the wavelength of the illuminating light and the numerical aperture of the imaging apparatus. Super-resolution microscopy techniques circumvented this limit based on different strategies to achieve nanoscale imaging. Some of these include Stimulated Emission Depletion (STED), Stochastic Optical Reconstruction Microscopy (STORM), and

143 Photoactivated Localization Microscopy (PALM), which are some of the standard

144 techniques to achieve 10–50 nm resolutions [45].

145   *4.1.1.1 Stimulated Emission Depletion (STED) Microscopy*

146   STED microscopy is a directed super-resolution imaging technique bypassing

147 diffraction limit in traditional fluorescence microscopy by stimulated emission

148 depletion. It was initially described by Stefan Hell and Jan Wichmann in 1994 [16].

149 The mechanism relies upon two lasers: a pumping excitation laser inducing

150 fluorophores into a state of excitement, a second doughnut-shaped laser beam de-

151 exciting fluorophores in a region outside the focal area of interest by stimulated

152 emission, effectively shrinking the effective point spread function [33].

153

154 The most striking advantage of STED microscopy comes from its capability of

155 reaching resolutions of as low as ~70 nm, demonstrated from intravital microscopy

156 of mouse brain tissue. This has made STED microscopy highly valuable in virus-

157 host interaction research, where the technique has been used in imaging viral

158 infection cellular structures at higher resolution [42]. STED microscopy has several

159 disadvantages, however, such as relatively strong laser intensities, resulting in

160 photochemical bleaching and phototoxicity. Solutions have been aimed at

161 optimizing the technique using reversible saturable/switchable optical linear

162 fluorescence transition (RESOLFT), allowing lower laser intensities while with no

163 loss in resolution [1,64].

164   *4.1.1.2 Stochastic Optical Reconstruction Microscopy (STORM)*

165   STORM is a stochastic super-resolution method predicated on the exact

166 localization of individual fluorescent molecules for reconstructing an image at the

167 nanoscale [44]. While STED makes use of structured illumination, STORM

168 accomplishes super-resolution by stochastically activating a sparse number of

169 fluorophores in such a manner that merely a few molecules are in the fluorescent

170 state at a particular instant of time. Consecutive thousands of images are gathered,

171 and the exact locations of individual molecules are reconstructed computationally to
172 construct a super-resolved image [58].

173

174 STORM has been widely applied in virology research, especially in the investigation
175 of virus-host interactions. Single-molecule super-resolution STORM imaging, for
176 instance, was employed to investigate CD4 redistribution in the plasma membrane
177 of T cells upon HIV-1 binding, giving an insight into receptor organization at the
178 nanoscale. It has enabled researchers to describe viral particle interaction with host
179 cell receptors with unprecedented spatial accuracy [46].
180

181 Although high resolution is achieved with STORM, it necessitates high
182 labeling densities and extended acquisition times and thus is less appropriate for
183 live-cell imaging [21]. Furthermore, photobleaching of fluorophores can restrict
184 imaging time, such that the utilization of photoswitchable dyes is necessary to
185 compensate for signal loss [18].

186 ### 4.1.1.3 Photoactivated Localization Microscopy (PALM)

187 Another single-molecule, single-molecule super-resolution technique, PALM
188 achieves this imaging through the recruitment of the stochastically activated
189 photoactivatable fluorescent proteins. Like STORM, PALM also relies upon the
190 single-molecule precise localization through repeatedly imaging the low numbers of
191 activated fluorophores [71].

192

193 The PALM has also been used extensively in cell biology and virology research, in
194 a bid to study the assembly, release, and maturation of the virus. PALM imaging, in
195 combination with other methods, has revolutionized the study of the structure of the
196 virus at a nanoscale, for instance, in HIV-1, where PALM was used in combination
197 with other imaging methods of high resolution [35].

198

199 Among the strengths of PALM is its compatibility with genetically encoded

200 fluorophores, making it highly compatible with live-cell imaging [24]. Like
201 STORM, however, PALM requires long image acquisition and computational post-
202 processing, which frustrates its real-time applications. Despite these drawbacks, the
203 technique is an extremely valuable tool for investigating dynamic viral and cellular
204 processes at the molecular level [14].

205   4.1.2 Single-Molecule Imaging: smFRET and TIRF Microscopy

206   Single-molecule imaging techniques have revolutionized the viewing of
207 dynamic molecular interactions in real time. These high-resolution techniques
208 circumvent ensemble averaging by detecting and tracking single molecules,
209 enabling researchers to examine intricate biological processes at previously
210 unimaginable resolutions in space and time. Two such techniques that are at the
211 forefront of this field are Single-Molecule Förster Resonance Energy Transfer
212 (smFRET) and Total Internal Reflection Fluorescence (TIRF) Microscopy. These
213 techniques have been instrumental in the progress of virus-host interaction studies,
214 especially in investigating viral membrane fusion and protein conformational change
215 [36].

216   *4.1.2.1 Single-Molecule Förster Resonance Energy Transfer (smFRET)*
217 *Imaging*

218   Single-Molecule Förster Resonance Energy Transfer (smFRET) is a
219 fluorescence microscopy that facilitates real-time imaging of biomolecular
220 interactions on the nanometer scale. smFRET has been most applicable in virus
221 research since it reveals dynamic conformational change in viral proteins, especially
222 virus   spike–host   interactions   [27].

223

224 Principle of smFRET is based on the Förster resonance energy transfer (FRET)
225 mechanism, which describes non-radiative energy transfer between two
226 fluorophores: a donor and an acceptor. The efficiency of energy transfer (E) is
227 inversely proportional to the sixth power of the distance (R) between the

228 fluorophores, following the equation:

230 $$E = 1 / (1 + (R/R0)^6)$$

232 This renders smFRET very sensitive to nanoscale molecular interactions, with
233 distance measurements as low as 1–10 nm.

