

Review

# Astrochemistry of the Molecular Gas in Dusty Star-Forming Galaxies at the Cosmic Noon

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**Abstract:** Far-infrared and submillimeter observations have established the fundamental role of dust-obscured star formation in the assembly of stellar mass over the past  $\sim 12$  billion years. At  $z = 2-4$ , the so-called “cosmic noon”, the bulk of star formation is enshrouded in dust, and dusty star-forming galaxies (DSFGs) contain  $\sim 50\%$  of the total stellar mass density. Star formation occurs in dense molecular clouds, and is regulated by a complex interplay between all the ISM components that contribute to the energy budget of a galaxy: gas, dust, cosmic rays, interstellar electromagnetic fields, gravitational field, and dark matter. Molecular gas is the actual link between star-forming gas and its complex environment: much of what we know about star formation comes from observations of molecular line emissions. They provide by far the richest information about the star formation process. However, their interpretation requires complex modeling of the astrochemical networks which regulate molecular formation and establish molecular abundances in a cloud, and a modeling of the physical conditions of the gas in which molecular energy levels become populated. This paper critically reviews the main astrochemical parameters needed to obtain predictions about molecular signals in DSFGs. Molecular lines can be very bright compared to the continuum emission, but radiative transfer models are required to properly interpret the observed brightness. We review the current knowledge and the open questions about the interstellar medium of DSFGs, outlining the key role of molecular gas as a tracer and shaper of the star formation process.

**Keywords:** ISM; dusty star-forming galaxies; astrochemistry

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## 1. Introduction

The first detection of high-redshift dusty star-forming galaxies (DSFGs) dates back to the SCUBA observations in the late 1990s [1–3]. It soon became clear that they constitute a cosmologically significant population of galaxies at  $z = 2-4$ , appearing extremely bright in the submm and IR ( $S_{870\ \mu\text{m}} \geq 1$  mJy, with typical  $L_{\text{IR}} \sim 10^{12} L_{\odot}$ ), but nearly invisible in the optical [4–10]. The brightest of these galaxies have infrared luminosities exceeding  $10^{13} L_{\odot}$ . Because of this, DSFGs were formerly known as submillimeter galaxies (SMGs). The impressive infrared luminosity of DSFGs reveals star formation rates (SFRs) as high as a few  $10^2-10^3 M_{\odot} \text{ yr}^{-1}$  [11,12].

The widespread interpretation is that SMGs are dominated by short-lived and extreme burst events, in which the high rate of star formation is accompanied by the rapid production of large amounts of dust. The dust grains in the interstellar medium (ISM) surrounding active star-forming regions are heated mostly by UV light from massive, young stars, and then cooled down via thermal emission of infrared radiation, producing the typical intense IR brightness observed (redshifted, at high  $z$ , to far infrared (FIR) and submm wavelengths), while obscuring 95% of the stellar emission (see, e.g., [9,13] for extensive reviews).

In the last two decades, a huge effort has been devoted to perform higher-resolution and multiband observations of DSFGs, which became available thanks to the advent of facilities such as the Acatama Large Millimeter Array (ALMA), Northern Extended Millimeter

Array (NOEMA), VLA, South Pole Telescope, Spitzer, *Herschel*, and the most recent James Webb Space Telescope. Ever deeper and wider look-back surveys allowed a fairly robust outline of the cosmic history of star formation (SF) to be established, which culminated at  $z \sim 2\text{--}3$  (10 billions year ago, or a few Gyrs after the Big Bang: often nicknamed the “cosmic noon”). At cosmic noon, the bulk of star formation activity is strongly enshrouded in dust (see, e.g., [9,14]), and chiefly dominated by the most luminous and massive DSFGs (with  $L_{\text{IR}} > 10^{12} L_{\odot}$ ), with DSFGs containing  $\sim 50\%$  of the total stellar mass density [15].

Furthermore, the redshift evolution of the cosmic SFR density remains dominated by dust-obscured SF at least over the past  $\sim 12$  billion years, back to  $z \sim 4$  [15–17].

Thus, characterizing the star formation process in the DSFGs population is of paramount importance to understand the stellar mass assembly of the young Universe: what triggered the fast, intense burst of star formation observed at the “cosmic noon”, and which is the mechanism that eventually quenched it? Despite two decades of observations and modeling, a unique explanation is not yet available. Star formation is the result of the interplay between diverse, though interconnected, complex physical processes occurring in the many phases of the interstellar medium (ISM) and intergalactic medium (IGM), eventually culminating in the fragmentation and collapse of molecular clouds (e.g., [18–20]): with the possible exception of population III stars, SF is ultimately fueled by molecular gas. Several global-scale and local-scale galactic parameters compete in the SF process and in shaping the initial mass function (IMF), such as dust, gas and stellar content, gas kinematics, environment and local radiation fields, magnetic fields, global and local cosmic ray flux, metallicity, balance of heating and cooling, and infall of cold gas from the IGM (see, e.g., [21–24]). Molecular clouds, potential cradles of stars, are supported by magnetic fields and turbulence against gravitational collapse, but the knowledge of the processes ruling the clouds’ lifecycles and their star formation efficiency (defined as the star formation rate per unit of interstellar gas) remains an open question [25].

Thus, the ultimate question necessarily involves the molecular component of the ISM (e.g., [26,27]): in which respects is the molecular gas of local star-forming galaxies (ULIRG and LIRG) different from that of high-redshift DSFGs? Is star formation described by a universal law which applies to different galaxy populations? How can the observation of molecular lines help in answering these questions? The answer requires a proper characterization of the diffuse and dense molecular ISM phases at high redshifts, which is generally observed through rotational transitions of the most abundant “tracer” molecules, whose brightness can still be detected even at high  $z$ .

Diagnostics based on molecular line intensities, and on their ratios, address the comparison between spectral observations and models of line emission from key molecular species, both in dense clouds and in the diffuse molecular medium. In turn, this requires an accurate numerical solution of the radiative transfer problem, implying the characterization of a plausible physical environment in which the emitted line radiation propagates. But this is still not sufficient: line intensity ratios between different molecular species may suffer from a degeneracy between excitation effects and abundance effects, even when they arise from the same physical region in the host galaxy. It is then necessary to provide a solid astrochemical model to predict the relative molecular abundances in a given environment and to compare them with real data. Since the discovery of the first interstellar molecules CH, CN,  $\text{CH}^+$  [28–30], hundreds of molecules and isotopologues have been detected, including the breakthrough discovery of complex organic molecules throughout the Milky Way and in nearby galaxies, as well as in some distant quasars, which opened new scenarios for the emergence of life on exoplanets (e.g., [31–37]). To date, several galaxies have been mapped with the emission lines of diatomic or more complex molecules. In particular, in the last two decades, DSFGs have been extensively observed in their dust continuum emission and in the CO [32,38–49],  $\text{H}_2\text{O}$ , neutral carbon, and [CII] emissions [50–58], while only a few detections of HCN have been established to date [27,59].

Stacked spectra of DSFG samples have been obtained by [60] (in which the average mm/submm rest-frame spectrum was constructed by stacking the ALMA spectra of

22 gravitationally lensed sources, spanning a redshift range of  $z = 2.0$ – $5.7$  and rest-frame frequencies of 250–770 GHz, or  $\lambda = 0.39$ – $1.2$  mm) and by [61], who built the average far-infrared spectra of a sample of 36 DSFGs at  $0.8 < z < 4$  with rest-frame frequencies of 1400–6200 GHz ( $\lambda = 48$ – $214$   $\mu\text{m}$ ). The analysis of FIR stacked spectra for the highest-redshift sources allows general information to be obtained about the typical state of the ISM in DSFGs, and it is suggestive of an intense FUV field dominating the diffuse gas (a factor of  $10^3$ – $10^5$  higher than the Milky Way FUV field) and of an average density of the neutral gas of about  $10^{4.5}$ – $10^{5.5}$   $\text{cm}^{-3}$ . The stacked submm spectrum revealed, for the first time at those high redshifts, the emission from the hydride CH and the linear molecule CCH, which may turn out to be important probes of astrochemistry in DSFGs. Furthermore, the stacking technique allowed the detection of emissions from the high-density molecules HCN, HNC,  $\text{HCO}^+$ , and CS, often elusive in observations of single sources at that redshift.

In some cases, relatively detailed observations of single sources were made possible thanks to the size stretching and intensity amplification offered by a foreground gravitational lens.

In parallel, astrochemistry underwent a major development, pushed by the need to identify the main mechanism driving the molecular enrichment in diverse ISM environments. The huge effort of the astrochemistry community has led to the identification of the main chemical reaction networks and their reaction rate coefficients, corresponding to the main physical driver of the reactions and, ultimately, to the physics of the ISM.

The first attempts to solve gas-phase and grain-surface chemical reaction networks in physical environments representative of external galaxies date back to the works of [62,63]. In order to decipher the information hidden in spectral lines from high- $z$  DSFGs, the methodology clearly needs to be reviewed with respect to the local observations. While sticking to the universality of the underlying physical chemistry, unlensed DSFGs' molecular lines represent source-integrated signals, showing up as surface-averaged molecular line fluxes. Thus, a drawback of extrapolating the local astrochemical fundamentals to the extragalactic context lies in the misleading use of the so-called “molecular tracers”: while the emission line fluxes of selected molecules, and their ratios, may be locally suggestive of specific ISM physical conditions (such as a high or low density, aligned with the critical density of the molecular transition line, or an interstellar radiation field dominated by the extreme emission of an active galactic nucleus), the unresolved emission from a distant galaxy will necessarily mix and integrate molecular emissions from different regions of the galaxy, plausibly pertaining to different ISM phases. The unavoidable lower resolution, with respect to nearer, local sources, forces us to put effort into simplifying the problem, e.g., waiving the detailed analysis of the individual hot cores or corinos, and trying to analyze clusters of forming stars, giant molecular clouds, and diffuse molecular components in a statistical, averaged way. The starting point, however, is the characterization of the ISM in which molecular clouds emerge.

If the evolution of each galaxy is a tale of star formation, then the exploitation of galaxy evolution cannot overlook the physics and chemistry of the ISM. In this respect, galaxy evolution is a tale of the ISM, and, ultimately, a tale of how molecules are built out of elements.

