

## 45

# Chemical Reaction Engineering Aspects of Homogeneous Hydrogenations

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### 45.1 Introduction

The proper design of a reactor should lead to processes where the intrinsic kinetics would play the dominant role, leading to the maximum allowable conversion and yield. In many practical reactors, however, physical processes limit the production or throughput of the system. Thus, the basic problem in chemical reactor design and scale-up is to distribute and control the reactants, products and catalyst concentrations, as well as the heat or other energy sources in specific cases (photochemistry, microwave-assisted reactions, etc.), throughout the reactor. Ideally, such a control would allow the maximization of conversion and yield without the formation of side-products, in addition to operating safely away from runaway zones. Therefore, chemical reactor design involves a knowledge not only of the intrinsic kinetics of the target synthesis, related thermodynamic data (e.g., solubilities, heat of reaction), reactor characteristics in terms of mass and heat transfer, flow pattern, phases hold up, but also their interactions.

For single liquid-phase reactors, knowledge of mixing in the reactor is generally sufficient to account for mass and heat distribution over the reactor volume. Furthermore, when the reaction is not too rapid compared to the mixing times, and there is no large exo- or endothermicity, knowledge of the intrinsic kinetics is the only information required for reactor scale-up, and this allows predictions to be made of reactor performance in a relatively straightforward manner. Scale-up issues are discussed elsewhere in details [1–4]. This is the case for homogeneous single-phase hydrogenations – that is, those conducted with a hydrogen transfer reagent such as isopropanol and which are carried out in one liquid phase with a soluble molecular catalyst and in the absence of a gas or an immiscible liquid. Such hydrogenations can be analyzed and treated like any other homogeneous reaction. In such a case – and because H-transfer catalytic hydrogenations are not very fast – scale-up is easily achieved.

Most hydrogenations are carried out using dihydrogen, a molecular catalyst, and the substrate dissolved in a liquid layer, leading to a gas–liquid process.

Among the chemical industries, gas–liquid reactors are very common. Indeed, they are used for a wide variety of applications, such as the production of chemicals by oxidation, hydrogenation, halogenation, sulfation, polymerization, for gas scrubbing of  $\text{CO}_2$ ,  $\text{H}_2\text{S}$ ,  $\text{SO}_2$ ,  $\text{NO}_x$ ,  $\text{HF}$ ,  $\text{Cl}_2$ , and also in bioprocesses such as aerobic fermentation and biological waste treatments [4]. Many types of gas–liquid reactors have been reported that are presently used in industry [5]; these include bubble columns, spray columns, multistage sieve plate bubble columns, falling film reactors, stirred-tank reactors and loop reactors [3]. In such reactors, in addition to mixing each phase, it is important to recognize other properties before a meaningful design can be proposed. The extent of the gas–liquid interface is one of the most important properties, as it governs mass transfer between the gas and liquid phases. Liquid phase hold-up is also important, since when catalytic hydrogenations take place in the liquid phase the phase hold-up will influence reactor productivity and heat transfer.

The aim of this chapter is to define the general requirements typical of gas–liquid hydrogenations – that is, the main problems of hydrogenations related to chemical engineering – and to analyze the influences of limiting physical phenomena on productivity and selectivity. Whilst the chapter may help chemical engineers, the main intention is to provide chemists with a degree of understanding to help in the design and choice of laboratory reactors, and to become more familiar with the scale-up of homogeneous hydrogenation processes. A preliminary, more generalized text – *Chemical Reaction Engineering Aspects of Homogeneous Catalyzed Processes* – has already been published [6], while other aspects such as catalyst separation are detailed elsewhere in this book. Multiphase hydrogenations (e.g., gas–liquid–liquid hydrogenations) are not detailed here, and similar multiphase hydroformylations have been analyzed elsewhere [7]. Other biphasic liquid–liquid hydrogenations using H-transfer reagents (sodium or ammonium formate, formic acid, etc.) are known, but are not used extensively on an industrial scale and will not be described here.