235 In viral research, smFRET has been used extensively to probe viral membrane fusion
236 and spike protein dynamics. It has been particularly useful in the study of viral
237 glycoprotein conformational changes that accompany entry into host cells. For
238 example, smFRET has uncovered dynamic conformational states of the HIV-1
239 envelope (Env) protein and the SARS-CoV-2 spike protein during host interactions.
240 The method has given an understanding of how viral proteins move through various
241 structural states, e.g., pre-fusion and post-fusion states, which are essential in the
242 development of antiviral therapies [36].

4.1.2.2 Total Internal Reflection Fluorescence (TIRF) Microscopy

244 Total Internal Reflection Fluorescence (TIRF) microscopy is an extremely
245 advanced imaging technique for biomolecules with high resolution near the plasma
246 membrane. It is particularly suitable to investigate cell surface interaction and
247 membrane-bound processes, e.g., endocytosis, exocytosis, and viral entry [46].

249 TIRF Microscopy relies on the principle of total internal reflection, whereby the
250 incident laser beam hits the interface between two media of different refractive
251 indices, e.g., glass and water. Total internal reflection happens at an angle of
252 incidence larger than a certain critical angle and creates an evanescent wave that
253 penetrates only an infinitesimal distance (~100 nm) into the sample. The wave
254 excites fluorophores at the interface, minimizing background fluorescence and
255 improving signal-to-noise ratio [13].

TIRF microscopy has seen extensive application in the study of viral interaction with the cell membrane. TIRF microscopy has been in wide use in the imaging of dynamic processes, which include virus entry and host cell interaction. TIRF has also been combined with single-molecule fluorescence methodologies, such as smFRET, to investigate real-time viral spike protein conformation dynamics during virus-host interaction. Together, they have enabled the HIV-1 and SARS-CoV-2 receptor-binding events to be investigated in depth to reveal viral membrane fusion and antibody neutralization mechanisms [22].

TIRF microscopy provides key benefits to live-cell imaging in that it restricts fluorescence excitation to a thin plane (~100 nm) near the coverslip, reducing background noise and phototoxicity. This provides a method well-suited for imaging activity at the plasma membrane, including receptor-ligand interactions and endocytosis. TIRF is restricted, however, in imaging deeper cellular structures since the evanescent wave only penetrates a short distance from the coverslip [61].

4.1.3 Fluorescence Microscopy

Fluorescence microscopy is a sophisticated imaging method that utilizes light emitted by fluorophores to follow particular molecules and cellular structures. The method has transformed biological research by enabling precise probing of cellular processes with improved contrast and specificity [35]. In comparison to conventional brightfield microscopy that is based on transmitted light, fluorescence microscopy selectively illuminates and images fluorescently labeled structures, rendering it an indispensable tool in cell biology, molecular biology, and virology [42].

The basic principle of fluorescence microscopy relies on fluorophore excitation and emission. A fluorophore, upon absorbing light at a particular wavelength, gets excited and, in doing so, transitions to the ground state by releasing light at a longer

285 wavelength [26]. The fluorescence emitted is captured with the help of optical filters,
286 and this enables scientists to view structures with decent spatial resolution.
287 Specificity for fluorescence microscopy is obtained by labeling fluorophores to
288 antibodies, proteins, or nucleic acids, enabling the examination of cellular structures
289 with great precision [42].

290 *4.1.3.1 Types of Fluorescence Microscopy*

291 Several fluorescence microscopy techniques have been designed to enhance
292 resolution, contrast, and specificity. The most common ones are:
293

294 1. Widefield Fluorescence Microscopy: The most common and simplest type of
295 fluorescence microscopy, where the whole sample is illuminated with a wide light
296 source. This refinement significantly enhances optical sectioning and produces
297 sharper, more detailed images—especially useful for analysing thicker samples. The
298 technique improves resolution and contrast by point-by-point scanning in the
299 sample, rendering crisp three-dimensional images. It is especially suitable for thick
300 samples and live-cell imaging [43].
301

302 2. Confocal Laser Scanning Microscopy (CLSM) overcomes a critical deficiency
303 present in widefield fluorescence, namely the effect of out-of-focus light masking
304 the quality of the image. By the addition of a very small pinhole designed to
305 eliminate the unwanted light from the system, as well as the scanning of the
306 specimen point by point, CLSM yields images with greatly enhanced resolution and
307 contrast [50]. The technique thus proves particularly useful in the examination of
308 thicker biological samples or the examination of living cells over time in real
309 time.[54]
310

311 3. Super-Resolution Microscopy: The diffraction limit, once a limitation on
312 traditional fluorescence microscopy, restricts resolution to about 200 nm. Yet, super-
313 resolution techniques such as Stimulated Emission Depletion (STED), Stochastic

314 Optical Reconstruction Microscopy (STORM), and Photoactivated Localization
315 Microscopy (PALM) have broken this barrier, allowing the imaging of structures at
316 resolutions of less than 50 nm [31].

317 ### 4.1.4 Live-Cell Imaging

318 Live-cell imaging is a sophisticated microscopy method that aims to study
319 dynamic biological processes in living cells over a period. In contrast to fixed-cell
320 imaging, which takes static images, live-cell imaging enables researchers to monitor
321 intracellular processes like protein trafficking, mitosis, autophagy, viral infection,
322 and immune cell function in real time [12]. Live-cell imaging has emerged as a key
323 strategy for observing intricate biological processes in situ, as they occur in the cell's
324 own internal environment. Using advanced microscopy techniques, researchers are
325 now capable of acquiring high-quality images of cells in real-time, which enable
326 them to see structure and function changing as it happens. What is distinct about this
327 method is that it retains the native cell state—by not using chemical fixation or
328 staining, it effectively reduces interference with normal cell function to a bare
329 minimum   [5].