Here, we want to provide some considerations to be accounted for when using astrochemical networks to model the molecular abundances in high-redshift DSFGs. The main question behind it is what is peculiar in the ISM of high- $z$  DSFGs with respect to the local star-forming galaxies, with an emphasis on the molecular gas: trivially, they are at higher redshifts than the Milky Way, so the CMB radiation was warmer than today; they have high rates of star formation, which means that the interstellar radiation field and the flux of cosmic rays are stronger than they are in quiescent galaxies, which plausibly deeply affects the molecular abundances; they harbor large amounts of dust, which catalyzes molecular formation on grain surfaces, affecting the gas-phase molecular abundances, and regulates, through continuum opacity, the onset of cosmic rays as chemical drivers at large enough optical depths in clouds.

We review some of the ISM characteristics in DSFGs at cosmic noon, as they emerge from observations, the influence of the environmental ISM in the molecular abundances, and the open questions that need to be solved in order to obtain reliable information from molecular observations in such extreme environments.

The structure of the paper is the following: in the first part (Sections 2–5), we present an overview of the ISM environment of high- $z$  DSFGs: in Section 2, we discuss the impact of the CMB temperature at cosmic noon on the molecular emission lines; in Section 3, we characterize the far-UV interstellar radiation field; in Section 4, we describe the role of cosmic rays as drivers of astrochemistry in the molecular clouds where the FUV field is attenuated, discussing observations and molecular signatures of cosmic ray ionization; and in Section 5, we describe the fundamental role of dust grains on the physics and chemistry of DSFGs. The second part of the paper summarizes the state-of-the-art in theory and observations of the principal molecules detected in high- $z$  DSFGs' molecular gas:  $H_2$  and CO in Section 6, water vapor in Section 7, and dense gas tracers in Section 8. Finally, in Section 9 we conclude with our final remarks.

## 2. The Effect of the CMB on the Molecular Gas of High- $z$ Galaxies

The standard hot Big Bang model predicts the linear increase with redshift of the cosmic microwave background (CMB) temperature, as a consequence of the adiabatic expansion of the Universe. As CMB photons propagate along null geodesics, the CMB temperature varies as  $T_{\text{CMB}} = T_{\text{CMB}}^0 \times (1 + z)$ , where the current value  $T_{\text{CMB}}^0 = 2.7251 \pm 0.002 \text{ K}$  [64] corresponds to a blackbody spectrum peaking at  $\nu_{\text{max}}^0 \sim 2.82 kT/h \sim 160 \text{ GHz}$ . At  $z = 4$ , this corresponds to  $T_{\text{CMB}} = 13.625 \text{ K}$  and to a blackbody spectrum peaking at  $\sim 800 \text{ GHz}$ .

The energy density of blackbody radiation, integrated over all the spectrum, is given by  $u(T) = a T^4$ , with  $a$  being the Stefan–Boltzmann constant  $a = 7.56 \times 10^{-15} \text{ erg cm}^{-3} \text{ K}^{-4}$ .

The current value of the CMB energy density is  $u = 4.19 \times 10^{-13} \text{ erg cm}^{-3}$ : in the Milky Way, the CMB dominates the galactic spectrum above 1 GHz and up to  $\sim 500 \text{ GHz}$ , where thermal emission from dust at  $T_{\text{dust}} \sim 18 \text{ K}$  takes over. Since the CMB energy density scales as  $T_{\text{CMB}}^4 \propto (1 + z)^4$ , in galaxies at, e.g.,  $z \sim 3$ , it was larger than its current value by a factor  $> 200$ . Similarly, the number density of blackbody photons, integrated over all the spectrum, scales as

$$n_{\gamma} = 16\pi\zeta(3) \left( \frac{kT}{hc} \right)^3 \quad (1)$$

where  $\zeta$  is the Riemann function, which has  $\zeta(3) \approx 1.202$ . From the above scaling relations, we should expect the CMB to have an impact on high- $z$  galaxies already at cosmic noon.

The CMB temperature sets the fundamental minimum temperature of the ISM (assuming local thermal equilibrium) and can affect the physical conditions of dust and gas, in particular in the molecular ISM. For instance, a remarkable thermometer of the CMB temperature in the Milky Way is the CN molecule [65–67].

A higher CMB temperature has two competing effects on the physics of molecular clouds: on one hand, the higher dust and gas temperatures correspond to a boosted luminosity of emission lines and of the dust continuum [68–71]. On the other hand, the warmer CMB builds a stronger background against which the dust continuum and emission lines are detected [70,72–75]: at increasing  $T_{\text{CMB}}$ , the thermal equilibrium between the CMB, the cold gas, and the dust progressively erases the spectral contrast which makes dust and line emissions detectable.

A full exploration of the CMB effects on the observability of emission lines and the dust continuum is presented in [76], with an emphasis on the carbon monoxide (CO) lines. Indeed, CO rotational levels have energy differences which are close to  $kT_{\text{CMB}}$  at high redshift; in general, if the molecular gas is permeated by a bath of photons whose frequencies are distributed according the Planck law for a blackbody at temperatures of about 13 K, there will be a large number of photons in the Rayleigh–Jeans tail of the distribution that may pump rotational levels of CO,  $H_2O$ , and other molecules frequently detected in the high- $z$  DSFGs. Ref. [76] found that the dominant effect is that of attenuating

the observed line and continuum flux because of the enhanced brightness temperature of the background. Neglecting the influence of the CMB effect on molecular-level populations and radiative transfer can result in errors of a few percent when estimating intrinsic line fluxes. For instance, using line fluxes, such as CO(1–0) or CO(2–1), to trace molecular gas mass can lead to inaccuracies in interpreting molecular gas properties, including total mass, density, and temperature. However, this effect, which is limited to millimeter/submillimeter wavelengths, cannot be addressed easily [77]. The impact of CMB temperature on high- $z$  observations has been treated numerically in the work of [78] in order to explain the observed deviations, at  $z \gtrsim 1.5$ , from the Gao–Salomon relation, which strongly correlates the FIR and HCN(1–0) luminosities over more than 10 orders of magnitude in the local universe. Ref. [78] concludes that the CMB is unlikely to explain the deviations reported in the literature, under reasonable conditions. However, the strength of the CMB effect is extremely sensitive to the kinetic temperature, density, and optical depth of the gas. The CMB attenuation of HCN line intensities has also been explored by [27] as a possible reason for the scarcity of HCN detections in DSFGs at cosmic noon (see Section 8): an attenuation of  $\sim 10$ – $30\%$  was found for a DSFG sample at  $z \sim 3$ , bringing them to the conclusion that, up to  $z \sim 3$ , the effect of the CMB on HCN detectability is almost negligible.

Another aspect that should be taken into consideration is the potential impact of enhanced dust temperature on the grain surface chemistry and on the desorption rates of species formed on grain ice mantles [79]. In the Milky Way, complex organic molecules have been detected in the gas phase of cold, prestellar cores [80], suggesting that desorption mechanisms can also be effective at low temperatures [81]. To date, this effect has not been investigated in high- $z$  galaxies yet.

### 3. Interstellar Radiation Field

Photodissociation regions (PDRs; also known as photon-dominated regions) are responsible for most of the IR radiation in galaxies. They consist of predominantly neutral gas and dust illuminated by far-ultraviolet (FUV) photons ( $6 < h\nu < 13.6$  eV) of the interstellar radiation field. In PDRs, heating and chemistry are dominated by FUV photons [82], which are attenuated in the denser, more obscured inner parts of a molecular cloud, where the chemistry is initiated by cosmic rays [83,84]. It is frequently assumed that the higher the SFR, the higher the unattenuated intensity of the FUV radiation field  $\chi$  will be [85] (and, as discussed in Section 4, the CR ionization rate is expected to increase in a similar fashion). However, attenuation is strongly related to the dust content per parcel of gas. Assuming a constant gas-to-dust ratio of 100, and that the dust grain column density scales linearly with metallicity, Ref. [86] shows that a visual attenuation  $A_V$  of a few tens can already be attained at densities  $n_H = 10^5$  cm $^{-3}$ . Thus, the dust component efficiently shields the dense gas from the ionizing FUV field which, in high- $z$  DSFGs, can be as high as  $\sim 10^5 \chi_0$  [55,87], with  $\chi_0$  being the Draine FUV field<sup>1</sup> [88]. The analysis of the FIR stacked spectrum of high- $z$  DSFGs presented in [61] is consistent with a value of the interstellar radiation field in PDR regions which is at least a factor of  $10^3$ – $10^5$  larger than the Milky Way. Despite the higher rates of star formation and of FUV radiation with respect to quiescent galaxies, high- $z$  DSFGs appear to be well shielded against the FUV field thanks to the large dust-to-stellar mass ratio, which, for this galaxy population, lies above local spirals and ULIRGs [89,90]. The consequences of the dust shielding on the molecular enrichment will be discussed in Section 5.

### 4. The Far-Reaching Effect of Cosmic Rays on Star Formation

In general, the interstellar radiation field impinging on a cloud is dominated by the UV radiation emitted by the more massive stars; as the most energetic photons are retained within the HII regions surrounding the brightest stars, the energy of the ionizing photons permeating the neutral ISM is lower than the hydrogen ionization threshold of 13.598 eV and, importantly, lower than the ionization potential of many abundant species such as O, He, N, and molecular hydrogen. In general, these species are not photoionized in the diffuse

clouds. The FUV radiation field becomes strongly attenuated by dust as it propagates into a cloud. For this reason, only a few species (such as carbon and sulfur) in the outer shells of a cloud and in the diffuse gas will be affected by direct photoionization, thus undergoing a quite limited chemistry. In these photon-dominated regions (PDRs), the dominant source of free electrons is  $C^+$  which, through associations with  $H_2$  and dissociative recombinations, can form neutral C, CH,  $CH_2$ , and  $CH_4$ . Importantly, the fast atom–radical reaction between O and CH can be a significant route to the important tracer molecule CO. At depths of about two magnitudes in clouds in the average interstellar radiation field,  $H_2$  becomes abundant and CO becomes a significant reservoir of the available carbon.

In the densest phase of the interstellar medium, where external starlight is excluded, chemistry is instead initiated by cosmic rays (CRs), which can penetrate large column densities of gas and dust and reach the molecular cloud core, maintaining, in the mostly neutral medium, a small fraction of gas ionization, which is sufficient to drive an extremely rich chemistry [91] and to couple the dense gas to the local magnetic field. The ionization fraction observed in the galactic dense MCs ( $\sim 10^{-7}$ ) can only be explained by CRs.