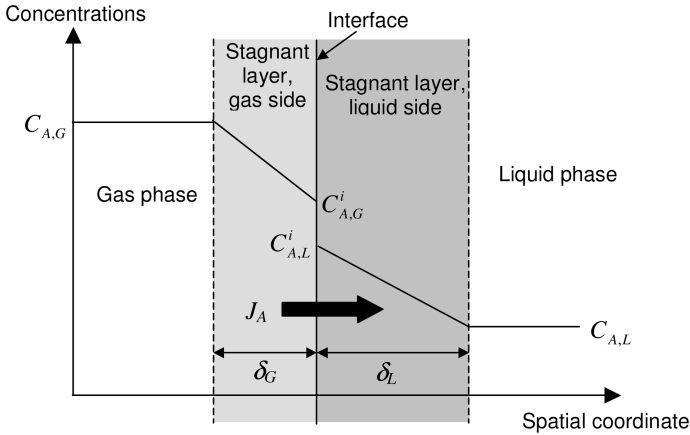
## 45.2

### Fundamentals

#### 45.2.1

##### Basics of Mass Transfer in Gas–Liquid Systems

First, we must consider a gas–liquid system separated by an interface. When the thermodynamic equilibrium concentration is not reached for a transferable solute A in the gas phase, a concentration gradient is established between the two phases, and this will create a mass transfer flow of A from the gas phase to the liquid phase. This is described by the “two-film” model proposed by W.G. Whitman, where interphase mass transfer is ensured by diffusion of the solute through two stagnant layers of thickness  $\delta_G$  and  $\delta_L$  on both sides of the interface (Fig. 45.1) [1–4].



**Fig. 45.1** Schematic presentation of the two stagnant films theory applied to gas–liquid systems, indicating the concentration profiles on both sides of the interface.

The application of Fick's law leads to the following description of mass transfer (Eq. (1)):

$$J_A = \frac{D_{A,G}}{\delta_G} (C_{A,G} - C_{A,G}^i) = \frac{D_{A,L}}{\delta_L} (C_{A,L}^i - C_{A,L}) \quad (1)$$

where  $J_A$  is the molar rate of mass transfer per unit of interfacial area ( $\text{mol s}^{-1} \text{m}^{-2}$ ) between the phases,  $D_{A,G}$  and  $D_{A,L}$  are the molecular diffusion coefficients ( $\text{m}^2 \cdot \text{s}^{-1}$ ),  $C_{A,G}$  and  $C_{A,L}$  are the actual concentrations ( $\text{mol m}^{-3}$ ) in the bulk of the liquid  $C_{A,G}^i$  and  $C_{A,L}^i$  are the concentrations of solute A at the interface in the gas and the liquid phase, respectively.

The molar transfer rate coefficient  $k_G$  (gas side) or  $k_L$  (liquid side) ( $\text{m s}^{-1}$ ) can be defined as the ratio between the intrinsic molecular diffusivity of the solute gas A in the gas or liquid matrix and the diffusion lengths  $\delta_G$  or  $\delta_L$  (Eqs. (2) and (3)). The diffusion lengths depend on the reactor flow and mixing properties.

$$\frac{D_{A,G}}{\delta_G} = k_G \quad (2)$$

$$\frac{D_{A,L}}{\delta_L} = k_L \quad (3)$$

Note that Eq. (3) (respectively Eq. (2)) is in fact the definition of the liquid (gas) film thickness  $\delta_L$  ( $\delta_G$ ), which cannot be measured because it does not really exist. The advantage of this model is its simplicity, its teaching power, and its ability to describe the coupling of mass transfer with chemical reactions sufficiently accurately for most practical cases.