330

331 This has made live-cell imaging a critical methodology in virology, neuroscience,
332 cancer biology, and drug discovery. One of the minimum requirements for effective
333 live-cell imaging is keeping cell viability in the microscope. This includes rigorous
334 temperature, pH, and osmotic balance control, typically provided by specialized
335 imaging chambers. Imaging methods must also keep phototoxicity to a minimum
336 since living cells can be harmed and their behaviors changed by being exposed to
337 light for extended periods [57]

338 #### 4.1.4.1 Techniques in Live-Cell Imaging

339 Fluorescence live-cell imaging is among the most popular methods used for
340 observing the beautiful ballet of cell dynamics. This technique relies either on
341 genetically encoded fluorescent proteins, like GFP and RFP, or on chemical dyes
342 with specific affinity for particular cellular structures.

343 Despite the exceptional specificity and contrast of these fluorescence-based
344 techniques, they are susceptible to photobleaching, a phenomenon in which ongoing
345 light exposure deteriorates fluorescence intensity over time [53]

346

347 One of the other widely utilized techniques is Total Internal Reflection Fluorescence
348 (TIRF) Microscopy, which is a technique for selective imaging of molecules close
349 to the plasma membrane. TIRF produces an evanescent wave that excites
350 fluorophores in only a thin layer, roughly 100 nanometers, close to the coverslip.
351 This unique characteristic makes it very suitable for examining membrane-
352 associated processes such as receptor-ligand interactions, endocytosis, and viral
353 entry [56]

354 Two-photon microscopy offers greater tissue penetration and reduced
355 phototoxicity compared to confocal microscopy. Near-infrared light is used to excite
356 fluorophores at deeper levels in this method and hence it is well suited for imaging
357 live tissues and organisms [50]. Two-photon microscopy has been instrumental in
358 neuroscience studies, especially in monitoring synaptic activity and interactions of
359 neural   networks.

360

361 The other techniques involve Fluorescence Recovery After Photobleaching
362 (FRAP), a technique that gauges the mobility and diffusion of proteins by
363 photobleaching a region and watching the recovery of ensuing fluorescence. Another
364 technique is Fluorescence Lifetime Imaging Microscopy (FLIM), which monitors
365 the decay of fluorescence to disclose details about the biochemical environment of
366 live cells [27].

367 ## 4.2 Electron Microscopy (EM) Techniques

368 Electron microscopy (EM) is a sophisticated method that employs electron
369 beams instead of light to obtain extremely high-resolution images of biological
370 specimens. Due to the much smaller wavelength of electrons, the technique provides
371 much better resolution than traditional light microscopy [68]. It allows the

372 examination of subcellular structures, viruses, and large molecular aggregates at the
373 nanometer resolution and, in some instances, even at the angstrom resolution.
374 Electron microscopy has become especially important in structural biology and
375 virology, where detailed fine structures need to be understood [23].

4.2.1 Transmission Electron Microscopy (TEM)

377 Transmission electron microscopy (TEM) is the most popular EM method of
378 analyzing biological samples. TEM involves directing a beam of high-energy
379 electrons through a specimen of 50-100 nm thickness that is made ultrathin. Contrast
380 due to electron scattering resulting from electron interaction in the specimen
381 produces high-image resolution of internal structures [59].

382 In virology, TEM was pivotal in the determination of viral structure,
383 morphology, and intracellular associations. TEM observations in early days, for
384 example, provided the initial direct observation of viruses like the poliovirus and the
385 influenza virus, revealing their capsid symmetry and surface topography. TEM was
386 also widely used to examine virus-induced changes in cells, e.g., replication
387 organelles, virus-host associations [24].

389 One major benefit of TEM is the possibility to image structures at near atomic
390 level resolution. Nevertheless, it involves complex sample preparation through
391 fixation, dehydration, and embedding in resin, which may introduce artifacts. TEM
392 is also generally performed on fixed samples and therefore is not appropriate for
393 live-cell imaging.

4.2.2 Scanning Electron Microscopy (SEM)

395 In contrast to TEM, SEM provides high-resolution images of the topography
396 of the biological samples' surfaces and not of internal structures. SEM operates by
397 scanning the surface of the specimen using a beam of focused electrons and
398 generating secondary and backscattered electrons in the creation of a three-
399 dimensional image [30].

400 SEM is also particularly beneficial in studying virus morphology, viral entry
401 mechanisms, and cell surface interactions [45]. SEM was used, for example, to study
402 how coronavirus attaches to host cell receptors and induces membrane fusion. SEM
403 was also used to study viral budding and cell egress of infected cells.

404 One of the significant advantages of SEM is that it is capable of generating
405 high-quality 3D cell structure reconstructions. Yet, like TEM, SEM also requires
406 complicated sample preparation involving chemical fixation of the samples, drying
407 or dehydration, and coating them in conductive materials, which are gold or
408 platinum, to prevent electron charging effects [72].

4.2.3 Cryo-Electron Microscopy (Cryo-EM)

410 Cryo-Electron Microscopy or Cryo-EM has led to a revolution in the study of
411 structural biology by enabling the imaging of biological macromolecules in their
412 natural state of hydration. Unlike TEM and SEM in which samples get processed
413 extensively, Cryo-EM quickly quenches samples in liquid ethane to immobilize the
414 structure without chemical fixation [11].