The Fermi Gamma-ray Space Telescope revealed that the diffuse  $\gamma$ -ray background is dominated by star-forming galaxies [92]. The  $\gamma$ -ray emission of a star-forming galaxy depends on its SFR, which determines the supernova rate, and thus, the rate at which CRs are injected into the ISM, where CRs collide with nuclei, producing  $\gamma$  photons. This suggests that the high SFR of high- $z$  DSFGs, both main sequence and starbursts, harbor enhanced CR fluxes with respect to quiescent galaxies. Understanding the paramount role of cosmic rays (CRs) in regulating the star formation efficiency of DSFGs is straightforward. An accurate characterization of their ionization rate can explain the mechanism fueling the extreme starbursts observed at the cosmic noon. Detailed reviews on the impact of CRs in MCs can be found in [93] and [94]. Since the cross-sections of the main molecular cloud processes (dissociation, ionization, and excitation of  $H_2$ ) peak at relatively low energies, star formation processes are mainly affected by low-energy CRs ( $E < 1$  TeV) [93–98].

Below, we summarize the current status of galactic and extragalactic observations and outline the primary impact of CRs on astrochemistry and molecular gas.

#### 4.1. CR Observations at Different Redshifts

Observations through different lines of sight in the Milky Way allowed the estimation of the galactic ionization rate of hydrogen molecules by CRs,  $\zeta_{H_2}$ , as a function of the  $H_2$  amount, covering  $H_2$  column densities ranging from values typical of diffuse clouds  $N_{H_2} < 10^{21} \text{ cm}^{-2}$ , up to the densest MCs,  $N_{H_2} \sim 10^{24} \text{ cm}^{-2}$ . These estimates assumed a galactic background of CRs propagating in the ISM, with an average value of  $\zeta_{H_2} \sim 10^{-17}–10^{-16} \text{ s}^{-1}$  [96,99]. Galactic observations have been complemented with extragalactic data of the nearest starbursts NGC 253 [100,101], ARP 220 [102], Mrk 231 and, remarkably, with two strongly lensed dusty galaxies at high  $z$ , in the range  $\sim 3.5–3.9$ , made possible recently thanks to the first detection of  $H_3O^+$  at such redshifts [59]. In most galactic sources, the CR flux, as  $\zeta_{H_2}$ , follows the expected decrease with increasing column densities, as CRs dissipatively collide with  $H_2$  molecules. However, a large number of outliers are found that cannot be explained by the average galactic CR flux: namely, in the galactic center [103], in a protostellar cluster [104], and in the vicinity of a supernova remnant [105,106], where the estimated  $\zeta_{H_2}$  is up to five orders of magnitude higher than the galactic average. These findings, firstly, opened the perspective for a local origin of low-energy CR acceleration. They suggest that the observed spread in the galactic CR flux compared to the average galactic value mirrors the local star formation state, and that the latter is the primary source of low-energy CRs.

However, the exact mechanisms responsible for their production remain debated, with proposals ranging from diffusive acceleration at supernova remnant shocks [107,108] to protostellar shocks and jets [109] or other mechanisms.

Noticeably, the five observed giant molecular clouds in the local starburst NGC 253 also reveal ionizing rates of about  $1–80 \times 10^{-14} \text{ s}^{-1}$ . Higher CR ionizing rates are, finally,

also estimated for ARP 220, Mrk 231, and for the two high-redshift sources observed by [59], confirming that, up to high redshifts, star formation is directly traced by cosmic rays. Going even further, the enhanced CR flux in SF regions may be the leading actor in shaping the initial mass function towards a top-heavy trend, because of the increased CR heating, at the expense of increased destruction of molecular hydrogen and of a rich interstellar chemistry. The burst event itself may indeed prove to be a self-sustaining process, underscoring the need for a quenching mechanism on the scale of the star-forming galaxy.

#### 4.2. Molecular Signatures of CR-Dominated ISM

Since different chemical drivers (either UV-X photons or CRs) lead to different characteristic molecules through different chemical reaction networks. One key aspect to consider when modeling integrated signals from unresolved high-*z* DSFGs is that of the unknown filling factors of PDRs with respect to CR-dominated regions. Viceversa, the observation of emission lines from tracers of a specific chemistry allow one to infer the main chemical spark of the ISM chemistry.

Focusing on dense clouds, where the bulk of star formation occurs, we assume that the chemistry is started by CR ionization:  $\zeta_{H_2}$  is the parameter generally used to quantify the CR intensity while implementing an astrochemical network. As shown in [83,95], it strongly affects the physics and chemistry of the ISM in many aspects, some of which are briefly summarized below:

- **Effects on the gas temperature:**  
Cosmic rays produce ions and excited molecules, which can significantly heat the gas and produce temperature gradients in prestellar cores (see, e.g., [96,110–112] and the reviews [113,114]). In a molecular environment, the available energy goes into ionization of  $H_2$ , vibrational and rotational  $H_2$  excitation, and the kinetic energy of the outgoing electron available for secondary ionization. About 50% of the CR energy is lost in gas heating [112,115]. Embedded protoclusters can also accelerate CRs from protostellar surfaces via accretion shocks, producing CR ionization rates (and gas heating) higher than the average value of the host galaxy [116]. Due to the importance of the molecular gas temperature on the reaction rates of chemical reactions, CR heating cannot be neglected when modeling the physical environment of a chemical network [112,113].
- **$H_2$  dissociation and H abundance in molecular clouds:**  
As discussed in [97], secondary electrons from primary CR ionization contribute to  $H_2$  dissociation, increasing the fractional abundance of atomic H and resulting in the only source of atomic H in dense clouds ( $N_{H_2} > 10^{21} \text{ cm}^{-2}$ ). This can severely alter the HCO abundance, the composition of grain mantles, and the formation of complex organic molecules [117].
- **Enhancement of C/CO in dense clouds:**  
Ref. [118] showed that CR penetration in dense molecular clouds can induce electronic excitation of the absorbing gas, particularly  $H_2$ , resulting in the emission of a chemically significant UV flux. The latter can photodissociate the CO reservoir, adding to the CO destruction process by  $He^+$  and recovering atomic neutral C, thus enhancing the abundance ratio C/CO in dense gas [119,120].
- **Effects on dust grains:**  
CR-induced UV photons can significantly alter the net electric charge distribution in submicron grains [121] and regulate the photodesorption process on dust [122,123]. During the lifetimes of about  $4\text{--}6 \times 10^8$  yr of interstellar ices on dust mantles within dense molecular clouds, the long exposure to ionizing radiation (CRs or CR-induced UV photons) can modify the pristine ices, favoring the formation of complex organic molecules [124–127].
- **Ionization of  $H_2$ :**  
The most remarkable effect is the ionization of molecular hydrogen, which, through the formation of the trihydrogen cation  $H_3^+$ , initiates a chain of ion-neutral reactions

that produce a large variety of chemical species. This pivotal ion is destroyed in diffuse clouds by dissociative recombination, and in dense clouds by a proton-hop reaction with the CO molecule. A more direct estimate of  $\zeta_{H_2}$  can be obtained by measuring the  $H_3^+$  column density (e.g., [128]) and either the CO abundance (in dense clouds) or the ionization fraction and the  $H_2$  fraction (for diffuse clouds), together with an estimate of the depth  $L$  of the cloud along the line of sight.

- **CR effects on oxygen chemistry:**

In diffuse clouds and at the edges of dark clouds, where there is still a non-negligible fraction of atomic H, CRs can ionize H, starting the oxygen chemistry. In dense clouds, the oxygen chemistry follows the  $H_3^+$  route, where the oxygen network is triggered by the CR ionization of  $H_2$ . In both cases, through a number of charge-transfer and abstraction reactions, this culminates with the dissociative recombination of  $H_3O^+$  into water and the hydroxyl radical, OH. The latter can then be used as a tracer of the CR ionization rate whenever CRs dominate over UV ionization. Intermediate ions of this reaction chain are the hydride cations  $OH^+$ ,  $H_3O^+$ , and  $H_2O^+$ : their use as CR tracers began following their detection by the Herschel Space Observatory [99,129,130].

- **Hydrogen deuteride, HD:**

In CR-dominated clouds, CR determines  $H^+$  formation, which defines the  $D^+$  abundance through charge-exchange reactions. HD is then produced by the fast ion–molecule reaction  $H_2 + D^+ \rightarrow HD + H^+$  [131,132]. HD is the main deuterium reservoir in molecular clouds. The HD abundance can then be used to infer the CR ionization rate of atomic hydrogen, which is slightly different than that for  $H_2$  [133].

- **Deuterium fractionation:**

Deuterium fractionation starts with the formation of the protonated molecular hydrogen  $H_3^+$  and its isotopic exchange with the HD molecule, which leads to  $H_2D^+$ . In low-temperature (<100 K) dense clouds, the endothermicity of the reverse reaction unbalances the number density ratio  $n(H_2D^+)/n(H_3^+)$  towards much larger values with respect to the cosmic elemental ratio  $n(D)/n(H) \sim 1.6^{-5}$ .  $H_2D^+$  is mainly destroyed by proton-hop reactions with CO, producing  $DCO^+$ , and by dissociative recombination. Similarly,  $H_3^+$  protonates CO to form  $HCO^+$ . It is possible to relate the deuterium fractionation of  $HCO^+$ , i.e., the ratio between the number densities  $n(DCO^+)/n(HCO^+)$ , to  $\zeta_{H_2}$ , making these two species important tracers of the CR effect on dense clouds [134–136].

## 5. Dust and Metallicity Environment of DSFGs' Molecular Clouds

A key parameter of any astrochemical modeling of molecular enrichment is the metallicity of the atomic environment out of which molecular clouds originate. High gas-phase metallicities promote the chemical production of oxygen-bearing and carbon-bearing molecular species, and, importantly, set the physical environment for dust production. Metals are added, removed, and redistributed in the ISM by star formation, supernovae, and winds, and are partially depleted from the gas phase through the condensation into dust grains. Estimates of metallicity ( $Z$ ) at high  $z$  are always extremely complicated and strongly affected by systematics due to calibration methods, which can vary the metallicity estimates, even by 0.7 dex [137]. What is nowadays accepted by the scientific community is that, from a statistical point of view, metallicity increases with the (total) stellar mass and decreases for increasing redshifts. The rapidity of this decrease, and its causes, are not yet completely understood. First observations pointed to a rapid decrease in  $Z$  at increasing redshifts for a fixed stellar mass. More recent works seem to suggest a slower decrease [138] and, importantly, that this decrease is related to the SFR rather than to the redshift. In other words, for a fixed stellar mass, galaxies with progressively higher SFR are selected at increasing  $z$ , and the SFR is observed to be anticorrelated with metallicity [139,140]: the  $Z$  evolution with redshifts can, thus, be described in terms of the SFR.