Using these definitions, Eq. (1) can be rewritten as Eq. (4):

$$J_A = k_G(C_{A,G} - C_{A,G}^i) = k_L(C_{A,L}^i - C_{A,L}) \quad (4)$$

It can be assumed for almost all practical cases that equilibrium exists at the interface between the two phases. The concentrations of solute A at the interface,  $C_{A,G}^i$  and  $C_{A,L}^i$ , are related by the equilibrium relation of Eq. (5) and which, for gases in general and hydrogen in particular, is often described using simplified Henry's law applied at the interface (Eq. (6)).

$$C_{A,L}^i = m_A C_{A,G}^i \quad (5)$$

$$C_{A,L}^i = \frac{P_{A,L}^i}{H_A} \quad (6)$$

Taking the Henry's coefficient  $H_A$  as constant, and with the definitions of the molar transfer coefficients  $k_G$  and  $k_L$  ( $\text{m s}^{-1}$ ), the concentrations at the interface, that cannot be measured, can be eliminated and Eq. (4) applied to the solute A rearranges to:

$$J_A = \left( \frac{RT}{k_G H_A} + \frac{1}{k_L} \right)^{-1} \left( \frac{P_{pA}}{H_A} - C_{A,L} \right) \quad (7)$$

Note that the groups  $\frac{RT}{k_G H_A}$  and  $\frac{1}{k_L}$  represent the mass transfer resistances on the gas and liquid sides, respectively.

In most of hydrogenation processes, the gas phase is mainly composed of hydrogen used in a pure form, often in a high gas phase concentration ( $\text{H}_2$  pressure  $> 0.1$  MPa). The other component is the solvent at the saturated vapor pressure, which can be often neglected since hydrogenations with molecular catalysts are performed at rather low temperatures (20–100 °C). Furthermore, the diffusion coefficient of hydrogen is high, leading to large values of  $k_G$ . Finally, hydrogen is poorly soluble in liquids, and this reflects in high values of  $H_A$ . All of these considerations support the assumption that gas-phase resistance against mass transfer is negligible for hydrogenations. Thus in practice, Eq. (7) reduces to:

$$J_H = k_L \left( \frac{P_{pH}}{H_H} - C_{H,L} \right) \quad \text{or} \quad J_H = k_L (C_{H,L}^{\text{eq}} - C_{H,L}) \quad (8)$$

Knowing the interfacial or contact area  $A$  ( $\text{m}^2$ ) between the gas and the liquid phase, the total molar flow  $\Phi_H$  ( $\text{mol s}^{-1}$ ) of transferred hydrogen is:

$$\Phi_H = k_L A \left( \frac{P_{pH}}{H_H} - C_{H,L} \right) \quad (9)$$

Of course, when designing reactors it is interesting to refer to the specific contact area  $a$  ( $\text{m}^2 \text{m}_{G+L}^{-3}$ ) – that is, the interfacial area per unit volume of gas–

liquid emulsion  $V_R = V_G + V_L$ . The contact area  $A$  and the specific contact area  $a$  are related by Eq. (10):

$$A = a V_R \quad (10)$$

In some cases, it can be useful to use other definitions for the specific contact area. For example, some authors use  $a_L$ , which is the interfacial area per unit volume of liquid ( $\text{m}^2 \text{m}_L^{-3}$ ) or  $a_G$ , the interfacial area per unit volume of gas ( $\text{m}^2 \text{m}_G^{-3}$ ). Note that the nomenclature  $a$ ,  $a_L$  or  $a_G$  is not always specified. The specific contact areas are related by:

$$A = a V_R = a_L V_L = a_G V_G = a_L \varepsilon_L V_R = a_G \varepsilon_G V_R = a_G (1 - \varepsilon_L) V_R \quad (11)$$

where  $\varepsilon_L$  is the liquid hold-up of the gas–liquid emulsion. Using the definition, the total molar flow  $\Phi_H$  becomes:

$$\Phi_H = k_L a \left( \frac{P_{pH}}{H_H} - C_{H,L} \right) V_R \quad (12)$$

Note that the ratio  $r_{\text{obs}} = \Phi_H / V_R$  ( $\text{mol s}^{-1} \text{m}^{-3}$ ) is the observed rate of hydrogen consumption from the gas phase.

This simplified description of molecular transfer of hydrogen from the gas phase into the bulk of the liquid phase will be used extensively to describe the coupling of mass transfer with the catalytic reaction. Beside the Henry coefficient (which will be described in Section 45.2.2.2 and is a thermodynamic constant independent of the reactor used), the key parameters governing the mass transfer process are the mass transfer coefficient  $k_L$  and the specific contact area  $a$ . Correlations used for the estimation of these parameters or their product (i.e., the volumetric mass transfer coefficient  $k_L a$ ) will be presented in Section 45.3 on industrial reactors and scale-up issues. Note that the reciprocal of the latter coefficient has a dimension of time and is the characteristic time for the diffusion mass transfer process  $t_{\text{diffGL}} = 1/k_L a$  (s).