415 Cryo-EM has also been the preferred approach for the determination of high-
416 resolution viral protein structures, e.g., SARS-CoV-2 spike proteins, influenza
417 hemagglutinin, and HIV-1 envelope glycoproteins. Single-particle imaging in the
418 thousands and computer-assisted 3D structure reconstruction by Cryo-EM allow
419 researchers to study the conformational dynamics of viral proteins and identify
420 potential drug targets [41].

421 Cryo-EM provides several advantages over traditional EM methods, e.g.,
422 fewer preparations of samples, imaging of samples in their state of hydration, and
423 the potential for near-atomic resolution. Specialized equipment is required, e.g.,
424 cryo-enabled microscopes and high-performance image processing computing
425 equipment [11].

4.2.4 Cryo-Electron Tomography (Cryo-ET)

427 Cryo-Electron Tomography (Cryo-ET) is the technologically advanced
428 extension of Cryo-EM for 3D imaging of cellular structures at the molecular

429 resolution level. Unlike single-particle Cryo-EM, where 3D structures are
430 reconstructed from average projections of extremely large particle numbers, Cryo-
431 ET includes the step of tilting a single specimen at various angles and
432 computationally reconstructing a 3D tomogram [28].

433 Cryo-ET has played a crucial role in investigating cell modifications induced
434 by viruses, including replication compartments and virus-host interactions. Cryo-
435 ET, for instance, gave detailed information on coronavirus replication
436 compartments' structure and unveiled the viral RNA synthesis machine. Cryo-ET
437 has also imaged viral entry processes, such as influenza virus particle membrane
438 fusion [62].

439 One of the advantages of Cryo-ET is that it can potentially yield high-
440 resolution 3D reconstructions of the full cell context. It is technically challenging,
441 however, and needs expert sample preparation, high-precision imaging, and
442 computationally intensive processing.

4.3 Correlative and Multiscale Imaging

444 Advances in imaging technologies have given rise to correlative and
445 multiscale imaging methodologies that use various microscopy methods to image
446 the molecular structures and interactions of cells in various resolutions and scales.
447 These methodologies bridge the gap between light microscopy (LM) and electron
448 microscopy (EM) and allow researchers to correlate dynamic live-cell imaging with
449 high-resolution structural information. These methods include Correlative Light and
450 Electron Microscopy (CLEM), FIB-SEM, SBF-SEM, and Helium-Ion Microscopy
451 (HIM), which are potent methodologies to explore virus-host interactions, cell
452 ultrastructure, and sub-cellular processes [3].

453 4.3.1 Correlative Light and Electron Microscopy (CLEM)

454 Correlative Light and Electron Microscopy combines the dynamic live-cell
455 imaging capabilities of fluorescence microscopy and the high resolution of electron
456 microscopy. It is particularly well adapted for tracking of viral infection, protein

457 localization, and ultrastructure of cells since it allows researchers to correlate
458 fluorescent-labeled molecules and ultrastructure in the same specimen [60].

459 In virology, CLEM has also come to be used in virus-host interactions by
460 initially imaging live cells by fluorescent microscopy to trace viral entry, replication,
461 and egress. These samples are subsequently prepared for electron microscopy to
462 capture ultrastructure of viral particles and host cell organelles [40]. For example,
463 CLEM has traditionally come to be used in studying SARS-CoV-2 replication
464 compartments and how viral RNA synthesis sites correlate to host cell organelles.

465 A significant strength of CLEM is that it allows both dynamic, live-cell
466 imaging and high-resolution structural data to be combined. It is, however, subject
467 to rigorous light and electron microscopy image registration and hence is technically
468 demanding [63].

469 4.3.2 Volume Electron Microscopy (FIB-SEM, SBF-SEM)

470 Volume Electron Microscopies (vEM) are methods by which 3D
471 reconstruction of biological specimens can be made in nanometer resolution.
472 Focused Ion Beam Scanning Electron Microscopy (FIB-SEM) and Serial Block-
473 Face Scanning Electron Microscopy (SBF-SEM) are the two popular vEM
474 technologies. Scientists use these technologies to study the architecture of the spatial
475 arrangement of subcellular components and large biological volumes, which is
476 beneficial in cell biology and virology [38].

477 FIB-SEM utilizes a focused ion beam serially to mill away samples in thin
478 layers in combination with SEM imaging of the exposed surface. It produces a high-
479 definition 3D structure data set of cells. FIB-SEM was used to study viral replication
480 compartments, mitochondrial reorganization, and viral inclusions in the cytoplasm
481 [69].

482 SBF-SEM employs a diamond knife to slice the sample in very thin sections
483 for SEM imaging. It is particularly beneficial in the examination of large tissue
484 samples, organoids, and whole infected cells since it allows cell changes caused by
485 the virus to be examined in whole cell populations.

486   Volume Electron Microscopy is also extremely useful in virus-host interaction
487 research because of the ultrastructural context it provides for viral replication and
488 assembly sites. Its drawback is that it is labor-intensive, equipment-dependent, and
489 generates incredibly large data sets that require high-level computational analysis
490 [38].

491   4.3.3 Helium-Ion Microscopy (HIM)

492   Helium-Ion Microscopy (HIM) is one of the new sub-nanometer resolution
493 imaging technologies that performs high-resolution imaging of biological samples
494 using very minimal sample preparation. While traditional SEM employs an electron
495 beam, HIM utilizes a helium ion beam that possesses numerous advantages like
496 increased surface sensitivity, decreased damage to the samples, and improved
497 contrast for biological samples [52].