We outline that the above picture gives a statistical view: the *average* cosmic metallicity decreases at higher redshifts because the average is dominated by many “small” (low total stellar mass) and metal-poor galaxies.

The situation is different when focusing on single objects (as DSFGs) since, ultimately, the metallicity is regulated by the combination of inflows of metal-poor gas, outflows of enriched material, and star formation. Almost all models predict an initial rapid increase in metallicity, up to the achievement of a saturation level, a sort of equilibrium value of  $Z$  where inflows, outflows, and star formation are balanced [23,141,142]. This equilibrium value depends on the metallicity of the inflow, on the mass-loading factor (which measures the efficiency of outflows in removing gas from the galaxy relative to the formation of stars), and on the SFR (the relative importance of these factors in determining  $Z$  has been the subject of numerical simulations in [143]). The point is that, in general, at any redshift there are, as a matter of fact, some galaxies which are more dusty and more metal-rich than the Milky Way, and this does not conflict with the cosmic trend, mentioned above, of an average metallicity decreasing at increasing  $z$ . As an explanatory example, we mention the observations of a sample of 30 distant quasars ( $z \sim 6$ ) by [144], in which the inferred metallicity of the host galaxies is as high as several times the solar metallicity.

The value of gas metallicity in high- $z$  DSFGs is still a matter of debate [90,145,146]. This is because in heavily dust-enshrouded galaxies metallicity diagnostics relying on rest-frame optical emission lines are not usable. However, observations of the FIR fine-structure emission lines [NII] 205  $\mu\text{m}$ , [CII] 158  $\mu\text{m}$  [147], [OI] 145  $\mu\text{m}$ , [OIII] 158  $\mu\text{m}$  [148], and of  $H_\alpha$  and [NII] 658.4  $\mu\text{m}$  [149], suggest that SMGs at  $z \sim 4$  are already chemically enriched nearly to the solar metallicity as a result of a rapid metal enrichment in the early phase of star formation. Recently, JWST observations delivered the first spatially resolved maps of gas-phase metallicity for two gravitationally lensed dust-obscured star-forming galaxies at  $z \sim 4$  [149], showing that dust surface density and gas surface density have spatial variations positively correlated with metallicity. This indicates that regions containing more gas and dust are also more metal-rich. The spatially averaged metallicity in the sample of [149] is conservatively estimated to have a value of  $Z \sim 0.7 Z_\odot$ . Of course, the average galactic metallicity is expected to follow the SFH and evolve on a timescale set by galactic dynamics [150], while the evolution of gas metallicity within a single molecular cloud evolves on the shorter timescales of the cloud’s lifecycle [25]. A star-forming galaxy is expected to host molecular clouds at different stages of their evolution, from starless, dark clouds to protostellar cores. These clouds may originate from atomic gas with differing metallicities. The statistical distribution of clouds’ evolutionary stages and of the environmental metallicity should be taken into account when modeling the integrated signal from high- $z$  DSFGs.

In addition to the gas metallicity, an important parameter needed to model the molecular enrichment in a cloud is the value of the  $M_{\text{dust}}/M_{\text{gas}}$  ratio,  $\delta_{\text{DGR}}$ , as it determines the opacity in a parcel of gas, thus regulating the chemical driver of molecular formation, as well as the amount of grains available for surface chemistry. We know that high- $z$  DSFGs are dust-rich, with dust-to-stellar mass ratios ( $M_{\text{dust}}/M_*$ ) higher than in spiral galaxies (by a factor of  $\sim 30$ ) or ULIRGs, and that they are gas-rich, with gas fractions ( $M_{\text{gas}}/M_*$ ) approaching 50% [151]: indeed, the high  $M_{\text{dust}}/M_*$  ratio plausibly mirrors their high gas content [89,90]. The findings outlined in [149] indicate that within each resolved region of the observed DSFGs the dust-to-gas ratio tends to increase with higher metallicity. This trend mirrors findings observed in local galaxies. Additionally, when spatially averaged, this ratio is found to be moderately lower than the canonical value typically adopted for local ULIRGs ( $\delta_{\text{DGR}} \sim 1/100$ , [152]), a result also discussed in [90]. What is relevant for our purposes is to note that, taken individually, the resolved ( $\sim 0.7$  Kpc) regions of [149] span about one order of magnitude in  $\delta_{\text{DGR}}$ , confirming that molecular clouds, with sizes spanning the range of 10–100 pc, are caught in different environments/evolutionary stages, where the timescale of evolution refers to the molecular cloud’s lifecycle (10–30 Myr, [25]): no single astrochemical model can fit the whole galactic signal, making it necessary to

use a statistical approach in the astrochemical modeling of high- $z$  galaxies' molecular abundances. The dominant provider of dust remains unclear: whether it is AGB stars, SNe, star-forming regions, or the processing coagulation and growth of dust facilitated in metal-rich gas is yet to be determined [153–155].

We know that dust is a fundamental player in the physical and chemical processes occurring in the ISM (see, e.g., [156]). In the ISM, dust grains show up as bare grains of refractory materials or covered by an ice mantle, depending on the environment. In diffuse clouds (50–100 K), the effect of the UV radiation favors the presence of bare grains, whereas ice mantles are typical in colder, shielded clouds. It is widely believed that dust grains divide into two main classes depending on their chemical composition: one carbon-based; and one dubbed “astronomical silicates”, dominated by O, Fe, Si, and Mg. Usually, the silicate class is represented by one elemental partition of olivine, namely,  $\text{MgFeSiO}_4$ . The most studied effects of dust in affecting galaxy evolution are the reprocessing of stellar radiation and the depletion of ISM metals (e.g., [157,158]). However, detailed dust properties, such as composition and size, can only be constrained by measured extinction curves along different sightlines, which are available, to date, only for the Milky Way and the Magellanic Clouds (e.g., [159]). Furthermore, these basic properties depend on the environment (i.e., they are not homogeneous throughout a galaxy's volume) and evolve with time. On the other hand, the composition and, even more, the size distribution of dust grains strongly affect the molecular formation rates through surface astrochemistry: for a fixed total mass of dust grains, smaller grains provide a larger surface area where molecules can form (in particular,  $\text{H}_2$ ), rapidly diffuse, and react, acting as a third body to dissipate the energy released in exothermic bond formations, and catalyzing reactions needing the activation barrier to be lowered (e.g., [81,160]). Only in the last decade has a complete treatment of grain size distribution for carbonaceous and silicate dust begun to be investigated through semi-analytical or numerical simulations [161], marking the beginning of the “dust cycle” models.

The general trend arising from the first studies is that dust *seeds*, produced via stellar channels (outlined later in this section), evolve from an initial distribution dominated by large grains ( $\gtrsim 0.1 \mu\text{m}$ ) to a broad size distribution, numerically dominated by small-radius grains. The size evolution can be followed reasonably well just considering two representative sizes, referred to as “large grains” and “small grains”, whose limiting radius is set at  $\approx 0.03 \mu\text{m}$  [162]. This simplification allowed the development of more sophisticated numerical simulations of dust evolution (e.g., [163,164] and references therein). The dust cosmic lifecycle mainly starts in the ejecta of evolved stars of mass  $\lesssim 8 M_{\odot}$  (the asymptotic giant branch, AGB, stars), and in their later evolutionary stages, in planetary nebulae, and in SNI (possibly also in SNIa explosions). In the hot circumstellar atmospheres of the AGB stars, the primary dust formation, forming grains with sizes from a few to tens of nanometers, occurs in the gas phase: the atmosphere is rich in carbon, oxygen, and silicon, which form in the stellar core and are ultimately dredged up to the stellar surface thanks to multiple convections of the stellar hot plasma. In oxygen-rich AGB stars' atmospheres, where  $n(\text{O})/n(\text{C}) > 1$ , carbon is predominantly trapped in CO: the formation of carbonates requires that three oxygen atoms are available for each C atom in the carbonate, but the extremely high bond energy of the CO molecule implies that this cannot happen in a carbon-rich element mixture if the oxygen is completely consumed by CO formation, so that oxygen atoms react with silicon and any other metals, forming amorphous and crystalline oxide and silicate grains [165,166]. Instead, carbon-rich stars, where the ejecta have  $n(\text{O})/n(\text{C}) < 1$ , are assumed to condense only graphite or amorphous carbon grains. Thus, primary grains consist of either carbonaceous materials [167,168] or silicates (refractory materials, [169]), depending on the C/O ratio in the gas phase where dust grains nucleate and form: the production of carbonates or silicates is mutually exclusive in AGB winds. In a single stellar population, stars with  $\sim 8 M_{\odot} < M < \sim 50 M_{\odot}$  undergo core collapse in a type II supernova already after  $\sim 5$  Myr. In type II SN, dust grains can nucleate and condense already in the heavy-element-rich mantle: in an onion-like model there is no molecular intermixing

between C and O layers, and SNe may produce both carbonate and silicate grains [170]. In contrast to AGB stars, in the outflows produced by SNe II and Ia explosions carbon and silicate dust can condense at the same time [171]. The classical picture is that the main contributors to carbonated dust are low-mass AGB stars [172], whereas SNe II are the main contributors of silicates in the ISM [173]. It is, however, important to outline that the subsequent thermal pulsations in AGB stars (due to the explosive ignition of the helium shell) cause multiple phases of dredging up, able to turn an O-rich giant into a C-rich one, and that, in general, the overall yield of dust in SNe and AGB stars is still highly unknown. For example, detailed nucleation calculations by [165] and [155] show that the dust yields from AGB stars are largely overestimated [174]. In any case, the dust cycle starts with the ejecta of AGB stars or SN, with the primary grains or “dust seeds”, consisting of large grains [175,176]. Once they are injected into the ISM, the primary grains undergo a series of physical processes able to change both their composition and their size: gaseous metal atoms can stick to the surfaces of the grains. Being a surface process, this accretion is particularly relevant for small grains, having a larger total area per unit mass. Accretion changes the size and composition of small grains. Grain–grain collisions can produce coagulation (when the collision occurs at low velocities, such as in the dense, cold ISM) or shattering (for high-velocity impacts), expected in the diffuse ISM: the former acts a source of large grains and a sink of small grains, and vice versa for the shattering. Sputtering is another surface process, thus relevant on small grains, due to the erosion of the grains by ions in the gas phase. This erosion can be due to collision with energetic ions or by SN shocks, with extreme effects bringing about total grain destruction, and dominates the hot plasma at  $T \gtrsim 10^5$  K. Astration is the last step of the dust cycle, returning processed dust to the stellar component.