#### 45.2.2

##### Physical and Chemical Data for Hydrogenations

The design of gas–liquid reactors requires the consideration of four sets of basic data:

- (i) the heat of reaction;
- (ii) distribution of the reagents between the phases at thermodynamic equilibrium – that is, hydrogen solubility in the liquid and the vapor pressure of the solvent in the gas phase;
- (iii) the physical rate at which hydrogen transfers from the gas phase to the liquid phase – that is, mainly driven by the hydrogen diffusivity in the liquid (see above) and the interfacial surface area; and
- (iv) the chemical rate of transformation that is the intrinsic kinetic; this last point is dealt with in Chapter 10, and will not be reviewed here.

Although a comprehensive review of the data cited in points (i), (ii) and (iii) is beyond the scope of this chapter, this section presents a selected collection of data specific to hydrogen. For a more extensive discussion on the topic, the reader is directed to textbooks in the field [8, 9].

#### 45.2.2.1 Heat of Reaction

Hydrogenation reactions are mild to highly exothermic (Table 45.1). The highly exothermic nitro-aromatic hydrogenations are generally performed with heterogeneous catalysts. Homogeneous hydrogenations concern almost exclusively the reduction of carbon-carbon double bonds, carbonyls and imines which are mildly exothermic. Furthermore, they are very selective so that in the case of large molecules featuring several chemical functions, only one is generally hydrogenated, with the corresponding exotherm.

The Benson group contribution method, and more recent methodologies, allow the computation of heat of hydrogenation reactions, even for large molecules (note that Benson method gives the reaction enthalpy assuming each species to be a perfect gas!). Software and database (e.g., NIST) are also available.

#### 45.2.2.2 Solubility

Many definitions are used to express the solubility of gases in liquids, but usually the equilibrium law is defined as:

$$H_A^x = \frac{P_{pA}}{x_A} \quad (13)$$

where  $x_A$  is the mole fraction of gas A dissolved in the liquid, and  $P_{pA}$  (MPa) is the partial pressure of the gas A.

This equilibrium can also be expressed by Eq. (14) using the concentration of A at the equilibrium in the liquid phase  $C_{A,L}^{eq}$  ( $\text{mol m}^{-3}$ ):

$$H_A = \frac{P_{pA}}{C_{A,L}^{eq}} \quad (14)$$

**Table 45.1** Heat of reaction for selected hydrogenations.

Reaction	Example	$\Delta H$ [ $\text{kJ mol}^{-1}$ ]
Alkenes to alkanes	$\text{RCH=CHR} \rightarrow \text{RCH}_2\text{-CH}_2\text{R}$	-117
	Cyclopentene $\rightarrow$ cyclopentane	-113
Nitriles to amines	$\text{RC}\equiv\text{N} \rightarrow \text{RCH}_2\text{-NH}_2$	-120
Alkynes to alkenes	$\text{RC}\equiv\text{CR} \rightarrow \text{RCH=CHR}$	-155
Aromatics to cycloalkanes	Benzene $\rightarrow$ cyclohexane	-208
Alkynes to alkanes	$\text{RC}\equiv\text{CR} \rightarrow \text{RCH}_2\text{-CH}_2\text{R}$	-274
Nitro-aromatics to amines	$\text{Ph-NO}_2 \rightarrow \text{Ph-NH}_2$	-493