498   HIM is particularly well-suited to image biological membranes, viruses, and
499 cell surfaces. It has also been used to study viral particle surface topology, host cell
500 entry, and structures of biofilms. Its ability to image without conductive coatings
501 makes it well-suited to image sensitive biological specimens [66].

502   However, HIM is still a relatively new technology, and application to
503 biological sciences is constrained by cost and requirement for specialized know-
504 how. In spite of these impediments, HIM holds the potential to revolutionize
505 nanoscale imaging of cell structures and viruses [19].

506   4.4 Molecular and Functional Imaging

507   Molecular and functional imaging technologies are strong methodologies for
508 the study of biomolecule localization, interactions, and functional activities in cells.
509 They find special application in cell biology and virology, where it is possible to
510 visualize the high-resolution spatial distribution of viral and host protein, nucleic
511 acid, and metabolism. Immunogold Labeling, In Situ Hybridization (ISH), and EM
512 Autoradiography are among the most frequently used methods, which utilize a
513 variety of molecular tagging and detection methods in dissecting the structure and
514 function of biological entities in infection and disease .

4.4.1 Immunogold Labeling

Immunogold labeling refers to a high-resolution electron microscopy (EM) technique applied in protein or biomolecule localisation in tissue and cells. It utilizes gold nanoparticles tagged to antibodies that selectively attach to the molecules of interest. Gold particles happen to be electron-dense and therefore under Transmission Electron Microscopy (TEM) or Scanning Electron Microscopy (SEM) provide high-contrast black spots, enabling protein localisation to the nanometer level [17].

In virology, immunogold labeling enabled the distribution of viral protein in infected cells to be mapped. For example, the method was used in investigating the localisation of the SARS-CoV-2 nucleocapsid protein in replication compartments, providing knowledge of how it interacts with host cell membranes [7]. It also enabled determination of protein-protein interactions in the ultrastructure, e.g., of viral polymerases with host cell ribosomes. However, one of the disadvantages of immunogold labeling is that the fixation and embedding of the samples may result in a loss of antigenicity, hence less efficient labeling. Dual or multi-labeling to examine interactions between several proteins also requires optimization of sizes of gold particles and of antibody concentrations [70].

4.4.2 In Situ Hybridization (ISH)

In Situ Hybridization (ISH) is a powerful molecular imaging tool that is used for the identification and localization of specific nucleic acid sequences (RNA or DNA) in cells and tissue. It allows for the study of gene expression, viral genome location, and genetic alteration through the hybridization of a labeled probe to complementary nucleic acid sequences [21].

ISH also finds extensive use in virology in the detection of viral RNA and DNA in virus-infected cells. For example, Fluorescence In Situ Hybridization (FISH) was applied in the study of HIV-1 RNA host nuclei distribution, where crucial replication sites of the virus were made known. FISH was also applied to examine host gene expression changes following viral infection, where cell defense

544 mechanism information was made available [25]. Oncology also greatly benefits
545 from ISH, where the method is applied in the detection of chromosomal aberrations
546 and oncogene amplification in cancer.

547 Although ISH is specific and sensitive, it also has some disadvantages. Cross-
548 hybridizations of probes may lead to false positives, and the method is also tedious.
549 ISH also requires proper RNA or DNA preservation, and therefore, preparation of
550 the samples is of extreme significance in obtaining reproducible results [15].

4.4.3 EM Autoradiography

552 Electron Microscopy (EM) Autoradiography is a cutting-edge molecular
553 imaging method used in tracing cellular metabolism and molecular dynamics. It
554 identifies the occurrence of radioactively labeled molecules on high-resolution EM
555 imaging.

556 This technique is of valuable application in following viral replication with
557 pulse-labeling at infection with radiolabeled nucleotides. EM autoradiography, for
558 instance, was used in demonstration of influenza virus RNA synthetic sites by
559 following the destiny of radiolabeled RNA precursors into nascent viral genomes.
560 This technique is also used in protein and lipid metabolic labeling where researchers
561 follow protein synthesis locations, lipid metabolism, and virus assembly places [49].

562 A significant advantage of EM autoradiography is that it can follow the
563 dynamics of molecules at high spatial resolution and is thus highly appropriate to
564 examine the intracellular trafficking and replication of viral genomes . The technique
565 is, however, outweighed by several disadvantages in the form of long exposure
566 times, demands of radioactive facilities, and time-consuming image analysis.

5. Applications of Imaging Techniques in Virus-Cell Interactions

568 Imaging modalities have revolutionized the way that scientists investigate
569 virus-host interactions since now for the first time ever it is possible to visualize
570 directly the critical viral processes of host cell entry, intracellular traffic, replication,
571 assembly, and host cell structural remodeling. Improvements in and optimization of
572 advanced microscopy techniques—particularly fluorescence microscopy, live-cell

573 imaging, electron microscopy, and correlative integrated imaging—have introduced
574 unprecedented new levels of investigation in the study of viral infections. These
575 techniques have enabled scientists to watch viral activity in real time, trace their path
576 through the host cell, and examine the fine structural organization of replication sites
577 with a precision never before attainable [34].

578 ### 5.1 Studying Viral Entry and Trafficking

579 Imaging of interaction of viruses with the host cell receptors, i.e., for HIV-1,
580 Influenza, and SARS-CoV-2, has made it more evident as for viral entry itself, which
581 constitutes the initial infection stage. Throughout this phase, viruses attach to
582 specific receptors of the host cell surface, prompting subsequent signaling inducing
583 membrane fusion or endocytic uptake. Advanced imaging technologies, particularly
584 single-molecule Förster Resonance Energy Transfer (smFRET), have been crucial
585 for recording conformational changes of viral spike proteins upon binding with host
586 receptors and progression toward membrane fusion [2]. SARS-CoV-2, HIV-1, and
587 influenza virus have been investigated to reveal that their spike proteins quickly
588 change their structure on binding with host receptors ACE2 (SARS-CoV-2), CD4
589 (HIV-1), and sialic acid residues (Influenza) [67].