It is obvious that the size distribution and composition, at a given evolutionary stage of a galaxy, is not easily predictable and requires accurate simulations of the above-mentioned opposing effects. The most recent simulations by [164] refer to objects with a dark matter halo mass up to 3 times that of the Milky Way (which is  $\sim 10^{12} M_{\odot}$ ), showing that, at a representative “cosmic noon” redshift of  $z \sim 3$ , or look-back time of  $\sim 12$  Gyr, the fraction of small to large grains is  $\gtrsim 10^{-2}$ , with a low dominance of silicates over carbonates. But high- $z$ , massive DSFGs’ dark halos may be up to 10 times larger than the values adopted in that simulation. So, the size distribution between large and small grains, and their compositions in DSFGs and, more generally, in high- $z$  galaxies, is still an open issue. As for the high- $z$  DSFGs, it may be that the large SFR, the enhanced SN rate and cosmic ionization rates, and the possible high fraction of diffuse vs. dense gas (see Section 8) plays a big part in primary grains evolving into small grains. This hypothesis needs, however, to be supported by more observations and/or detailed simulations on small scales. Noticeably, the most recent observations by JWST are providing interesting challenges to the dust-cycle picture while exploring the most extreme distances observed in the galactic framework. An absorption feature around a rest-frame wavelength of  $\lambda = 2175$  was found in the spectrum of a galaxy at  $z = 6.71$  [177], i.e., just 800 Myr after the Big Bang. This feature, known as the ultraviolet (UV) bump, was first discovered along the lines of sight in the Milky Way and generally attributed to small carbonaceous dust grains, specifically PAHs (size 0.3–5 nm) or nano-sized graphitic grains. The puzzle resides in the fact that, at such redshifts, AGB stars have not formed yet, so that the only plausible source of dust seeds is SNe [59], which, in the local Universe, are more prone to produce silicates in larger amounts than carbonates. The latter are, however, a non-negligible SN ejecta. In light of the processes summarized above, we may argue that the “down-sizing” fragmentation processes acting on the large seeds grains ( $\sim 0.1 \mu\text{m}$ ) to produce nano-carbons or PAHs must be much more effective at those high redshifts, due to a combination of shattering possibly followed by sputtering. This investigation goes well beyond the purpose of this paper, but make us reflect on possible scenarios justifying the efficient formation of PAHs in high-redshift sources.

Whatever the main factory is, dust plays a paramount role in the ISM’s molecular enrichment, both for its thermal effects on the gas and for the several chemical processes

occurring on the dust grains' surfaces. Dust regulates the balance of heating and cooling in the ISM, as a massive gas reservoir, and the efficient dust shielding from the FUV field, described in Section 3, implies that a large amount of gas, in the form of diffuse clouds (atoms and simple diatomic molecules, with characteristic temperatures of 30–100 K and gas density  $n_H \sim 500\text{--}1000 \text{ cm}^{-3}$ ) will undergo the necessary cooling for gravitational collapse, allowing the formation of dense, cold gas clouds with temperatures of 5–10 K and  $n_H > 10^4 \text{ cm}^{-3}$ , pristine cradles for star-forming regions.

#### *Impact on Molecular Chemistry*

In the diffuse gas, dust grains are solid-state, sub-micron-sized, bare silicates and carbonaceous refractory compounds, while prestellar grains (in dense cores) are coated with thick ice mantles, cradles of complex organic molecules. We summarize below the main roles of dust on molecular chemistry.

- **Regulator of chemical drivers:** the dust-to-gas ratio and the chemical composition and size of dust grains results in the visual attenuation  $A_V$  against the FUV interstellar field, thus determining the “thickness” of the PDR regions, layers of neutral gas separating photon-dominated chemistry from CR-dominated chemistry, as discussed in Section 3 (see also [59,95,178]). For  $A_V > 1 - 2$ , carbon is mainly in the neutral form, and increasingly incorporated into CO molecules for increasing depths in the cloud. While the chemistry in PDR regions is limited to the formation of few simple molecular species, the transition to dense cores comes together with a very rich molecular scenario [83]. For this reason, for a given interstellar FUV field, the dust-to-gas ratio and the grain composition are of paramount importance in regulating the overall filling factor of the PDR regions with respect to dense molecular cores.
- **Regulator of atomic-to-molecular transition:** in dense clouds, the atomic-to-molecular transition is regulated by the balance between the formation of  $H_2$  on grain surfaces and on the  $H_2$  destruction by the FUV external radiation field. Increasing the optical depth in the cloud, photodissociation is reduced by dust and by  $H_2$  self-shielding (through absorption in the Lyman–Werner bands). The formation rate is proportional to the gas density, thus the primary controllers of the transition from atomic to molecular gas are the dust-to-gas ratio or the metallicity of the gas (which determine the dust absorption opacity), the gas density, and the intensity of the FUV field [18].
- **Factory of  $H_2$ ,  $H_2O$ ,  $O_2$ , and complex organic molecules:** with  $H_2$  being the most abundant molecule in the ISM, it provides an important contribution to the cooling of collapsing gas, necessary for star formation. The primary route for  $H_2$  formation is grain-surface chemistry [179–184].

Grain-surface chemistry is also required to explain the observed abundances of water in molecular clouds [185,186] because of the inefficiency of the gas-phase routes for its formation. In the cold phase of the collapsing gas, dust grains are covered by thick icy mantles. The prestellar grain surface chemistry is dominated by hydrogenation processes: simple hydrogenated molecules, like  $H_2O$  [187,188] and  $CH_3OH$  [189,190], form in this phase by hydrogenation of O,  $O_2$ ,  $O_3$ , and CO. Molecules formed on icy grain mantles during the prestellar phase remain frozen in the grain mantle until the densest, central core of the collapsing cloud starts to heat up when forming a protostar, a central hot core with temperatures of about 100–300 K. During this protostellar switch-on phase, grain-surface chemistry is thought to be responsible, together with gas-phase processes, for the formation of many complex organic compounds, the so-called “interstellar complex organic molecules” (iCOMS), carbon-bearing molecules with at least six atoms (see [191] for a review). Many common organic compounds are thought to form in this phase, such as methyl formate,  $HCOOCH_3$ ; formic acid,  $HCOOH$ ; and dimethyl ether,  $CH_3OCH_3$ . The relative importance of grain-surface and gas processes may increase with the duration of the warm-up phase from prestellar to protostellar core [192], although more recent observations found that iCOMS are numerous and relatively abundant (fractional abundance as large as  $\sim 10^{-10}$ ) already

in the cold phase, before the switch-on of the protostar [80,193,194]. Finally, the warm-up phase generates ice sublimation, which injects the icy mantle molecules in the gas phase, where they can be detected through their rotational lines. The evolution continues with dissipation of the protostellar envelope, converted into a protoplanetary disk. Although we can expect high- $z$  DSFGs to be huge sources of iCOMS, unfortunately the low scales of hot corinos and hot cores are very compact (size less than 0.1 pc), and the strongest transitions of these large molecules are located between  $\sim 30$  and 50 GHz rest-frame frequency, which makes their direct detection in high- $z$  DSFGs out of reach of the current astronomical facilities (but see, e.g., [195] for the observational perspectives of the Square Kilometer Array, SKA). However, it has been estimated by [196] that if the number of hot cores is a factor of  $\sim 1000$  larger than in the Milky Way, specific signatures of hot core chemistry may be detectable even at high  $z$ .

Despite chemical networks for surface reactions still being developed by the astrochemical community, it is now widely accepted that chemistry on dust can have a high impact on the molecular composition of the ISM gas. In particular, the high ionization rates and FUV fluxes of DSFGs are expected to play a role in the non-thermal desorption from grain mantles. This is why, when dealing with high- $z$  DSFGs and with their large dust content and extreme environmental conditions, surface chemistry should always be considered together with the gas routes for molecular formation.

## 6. The Molecular Gas Reservoir: $H_2$ as Traced by CO

The fundamental properties of galaxies traditionally adopted to trace their star formation cycle are the star formation rate (SFR), the stellar mass  $M_*$ , and the molecular gas mass  $M_{H_2}$ . They are connected by three scaling relations. The Kennicutt–Schmidt (KS) relation [197,198] assumes that star formation is fueled by molecular gas [199] and illustrates how an increase in molecular gas corresponds to an increase in the star formation rate. The molecular gas main sequence (MGMS) [200] shows that an increase in molecular gas is correlated to an increase in the stellar mass: a plausible interpretation is that higher stellar masses trace higher gravitational potentials, which retain higher gas amounts, fostering the conversion from atomic to molecular hydrogen through enhanced pressure and densities. Finally, the star-forming main sequence (SFMS) [201–204] illustrates the observed correlation between the stellar mass and the star formation rate. DSFGs form a heterogeneous class of galaxies: for the majority of known DSFGs, SFR and  $M_*$  follow an approximately linear relation along the SFMS. Positive outliers, having boosted specific SFR ( $sSFR \equiv SFR/M_*$ ), form the so-called starbursts (SBs). The interpretation of these characteristics within the main-sequence paradigm provides key constraints on the history of DSFGs' stellar mass assembly [205–210]. Molecular gas in high- $z$  DSFGs is warmer than in less active objects, and has column densities higher than quiescent galaxies. A negative correlation is observed between molecular gas depletion time and excitation (e.g., [211]), and a positive correlation is found between gas density and the star formation rate (e.g., [212]). This shows that the density and temperature of the molecular gas are related to star formation activity: the average densities and temperatures of the molecular clouds in starburst nuclei are higher than those in more quiescent galaxies. There is still debate in the literature on the nature of the main scaling relations, on whether they are intrinsic and fundamental, or whether some of them are just indirect by-products of the others [205,213,214]. But, whatever their nature is, we know that the characterization of the star formation process needs to start from a reliable estimate of the molecular gas mass and, ultimately, of the molecular hydrogen content. Molecular hydrogen is the most abundant molecule in the Universe and plays a central role in the evolution of stellar systems and galaxies. It is found in all regions where the attenuation  $A_V > 0.01$ – $0.1$  mag, shielding the gas against the ultraviolet (UV) photons responsible for its photodissociation (requiring an energy of about 12 eV). However,  $H_2$  is a diatomic homonuclear molecule, and it has no permanent dipole moment and no dipolar rotational transitions. All ro-vibrational transitions within the electronic ground state are quadrupolar with low Einstein coefficients

for spontaneous emission, emitting radiation very weakly [215,216]. More importantly, the two lowest para and ortho purely rotational quadrupole transitions are only excited at temperatures higher than a few hundred K: the cold molecular component of the ISM is, therefore, invisible in H<sub>2</sub> emission at the characteristic temperatures of typical giant molecular clouds (GMCs) (10–20 K, [217]). The strong dipole-allowed H<sub>2</sub> transitions in the Lyman ( $B^1\Sigma_u^+ - X^1\Sigma_g^+(v', v'')$ ) and Werner ( $C^1\Pi_u - X^1\Sigma_g^+(v', v'')$ ) systems fall in the range of the vacuum ultraviolet (10–200 nm).