590 In addition to smFRET, live-cell fluorescence microscopy has also been
591 crucial in the tracking of real-time virus particle motion on the cell surface. Total
592 Internal Reflection Fluorescence Microscopy (TIRF) has been particularly helpful
593 in imaging on or near the plasma membrane and in providing high-resolution views
594 of viral particle attachment to host receptors and into entry. Apart from that,
595 development of super-resolution microscopy methods like Stochastic Optical
596 Reconstruction Microscopy (STORM) and Photoactivated Localization Microscopy
597 (PALM) made the visualization possible of individual isolated viral particles to a
598 nanometer resolution, and so the viral receptors' cell surface spatial organization and
599 clustering pattern are revealed [48].

600 Viral genomes delivery to the sites of replication in the cytoplasm constitutes
601 a crucial event of the infecting process when the entry into cells is efficient. Imaging

602 techniques involving fluorescently labeled viral nucleic acids enabled researchers to
603 monitor intracellular dynamics of these genomes in real time. Live-cell microscopy,
604 for instance, has demonstrated how HIV-1 reverse transcription complexes are
605 transported actively along microtubule tracks to the nucleus, a process mediated by
606 dynein motor protein. Building on these findings, electron microscopy has allowed
607 imaging of virus-containing vesicles and their targeted delivery to specific
608 subcellular compartments, resolving further our understanding of intracellular viral
609 transport [3].

5.2 Visualization of Viral Replication and Assembly

611 Electron tomography of coronavirus, enterovirus, and flavivirus replication
612 factories. Upon entry into the cell, viruses reorganize host cell membranes to create
613 replication organelles (ROs), which serve as platforms for viral genome replication.
614 Multiscale electron microscopy techniques, such as electron tomography and
615 volume scanning electron microscopy (SEM), have provided 3D reconstructions of
616 such replication structures. Studies of coronaviruses (SARS-CoV-2, MERS-CoV),
617 enteroviruses (coxsackievirus, polio), and flaviviruses (Dengue, Zika) have revealed
618 complex networks of membranes facilitating viral genome formation [68]. For
619 instance, electron tomography demonstrated that SARS-CoV-2 induces
620 endoplasmic reticulum-derived double-membrane vesicles (DMVs), which are
621 special sites for viral RNA replication. These are likely protected from host immune
622 sensors, thus allowing for efficient replication while evading detection [65].

623

624 Live-cell microscopy for viral protein localization tracking. Live-cell imaging has
625 been important in elucidating the spatiotemporal dynamics of viral protein
626 localization in infection. Fluorescently labeled viral proteins allow researchers to
627 monitor their motion and interactions with host factors in real time [57]. For
628 example, fluorescently tagged Ebola virus matrix proteins have been employed to
629 illustrate how these proteins accumulate at the plasma membrane before virus

630 budding. Likewise, GFP-labeled influenza nucleoproteins have been followed to
631 discern their nuclear import during replication.

632 ### 5.3 Host Cell Remodeling During Infection

633 Viral replication organelles (ROs) and their effects on cell structure. The
634 majority of viruses induce extreme modifications of host cell structure to facilitate
635 proper conditions for replication. Imaging studies have shown that positive-strand
636 RNA viruses such as coronaviruses and flaviviruses form complex membrane-bound
637 structures in which viral replication occurs. Cryo-electron tomography (Cryo-ET)
638 has provided high-resolution data on how such viral ROs assemble and are
639 organized, including the illustration of specialized channels that permit RNA export
640 but protect viral genomes from host immunity [28].

641

642 Besides membrane restructuring, certain viruses even hijack host cytoskeletal
643 components. For example, live-cell imaging studies of Herpes Simplex Virus (HSV-
644 1) have shown the virus reorganizes the networks of actin and microtubules actively
645 to facilitate intracellular trafficking and egress.
646 3D visualization of virus-induced changes in the membrane. FIB-SEM and SBF-
647 SEM are ultra-high-resolution imaging techniques that have been used to visualize
648 3D virus-induced changes in membranes. These technologies have revealed that
649 Dengue virus-infected cells develop invaginated spherules, which serve as
650 replicative sites as well as aid viral genome synthesis in a safe environment [67].

651 ### 6. Challenges and Limitations in Virus Imaging

652 Despite dramatic advances in imaging techniques, there are several challenges
653 and limitations in virus imaging. These arise due to the resolution-sample
654 preparation trade-off, problems with labeling and contrast enhancement, limitations
655 in capturing dynamic virus-host interactions, and biosafety concerns. Enhancing the
656 accuracy and efficiency of virus imaging, particularly for highly pathogenic viruses
657 such as SARS-CoV-2, Ebola, and HIV-1, therefore relies on addressing these issues
658 [34].

6.1 Resolution vs. Sample Preparation Trade-offs

The one largest limitation to virus imaging is the resolution-vs-sophisticic sample preparation trade-off. While, with high resolutions such as Cryo-Electron Microscopy (Cryo-EM) and Electron Tomography (Cryo-ET), imaging modes provide near atomic-level resolutions, they also require a sophisticated level of sample preparation [4].

• Complex sample processing is required for high-resolution Electron Microscopy (EM). Standard Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) involve complicated sample preparation, i.e., chemical fixation, dehydration, staining, resin embedding, and ultrathin sectioning. These steps can cause artifacts that lead to misinterpretation of viral structures.

• Cryo-EM is low-throughput and expensive. Cryo-EM has transformed structural virology with the facility to image native hydrated viruses without chemical fixation. However, Cryo-EM requires expensive equipment, specialized expertise, and is low-throughput and, therefore, not readily adoptable by the majority of research labs. Cryo-ET datasets are also large and computationally demanding and require advanced image processing software for 3D structure reconstruction.

The need for enhanced sample preparation techniques which preserve ultrastructure and are timesaving is crucial in order to improve virus imaging efficiency [45].

6.2 Limitations in Labeling and Contrast Enhancement

Labeling and contrast enhancement are crucial for visualizing viral components, but existing techniques have several limitations. Electron Microscopy (EM) lacks natural contrast for biological samples, requiring the use of heavy metal stains, while fluorescence-based imaging is limited by photobleaching and labeling specificity.

• Immunolabeling challenges in EM. Immunogold labeling is widely used to detect viral proteins, but it suffers from low labeling efficiency, steric hindrance, and antigen loss during sample preparation. Furthermore, multiple

688 labeling for co-localization studies is difficult, as different-sized gold particles must

689 be used to distinguish between various proteins.

690 • Need for new probes and staining methods. In fluorescence microscopy,

691 genetically encoded fluorescent proteins (e.g., GFP, RFP) provide high specificity

692 but may alter protein function. Chemical dyes can be non-specific, leading to

693 background fluorescence. Developing novel, brighter, and more photostable probes

694 is essential for improving virus imaging.

695 Future advancements in super-resolution microscopy and correlative imaging

696 techniques may help overcome these labeling limitations by enabling higher

697 specificity and contrast in virus imaging [38].

698 ### 6.3 Difficulties in Studying Dynamic Virus-Host Interactions

699 Virus-host interactions to be replicated in real time remain a significant issue,

700 mainly due to the incredible speeds at which viral processes are carried out and the

701 constraints at the moment on available imaging technologies. Processes like

702 membrane fusion, emission of the viral genome, and RNA synthesis are carried out

703 in a millisecond to a few seconds and are thus events stupendously difficult to image

704 through conventional microscopy. These transient dynamics not only need

705 sophisticated imaging devices with ultra-high temporal resolution but also

706 innovative approaches to preserve biological relevance with visualization.

707

708 • Imaging of fast processes like viral fusion and RNA replication. Live-cell

709 fluorescence microscopy single-virus tracking approaches have provided insights

710 into viral entry and traffic. They are hindered by limited temporal resolution,

711 photobleaching, and phototoxicity. Microscopic strategies like smFRET (single-

712 molecule FRET) and TIRF (Total Internal Reflection Fluorescence Microscopy)

713 improved the resolution but still have a hard time to image sub-second events.

714 • Blending live-cell imaging and high-resolution EM remains a challenge.

715 Correlative Light and Electron Microscopy (CLEM) has emerged as a promising

716 approach for correlating live-cell fluorescence imaging and ultrastructural EM, yet

717 it remains technically challenging and time-consuming.

718   To overcome these challenges, AI-assisted image analysis and high-speed

719 super-resolution imaging can hopefully create a more precise picture of viral

720 dynamics in the future [42].

721   6.4 Biosafety Concerns and Access to Advanced Imaging Facilities

722   Handling highly pathogenic viruses requires strict biosafety protocols, and

723 imaging availability is severely limited thereby. High-level biosafety laboratories

724 (BSL-3 and BSL-4) are needed for handling viruses like SARS-CoV-2, Ebola, and

725 Marburg virus, making the experiment difficulty and resource demand higher.

726 • Working with highly pathogenic viruses (e.g., SARS-CoV-2, Ebola). Cryo-EM,

727 live-cell imaging, and super-resolution microscopy require special containment

728 measures to prevent exposure. Fixation and inactivation methods must be optimized

729 to preserve viral structure while ensuring biosafety.

730 • Requirement of high-containment biosafety facilities for imaging. Imaging

731 infectious viruses in a living form require access to BSL-3 or BSL-4 level facilities,

732 which are available only at centers of special expertise. Some imaging techniques

733 such as cryo-EM and FIB-SEM also require expensive instrumentation available

734 only   at   premier   institutes.

735

736   To overcome these limitations, other virus models such as pseudoviruses and

737 virus-like particles (VLPs) are underway to utilize for imaging studies under lower

738 biosafety conditions. Certain initiatives towards developing more accessible

739 imaging core facilities also help in democratising the access of advanced virus

740 imaging technologies [6].

741   Conclusion

742   Imaging techniques have transformed virus-cell interaction research, enabling

743 scientists to track viral entry, replication, assembly, and host response with

744 unprecedented resolution [68]. Light microscopy, including fluorescence and super-

745 resolution microscopy, has provided real-time viral dynamic information, whereas
746 electron microscopy (EM) methods have yielded high-resolution structural
747 information on viral particles and replication sites. The correlative application of
748 imaging modalities has also bridged the gap between molecular and ultrastructural
749 virology and has yielded a composite picture of viral infection [41].
750 Despite these advances, there are still some challenges, for instance, in achieving an
751 optimum resolution-sample preparation trade-off, enhancing labeling efficiency,
752 and capturing fast virus-host interactions. Biosafety level high-containment
753 requirements for imaging highly pathogenic viruses also impose accessibility
754 restrictions. However, ongoing development of AI-driven image analysis,
755 nanotechnology-based imaging probes, and high-speed live-cell imaging will bypass
756 many   of   these   restrictions   [53].
757 Moving ahead, the future of viral imaging lies in integrating multiple imaging
758 modalities with computational and molecular approaches to obtain an even more
759 comprehensive and dynamic view of viral infection [1]. By continuing to advance
760 imaging approaches and overcome current challenges, scientists will certainly
761 continue to clarify important details of viral pathogenesis, which will in turn aid in
762 the development of effective antiviral therapies, vaccines, and diagnostics.