Due to the difficulties in having a direct measure of the H<sub>2</sub> content, carbon monoxide is routinely used as an observable tracer of H<sub>2</sub> [218], being the second most abundant molecule in the ISM, with the advantage of a weak permanent dipole ( $\mu \sim 0.11D$ ) and a ground rotational transition CO(1–0) of  $\sim 5.53$  K ( $\lambda = 2.6$  mm, rest-frame frequency of 115.22 GHz). The CO ground transition has a critical density for collisional excitation of  $n_{crit} = 3.9 \times 10^2 \text{ cm}^{-3}$ , further reduced by radiative trapping, due to its high optical depth. The low excitation temperature and critical density makes CO(1–0) a relatively strong, easily excited millimeter (mm) emission line, traditionally used to trace the bulk of the molecular content. With respect to mid- and high-J CO transitions, it is the least affected by the excitation conditions of the gas, thus fully revealing the widely distributed reservoirs of less dense, sub-thermally excited gas (e.g., [219–221]). In high-*z* star-forming galaxies, observations of CO(1–0) require observing capabilities in the 20–50 GHz regime (wavelength 6–20 mm). The standard methodology to infer  $M_{H_2}$  from CO assumes a simple relationship between the H<sub>2</sub> column density,  $N_{H_2}$ , and the integrated line intensity  $W(\text{CO})$  of the  $J = 1 \rightarrow 0$  purely rotational transition of the most common isotopologue <sup>12</sup>C<sup>16</sup>O (hereafter, CO). In nearby clouds throughout the Milky Way disk, the CO-to-H<sub>2</sub> conversion factor shows little variation and is given approximately by [222–224]

$$X_{CO,gal} = \frac{N_{H_2}}{W_{CO}} = 2 \times 10^{20} \text{ cm}^{-2} \text{ K}^{-1} \text{ km}^{-1} \text{ s} \quad (2)$$

As a corollary, integrating over the emitting area,  $M_{mol} = \alpha_{CO} L_{CO}$ , with  $\alpha_{CO} = 4.3 M_{\odot} (\text{K}^{-1} \text{ km}^{-1} \text{ s pc}^{-2})$ . Independent estimates of the molecular mass in local observations usually come from virial mass measurements, or from measurements (or assumptions) about the dust-to-gas ratio (where the dust mass is estimated from the IR SED of the dust component, when available), and  $\gamma$ -ray observations of the bremsstrahlung radiation emitted by the cosmic rays' interaction with the dense molecular gas [225]. Significant deviations from the typically observed relative constancy of the galactic X factor have been found in regions of high SFR density, where  $X_{CO} < X_{CO,gal}$  by a factor  $\sim 4$ –20 (e.g., [226]) in nearby mergers and starbursts. For a long time, the custom in the literature has been to assume a bimodality in the CO-to-H<sub>2</sub> conversion factor, with  $\alpha_{CO} \approx 4$  for normal star-forming systems (similar to the typical value of local giant molecular clouds) and  $\alpha_{CO} \approx 0.8$  for boosted-star-formation systems. When considering high-*z* systems, however, the combined measurement of dynamical mass and high-resolution CO(1–0) observations leads to a broad range of X factors, from lower to higher values compared to local ULIRGs (e.g., [151,205,227]), with no evidence of a strict bimodality, nor of a single conversion factor applicable to high-*z* DSFGs.

If one sticks to the aforementioned bimodal conversion factor, the Kennicutt–Schmidt (KS) relation between SFR density and surface density of the cold molecular gas, as traced by CO(1–0), separates into two distinct regimes, where ULIRGs and high-*z* SBs lie above the more quiescent galaxies [9]. This appears to reflect the bimodality in the SFMS between MSs and SBs. In turn, the SFMS estimates the stellar mass in obscured star formation environments by assuming a given relation between the stellar mass and gas mass, and, ultimately, assuming a constant dust-to-gas ratio. Viceversa, accurately modeling  $X_{CO}$  as a smoothly varying function of the gas surface density, so accounting for the boosted  $W_{CO}$  due to higher velocity dispersions in heavily star-forming environments [228–230], the KS relation becomes unimodal. The conclusion is that in order to use CO(1–0) as a proxy for H<sub>2</sub>, some caution must be adopted, especially in the extreme ISM conditions of high-*z*

DSFGs. The “X factor” is explicitly dependent on the H<sub>2</sub> column density, the peak CO intensity (brightness temperature) and range in velocities, and, implicitly, dependent on density and kinetic temperature. In the physical environment of high-*z* DSFGs, how does the chemistry affect the relative abundances of H<sub>2</sub> and CO and the value of the conversion factor?

In the diffuse molecular medium, dominated by photochemistry, both CO and H<sub>2</sub> are easily dissociated by FUV photons, making the abundances of these molecules small in low-density ( $n_H = 100\text{--}500\text{ cm}^{-3}$ ) and low-extinction ( $A_V \lesssim 1$ ) gas [231]. In low-extinction regions of the clouds, photoelectric heating is dominated by photons with energies above 6 eV, while photons with energies above 11.2 eV and 11.5 eV are responsible for H<sub>2</sub> and CO dissociation, respectively.

However, H<sub>2</sub> can exist at lower column densities than CO because, being more abundant, it is more easily self-shielded than CO [232–234]. There is a range of column densities ( $10^{20}\text{--}10^{21}\text{ cm}^{-2}$ ) where the gas is potentially undetectable with the CO line (“CO-dark clouds”), so that the use of the galactic  $X_{CO}$  factor would underestimate the total molecular mass if the filling factor of this ISM component was non-negligible. This range of column densities is dependent on the thickness of the transition region and, ultimately, on the intensity of the FUV field.

CO photodissociation is also more effective in low-metallicity environments: in this case, also the H<sub>2</sub> abundance may be reduced, but its higher self-shielding makes H<sub>2</sub> less sensitive to changes in metallicity. In low-metallicity systems, CO traces the regions of a cloud that have extinction greater than  $\sim 2$  but does not trace the surrounding diffuse envelope, which can be CO-dark while containing a large fraction of molecular gas [235,236]. For the typical dusty and heavily star-forming systems at hand, we can expect that the metallicity plays a negligible role in boosting the CO photodissociation, while we argue that the relative size of the CO-emitting region in a molecular cloud shrinks because of the boosted value of the environmental FUV associated with the high SFR.

It is reasonable to assume that, concerning the temperature and chemistry of the gas, the relevant FUV interstellar radiation field comes from massive, young stars, so that the FUV intensity scales linearly with the star formation rate. Similarly, if cosmic rays are associated with SN remnants, the ionization rate  $\zeta_{CR}$  can be assumed to track the SFR. Moving to environments which may be typical of DSFGs, in which molecular clouds are embedded in strong FUV and CR fluxes, more CO photodissociation will occur, decreasing the filling factor of the CO emission and, if CO is not distributed throughout all the cloud volume, decreasing the line width, leading to an overall increase in  $X_{CO}$  with respect to the galactic value. On the other hand, the higher photodissociation and the higher CR heating in low- $A_V$  regions will increase the brightness temperature of the CO emission, decreasing  $X_{CO}$ .

In order to determine the total effect on the conversion factor in different environmental FUV fields and CR fluxes, Ref. [237] presented a series of simulations which incorporates a time-dependent astrochemistry network into a smoothed-particle hydrodynamics code, finding that for virialized clouds with masses of  $10^5 M_\odot$  and mean density of  $100\text{ cm}^{-3}$ , the  $X_{CO}$  factor increases by one order of magnitude over an SFR increase of two orders of magnitude. Remarkably, the inclusion of CO destruction by dissociative charge transfer with He<sup>+</sup>, occurring for large CR ionization rates, leads to a dependence on SFR even in the portions of the cloud which are highly shielded and CO-bright. In general, for high column densities (mean extinction  $A_V$  above  $\sim 6$ )  $X_{CO}$  becomes almost independent of the external FUV field [238] but retains a dependence on the CR ionization rate.

These simulations did not account for turbulence and density effects, though, and may be altered if the clouds in DSFGs are systematically denser and/or more turbulent than less actively star-forming galaxies: while a high SFR tends to increase  $X_{CO}$  (reducing the CO abundance), higher densities and turbulent velocities may counterbalance this effect by increasing  $W_{CO}$ . In contrast to the diffuse gas, the high-density core of the molecular cloud is less affected by the external FUV field, and density and temperature play a major

role: this has to be taken into account for molecular gas in high- $z$  DSFGs, which are on average warmer than less active objects, and have column densities higher than more quiescent galaxies.

These effects were analyzed by [239]. Observations of galactic CO show that due to the large optical thickness of the CO(1–0) line,  $W_{CO}$  saturates beyond a threshold column density [240,241]. When the CO line saturates, it no longer traces gas mass, and  $W_{CO}$  scales linearly with  $N_{H_2}$ . In the Milky Way, this saturation occurs at  $N_{H_2} \lesssim 10^{21} \text{ cm}^{-2}$ . In general, the CO line becomes saturated in regions with the highest CO abundance, so the corresponding  $H_2$  column density depends on the  $f_{CO} = n_{CO}/n_{H_2}$  ratio which, in turn, is related to the level of CO destruction by CRs and, ultimately, on the SFR. Also, the high dust content in DSFGs may alter this ratio by increasing the shielding of CO.

Given all the physical parameters involved, and the still unclear indications from simulations, it is clear that much caution is required when extrapolating the local  $X_{CO}$  to the extreme environments of high- $z$  DSFGs, where our interpretation of the Kennicutt–Schmidt relation should be rethought.

#### *Other CO Rotational Lines*

Although CO(1–0) could provide, with some caveats, a robust estimate of the bulk of the extended, low-excitation molecular gas reservoir, it is an intrinsically faint line, whose detection in high- $z$  DSFGs involves large observing times. The situation with high- $z$  DSFGs is also particularly murky because the ground-state CO transition is redshifted out of many typical instrumental bandpasses. For this reason, mid- and high- $J$  CO transitions are often used: they are typically brighter than the ground transition, tracing dense (e.g., for CO(5–4),  $n_{crit} = 1.7 \times 10^5 \text{ cm}^{-3}$ ) and thermally excited gas in actively star-forming regions. If many of those lines are observed, one can determine the thermal state of the gas and extrapolate down the observed CO excitation to infer the CO(1–0) excitation. However, the full CO spectral line energy distribution (SLED) is rarely observed: when it is available, it turns out that high- $z$  DSFGs exhibit a large diversity in the CO SLED, ranging from nearly thermalized through  $J = 6$ , through subthermal even at the  $J = 3-2$  line [9]. This is because CO has a non-zero dipole moment (0.1 Debye), so that it will not reach equilibrium with the kinetic temperature of the gas via collisions, because spontaneous emission has some effect instead [242–245]. It follows that there is no universal conversion from mid- and high- $J$  CO lines to CO(1–0) for DSFGs: converting down to CO(1–0) leads to significant dispersions, which makes these lines unreliable tracers of the cold molecular gas. Furthermore, the densities and temperatures required to excite these higher transitions may not be reached by the majority of the molecular gas, so that significant amounts of low-excitation gas may lurk in DSFG environments. Also, the non-collisional excitation of these lines prevents us from finding a clear connection with the dense gas, for which other tracing molecules are traditionally used.

### **7. H<sub>2</sub>O: The Beacon of Star Formation**

Water is expected to be one of the most abundant molecules in molecular clouds, after  $H_2$  and CO. In the coldest clouds, where  $H_2O$  freezes-out onto dust grains, its fractional abundance is  $<10^{-8}$ , raising to  $>10^{-4}$  in warm gas and shocks, due to ice evaporation or sputtering and exothermic gas-phase reactions (see, e.g., [102,246–250]).

The water molecule has a very large dipole moment of 1.84 D, which allows a strong coupling with the radiation field. Furthermore, due to the high spacing between rotational levels (compared to other molecules with low-level transitions in the millimeter range),  $H_2O$  has a large number of rotational transitions lying in the submm and FIR wavelength regime. This combination of high dipole moment and peculiar rotational ladder makes water a very powerful tracer of dense ( $n_H = 10^5-10^6 \text{ cm}^{-3}$ ), warm ( $T_{dust} \sim 50-100 \text{ K}$ ,  $T_{gas} = 100-200 \text{ K}$ ) star formation regions and, in general, of highly energetic processes, such as starbursts, shocks, and AGN. This is not only because in these conditions the dust temperature is raised above the ice evaporation temperature, boosting the  $H_2O$  abundance; but, most

importantly, the environmental FIR radiation emitted by warm dust is able to populate high- $J$  ( $E_{\text{up}} > 200$  K) levels of ortho- and para- $\text{H}_2\text{O}$  (FIR pumping, [251–258]), which then relax via a cascade down to lower rotational levels, emitting intense submm lines.

The high dipole moment of  $\text{H}_2\text{O}$  corresponds to large Einstein coefficients for spontaneous emission, which, under the optically thin case, implies critical densities of the order of  $10^8$ – $10^9$   $\text{cm}^{-3}$  [259]. Radiative trapping reduces the effective density for collisional excitation of the optically thick lines. For example, the warm gas model by [260] shows that for  $n_{\text{H}} = 10^5$   $\text{cm}^{-3}$ , kinetic gas temperature  $T_{\text{gas}} = 50$  K, and fractional abundance  $X(\text{H}_2\text{O}) = 10^{-7}$ , the FIR pumping from the dust continuum drives the thermalization up to levels of increasing  $E_J$  for increasing dust temperature. The low-excitation lines become weaker in the warm and hot regions, where infrared pumping dominates over collisions.

As  $T_{\text{dust}}$  approaches  $T_{\text{gas}}$ , the combination of collisions and pumping populates the levels in such a way that collisions drive the o- $\text{H}_2\text{O}$  (p- $\text{H}_2\text{O}$ ) toward thermalization at  $T_{\text{gas}}$  for levels with  $E_J \leq 200$  (100) K: collisions still dominate over FIR pumping in populating the o- $\text{H}_2\text{O}$  (p- $\text{H}_2\text{O}$ ) levels with  $E_J \leq 350$  (250) K, but the radiative pumping becomes the dominant source of excitation for the levels with  $E_J \geq 350$  (250) K. Viceversa, in the absence of the FIR continuum, and under the same gas conditions, the o- $\text{H}_2\text{O}$  (p- $\text{H}_2\text{O}$ ) populations can be excited by collisions only up to levels with energies up to 350K (250 K), corresponding to the o-4<sub>14</sub> (p-3<sub>13</sub>) level. The low- $J$  lines can then be collisionally excited, and observed in emission, also in regions where the other lines do not emit owing to a weak far-IR continuum.

In general, the observed intensities of molecular emission depend on a complex competition between radiative and collisional processes. This is particularly true for the excitation of  $\text{H}_2\text{O}$ , where the FIR radiation from dust strongly affects the level populations, so that the interpretation of optically thick water emission lines requires a full radiative transfer calculation and an accurate modeling of the environmental gas and dust mixture. High- $z$  DSFGs have been investigated using their water emission lines, often detected in strongly lensed sources, in several studies, [41,58,261–272], which confirmed that those lines are among the brightest ones in the extreme star-forming environments of this galaxy population. Water lines have also been detected in absorption, and related to massive galactic outflows, a possible quenching mechanism for star formation [273].

With water being a unique tracer of the FIR radiation field, it is not surprising that a strong correlation has been found (see [268,272,274]) between the IR luminosity and the submm  $\text{H}_2\text{O}$  emission (with the exception of the ground-state emissions of para- and ortho-water, which, as we said, are largely affected by collisional excitation). This dependence extends over four orders of magnitude of the luminosity range, regardless of the presence of a strong AGN signature. In particular, the sample of strongly lensed high- $z$  DSFGs presented in [268,274] and discovered in the Herschel Astrophysical Terahertz Large Area Survey (H-ATLAS) shows this correlation of the p- $\text{H}_2\text{O}$  2<sub>11</sub>–2<sub>02</sub> ( $\nu_{\text{rest}} = 752.033$  GHz,  $E_{\text{up}} = 137$  K) and the p- $\text{H}_2\text{O}$  2<sub>02</sub>–2<sub>11</sub> ( $\nu_{\text{rest}} = 987.927$  GHz,  $E_{\text{up}} = 101$  K), finding that, for these lines,  $L_{\text{IR}}$  varies approximately as  $\sim L_{\text{H}_2\text{O}}^{1.2}$ . As discussed in [58], this superlinear relation may be suggestive of the fact that these lines are still partially excited by collisions, so that they do not just trace the star formation through FIR pumping. Indeed, it was suggested in [58] that a linear, more direct correlation between the star formation process, as traced by the FIR luminosity and the water excitation, can arise when considering those lines which are only associated with FIR pumping, i.e., the higher  $E_{\text{up}}$  lines.

We wish to emphasize that obtaining relatively high-resolution images of molecular emission from high- $z$  DSFGs inevitably requires relying on the selection of strongly lensed sources. This introduces the additional complication of reconstructing the unlensed image of the galaxy. Despite the difficulties in lens modeling, recent works by [43,58] could analyze high-resolution ( $\lesssim 0.1$ – $0.3$  arcsec) ALMA observations of the strongly lensed galaxy HATLASJ113526.2-01460, an optical/near-IR-dark SB (with SFR of  $\sim 900$   $M_{\odot} \text{ yr}^{-1}$ ) at redshift  $z \sim 3.1$  discovered in the GAMA 12th field of the H-ATLAS survey. Accurate lens modeling and source morphology reconstruction in three different submillimeter

continuum bands and in the C[II], CO(8–7), and in three water emission lines (the low-J p-H<sub>2</sub>O 2<sub>02</sub>–1<sub>11</sub> line, the mid-J o-H<sub>2</sub>O 3<sub>21</sub>–3<sub>12</sub> line, and the high-J p-H<sub>2</sub>O 4<sub>22</sub>–4<sub>13</sub> line) led to the first high-resolution spatial map of the water emission in a high-z SB. While the low-, medium-, and high-J water emission lines appear to peak in a compact nucleus of ~500 kpc, where the FIR continuum also peaks, the image show a more extended molecular region where the p-H<sub>2</sub>O 2<sub>02</sub>–1<sub>11</sub> line is excited. The existence of plausibly cold molecular gas, exhibiting water excitation at low energy levels at large distances (~1 Kpc) from the compact, star-forming core, surely deserves a deeper investigation.

## 8. Dense Gas Tracers

In [275], the actual link between star formation and molecular gas resides in the high-density gas. The first investigations of the role of dense gas in molecular clouds were motivated by early galactic observation, which found a correlation between the dense gas component and young stellar objects [276]. One key question is how much dense gas is needed to trigger star formation, and whether the ratio between dense and diffuse molecular gas is correlated to the star formation efficiency [277].

Direct tracers of dense gas include emission lines from molecules with high electric dipoles, such as HCN, HNC, HCO<sup>+</sup>, and CS, since the ground-state rotational transition of these molecules has a critical density for collisional excitations with H<sub>2</sub> of about 10<sup>5</sup> cm<sup>-3</sup> (see [9,212] and references therein).

Although CO is much more abundant than these molecules, the low critical density of low-J CO transitions ( $n_{crit} \sim 10^2$  cm<sup>-3</sup>) makes CO(1–0) a reliable tracer of the bulk of the molecular gas reservoir (diffuse molecular phase, with  $A_V \sim 2$ ,  $n_H \sim 10^2$  cm<sup>-3</sup>,  $T \sim 100$  K) rather than of the dense cores where stars form ( $n_H > 10^5$  cm<sup>-3</sup>). On the other hand, the mid- and high-J CO emission lines are much more affected by non-collisional excitation, preventing them from directly tracing high-density environments [278–280] (see Section 6).

Assuming that HCN(1–0)/CO(1–0) measures the dense gas fraction with respect to the diffuse gas, Ref. [212] found that, in nearby galaxies, the emission ratio HCN(1–0)/CO(1–0) increases with the star formation rate. Moving to DSFGs at  $z \geq 1$ , it is not yet clear whether the SFR is correlated with the dense molecular gas fraction [281] or with the total molecular gas [27], because of the sparse detections of HCN(1–0) in such galaxies: only three DSFGs have been detected in HCN(1–0) to date (J1202 [27], J16359 [282], and SDP.9 [281]). The inferred HCN/CO ratio in these galaxies is not consistent with a universally high dense gas fraction in DSFGs [27].