РИСУНКИ

Fig 1. Imaging methods utilized to investigate virus-host interactions throughout the viral life cycle. The illustration presents the RSV, a negative-sense single-stranded RNA (–ssRNA) enveloped virus, replication cycle as a model.
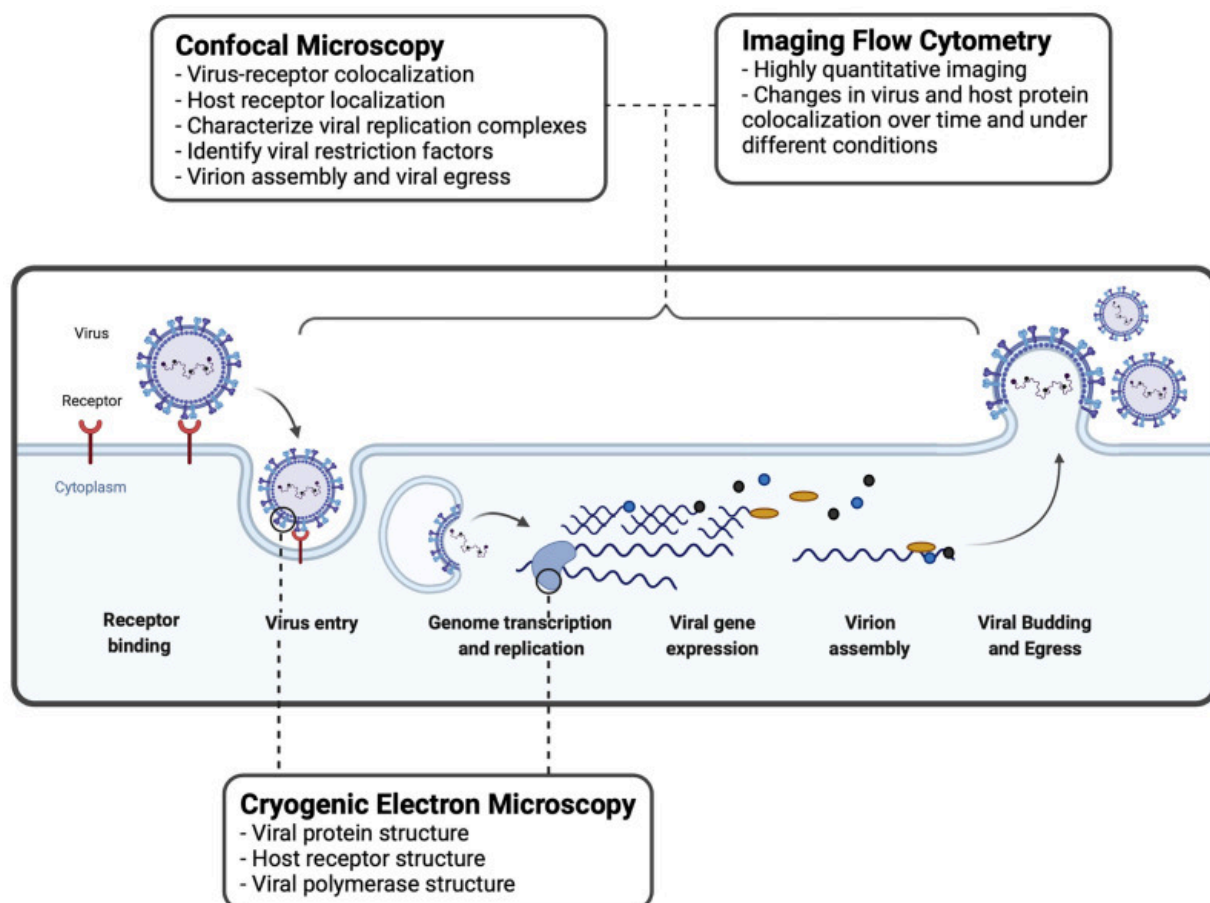
ТИТУЛЬНЫЙ ЛИСТ_МЕТАДАННЫЕ

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IMAGING TECHNIQUES FOR STUDYING VIRUS -CELL INTERACTIONS
МЕТОДЫ ВИЗУАЛИЗАЦИИ ДЛЯ ИЗУЧЕНИЯ ВЗАИМОДЕЙСТВИЯ ВИРУСОВ И КЛЕТОК

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Блок 3. Метаданные статьи

IMAGING TECHNIQUES FOR STUDYING VIRUS-CELL INTERACTIONS: A REVIEW OF CURRENT METHODS AND CHALLENGES

МЕТОДЫ ВИЗУАЛИЗАЦИИ ДЛЯ ИЗУЧЕНИЯ ВЗАИМОДЕЙСТВИЙ ВИРУС-КЛЕТКА: ОБЗОР СОВРЕМЕННЫХ МЕТОДОВ И ПРОБЛЕМ

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МЕТОДЫ ВИЗУАЛИЗАЦИИ ДЛЯ ИЗУЧЕНИЯ ВЗАИМОДЕЙСТВИЯ ВИРУСОВ И КЛЕТОК

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Ключевые слова: молекулярные механизмы, просвечивающая электронная микроскопия, вирус, методы визуализации, криоэлектронная томография, микроорганизмы.

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