As for  $L_{\text{HCN}(1-0)} / L_{\text{FIR}}$ , assumed to be a proxy for dense gas star formation efficiency, there are indications for a sublinear relation at high redshifts [27], which corroborates theoretical predictions by [283] and [284]. However, more statistics is needed to analyze the role of dense gas in the efficiency of star formation.

It is important to note that all these considerations rely on the assumption that the HCN(1–0) transition is unambiguously associated with gas at H<sub>2</sub> densities  $\gg 10^4$  cm<sup>-3</sup>. If this is true, the mass of gas at densities  $\gg 10^4$  cm<sup>-3</sup> can be inferred from the luminosity of this emission line. However, observations of the Orion A molecular cloud suggest that this line is actually associated with moderate gas densities, of about 10<sup>3</sup> cm<sup>-3</sup> [277], and that the only molecule really tracing dense gas is N<sub>2</sub>H<sup>+</sup>. In Orion A, the characteristic densities derived for the HCN(1–0) line are about two orders of magnitude below values commonly adopted in extragalactic environments, suggesting that only a fraction of the HCN(1–0) luminosity traces the dense gas, while about half of the emission is related to the gas surrounding the densest clouds. On the other hand, in high-z DSFGs there is not sufficient angular resolution to analyze the single molecular clouds: once again, local observations and astrochemical modeling of the molecular ISM have to be the primer for any attempt at high-z molecular spectra interpretation.

A recent deep spectral line survey, using NOEMA, targeted the strongly lensed DSFG NCv1.143 [59], and revealed an unprecedented large inventory of molecular species for a starburst at  $z = 3.655$ . Mid-J lines of HCN were detected, together with other dense gas

tracers. The analysis of the spectral lines is suggestive of a top-heavy stellar initial mass function and of high cosmic ray ionization rates. However, we outline again that in order to remove the degeneracy between molecular abundances and excitation of molecular lines and to obtain the correct interpretation of the ISM physics, a solid chemical network including dust surface chemistry, and high-angular-resolution observations are needed.

### AGN Tracers

Dense gas acts as a reservoir for sites of massive star formation, but it is also a fuel for active galactic nuclei (AGN). In the framework of galaxy evolution, the study of high-redshift DSFGs is of paramount importance to address the issue of coevolution between galaxies and supermassive BHs [285–287]. As heating sources, AGNs can radiatively and mechanically alter the chemical composition and the excitation state of the surrounding molecular medium. It has been proposed that different heating mechanisms produce specific, distinguishable signatures in the surrounding interstellar medium. Specifically, the main power source in starbursts comes from nuclear fusion, with the intense UV flux producing photodissociation regions (PDRs) around massive stars, while, in the vicinity of an AGN, the strong X-ray emission produces, thanks to the higher penetrating capabilities of this radiation, X-ray-dominated regions (XDRs), larger in volume than PDRs. Mechanical heating due to AGN outflows or to supernovae, as well as cosmic rays, also shapes the chemical composition and the molecular excitation state. This should lead to distinguishable properties of the dust and molecules surrounding the gas.

One key problem lies in the high resolution needed to probe the very central region of AGNs: the kinematics of the gas flow in the central  $\lesssim 100$  pc is crucial information to account for the different physical conditions [288]. This makes it necessary to rely on millimeter/submillimeter interferometric spectroscopic observations, because of their high spatial and spectral resolution. Also, such wavelengths are not affected by dust extinction, which is of paramount importance if the target AGN is enshrouded in dust.

Following this idea, it has been proposed to use the line ratios of specific transitions of dense-gas-tracing molecules as a possible diagnostic to discriminate the main heating source in galactic nuclei. An enhanced intensity of HCN(1–0) compared to HCO<sup>+</sup>(1–0) has been proposed as a feature unique to AGNs [281,289–297]. However, low values of HCN(1–0)/HCO<sup>+</sup>(1–0) [298] have been detected in AGNs, as well as high values in non-AGNs [299,300]. This diagnostic has been later questioned by [301], showing that the ratio of the HCN(1–0) and HCO<sup>+</sup>(1–0) integrated intensity emission cannot be simply interpreted in terms of the AGN or starburst dominance, because it is likely affected by multiple processes, including contamination from a coexisting starburst, effects of density, opacities, temperature, radiative effects (non-collisional excitation), out-flowing material, and abundances.

Following the indication by [277] that the  $J = 1 \rightarrow 0$  emission of HCN and HCO<sup>+</sup> could be dominated by low gas densities, Ref. [302] argued that a more suitable star formation tracer is the  $J = 2 \rightarrow 1$  transition, having a higher critical density ( $1.6 \times 10^6$  and  $2.8 \times 10^5$  cm<sup>-3</sup>, respectively, for HCN and HCO<sup>+</sup>). However, no significant difference was found between the average HCN/HCO<sup>+</sup> ratio in a sample of eight AGN-dominated galaxies and eleven nearby star-formation-dominated galaxies.

In this view, Refs. [303–306] examined higher rotational lines of dense-gas-tracing molecules, since higher resolution is achievable for these lines compared to the fundamental (1–0) transition. Specifically, the integrated line intensity ratios HCN(4–3)/HCO<sup>+</sup>(4–3) and HCN(4–3)/CS(7–6) seem to be enhanced in AGN when compared to pure starbursts (*submillimeter HCN enhancement*). The physical interpretation is not unique, though: a chemical layout focusing on high-temperature chemistry was invoked by, e.g., [304] and [101], to explain the HCN/HCO<sup>+</sup> enhancement through an astrochemical mechanism that boosts the HCN abundance relative to HCO<sup>+</sup>.

The neutral–neutral reactions:  $O+H_2 \rightarrow OH+H$  and  $OH+H_2 \rightarrow H_2O+H$  are efficiently activated in high-temperature environments, especially at  $T > 300$  K, indicating

that much of the elemental oxygen is in the form of water. The hydrogenation of CN reacting with molecular hydrogen to produce HCN is a slightly endothermic reaction, which enhances the HCN abundances at high temperatures, whatever the heating source:  $\text{CN} + \text{H}_2 \rightarrow \text{HCN} + \text{H}$ . The  $\text{HCO}^+$  ion is generally created by the reaction  $\text{CO} + \text{H}_3^+ \rightarrow \text{HCO}^+ + \text{H}_2$ . Although this ion tends to dissociatively protonate a water molecule, producing a CO molecule, the abundance of  $\text{HCO}^+$  with respect to  $\text{H}_2$  at high temperatures remains approximately constant. Thus, once water formation is promoted by the high temperatures, the water-induced reactions facilitate HCN enhancement with respect to  $\text{HCO}^+$ . This could explain why the observed abundance ratio of HCN-to- $\text{HCO}^+$  in the nucleus of AGNs seems to be enhanced by a factor of a few to even  $\gtrsim 10$ . However, X-rays are not the only possible heating mechanism, as mechanical heating due to an AGN jet could contribute significantly.

## 9. Summary and Concluding Remarks

We have discussed the wealth and robustness of the information provided by the current molecular line observations in high-*z* DSFGs. What arises from this review is that there are still many open questions that molecular line data cannot clarify yet. The main problem in the interpretation of spectroscopic lines from high-*z* sources resides in the fact that, even for gravitationally lensed sources, there is a limit in the spatial resolution that prevents us from the characterization of single molecular clouds. So, we receive integrated signals, emitted by gas in different physical conditions. For this reason, we focus on those molecular lines which better trace specific densities and temperatures of the gas.

To properly interpret molecular line observations, the modeled intrinsic line emission has to be implemented in a radiative transfer equation which, in turn, encodes the ISM properties along the line of sight. As a matter of fact, the ISM in high-*z* DSFGs differs from that of local or more quiescent galaxies in several respects. At high redshifts, the CMB radiation can affect the observability of molecular lines, as well as the population of excited rotational levels. The high rates of star formation typical of DSFGs boost the flux of FUV radiation, which regulates the physics and chemistry of PDR regions. The strong interplay between the FUV radiation and the large amount of dust, also typical of this population, allows an efficient shielding against ionizing radiation for large parts of the gas, which can turn from atomic to predominantly molecular. In dark molecular clouds, cradles of simple molecules as well as complex organic molecules, a key role is played by cosmic rays: at the typical SFRs of this galaxy population, their flux is expected to be enhanced compared to quiescent galaxies, as observations seem to indicate. Cosmic rays deeply affect molecular chemistry, starting from the production of the pivotal ion  $\text{H}_3^+$ , whose abundance drives all the chain of chemical reaction networks to the equilibrium molecular abundances. Notably, cosmic rays impact the photodesorption in dust grains, so that gas chemistry is deeply linked to surface chemistry even in a starless molecular core.

In summary, the unique and extreme ISM of DSFGs not only influences the radiative transport of emission lines and their observed brightness but also significantly impacts the underlying chemistry and molecular abundances. We have then to face a problem of degeneracy between the radiative transport process and the molecular abundances: for example, unless a line is optically thin, a single bright emission line may indicate either a high excitation of the corresponding upper energy level, or just an increase in the molecular abundance for that particular species. In order to disentangle these two effects, it is crucial to have large spectral coverage and high-spectral-resolution observations, and to carefully insert all the “ingredients” into the astrochemical networks when implementing simulations of molecular clouds. This problem is exacerbated by a lack of spatial resolution, which forces us to interpret the integrated emission lines in a statistical approach, rather than as indicators or thermometers of a single molecular cloud.

For all these reasons, caution needs to be taken when using an  $\text{H}_2$ -to-CO conversion factor to estimate the molecular content of a whole galaxy, or when inferring global proper-

ties of the unresolved source from tracer molecules which are affected by different local environments through the ISM.

In view of future higher-resolution spectral observations, a statistical approach will be needed, in which the filling factors of the several phases of the ISM are estimated and used as inputs for astrochemical and radiative transfer models, to allow for an improved interpretation of the molecular lines and of the wealth of information they can potentially deliver.

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## Notes

- <sup>1</sup>  $G_0$  is the FUV radiation field in Habing units;  $G_0 = 1$  corresponds to a flux of  $1.6 \times 10^{-3} \text{ erg cm}^{-2} \text{ s}^{-1}$ . As an example, the median value in the Milky Way is  $G_0 = 1.7$ , corresponding to a flux of  $2.72 \times 10^{-3} \text{ erg cm}^{-2} \text{ s}^{-1} \equiv \chi_0$ .

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