**Table 45.2** Examples of experimental correlations for hydrogen solubility.

Solvent	Range/Units	$C_{H,L}^{eq}$ or $H_H^x$	Reference
Ethanol	293–333 K	$C_{H,L}^{eq} = 0.0099 \exp\left(-\frac{2640}{RT}\right) P_{pH}$	10
Cyclohexane	283–323 K	$C_{H,L}^{eq} = 0.00529 \exp\left(-\frac{3773}{RT}\right) P_{pH}$	10
$\alpha$ -Methylstyrene		$C_{H,L}^{eq} = (0.145T - 16.985) P_{pH}$	11
Toluene/ethyl pyruvate	$C_{Etpy}$ (mol m <sup>-3</sup> ) 2–10 MPa 293–343 K	$C_{H,L}^{eq} = (357.2 - 10173 C_{Etpy}) \exp\left(-\frac{6352}{RT}\right) P_{pH}$	12
Rapeseed oil	0.03–1 MPa 413–473 K	$C_{H,L}^{eq} = 0.203 \exp\left(-\frac{5900}{RT}\right) P_{pH}$	13
Methanol	$H_H^x$ (MPa) $P_{pH}$ (Pa) 0.1–1.6 MPa 20–140 °C	$H_H^x = \exp\left(-122.3 + \frac{4815.6}{T} + 17.5 \ln(T) - 1.4 \times 10^{-7} P_{pH}\right)$	14

All correlations adapted to SI units:  $C_{H,L}^{eq}$  (mol m<sup>-3</sup>),  $T$ (K),  $P_{pH}$  (MPa) unless otherwise stated.

$H_A^x$  (MPa) (Eq. (13)) and  $H_A$  (MPa m<sup>3</sup> mol<sup>-1</sup>) (Eq. (14)) are often referred to as “Henry’s constant”, but they are in fact definitions which can be used for any composition of the phases. They reduce to Henry’s law for an ideal gas phase (low pressure) and for infinitely dilute solution, and are “Henry’s constant” as they are the limit when  $C_{A,L}^{eq}$  (or  $x_A$ ) goes to zero. When both phases behave ideally,  $H$  depends on temperature only; for a dilute dissolving gas,  $H$  depends also on pressure when the gas phase deviates from a perfect gas; finally, for a non-ideal solution (gas or liquid),  $H$  depends on the composition. This clearly shows that  $H$  is not a “classical” thermodynamic constant and it should be called “Henry’s coefficient”.

For hydrogen, and within the temperature range used for homogeneous hydrogenations,  $H$  decreases when temperature increases and is only slightly dependent on pressure and composition when an excess of solvent is used (Table 45.2). Although it is rarely encountered in homogeneous hydrogenations, examples of the pressure dependence on hydrogen solubility are also provided.

$H_A$  and  $H_A^x$  are related by the expression:

$$H_A = \frac{H_A^x}{C_L} \quad (15)$$

where  $C_L$  (mol m<sup>-3</sup>) is the total concentration of the liquid phase. Often, only  $H_A^x$  is available. In order to compute  $C_{A,L}^{eq}$ ,  $C_L$  must be calculated or estimated which can be difficult for mixed solvents and/or for real liquid phase containing high concentrated reaction species for hydrogenation reaction. For example, the calculation of  $C_L$ ,  $H_A$  then  $C_{A,L}^{eq}$  requires a knowledge of the liquid density at the working temperature.

As discussed above, the hydrogen concentration increases with temperature, and that contributes to the overall activation energy up to 6.4 kJ mol<sup>-1</sup>, far from

being negligible. It is thus advisable to correct the measured activation energy from that of hydrogen dissolution in order to obtain the true chemical activation energy of the catalytic process.

No comprehensive compilation of published hydrogen solubility data is available. However, useful data sources can be found elsewhere [7, 8, 15, 16]. As a well-known general trend for mono- or di-atomic non-polar gases, the solubility

**Table 45.3** Examples of H<sub>2</sub> solubility at 25 °C and <0.1 MPa. <sup>a)</sup>

Type	Solvent	C <sub>H<sub>2</sub>,L</sub> <sup>eq</sup> [mol m <sup>-3</sup> ]	Reference
Ionic liquids	Various	0.62 to 0.98	17
Water	Water	0.81	14
Alcohols	Methanol	3.40 to 3.70	17, 18
	Ethanol	3.00 to 3.50	17–20
	2-Propanol	3.27	18
	1-Butanol	2.90	18
	Cyclohexanol	1.60	19
Ethers	1,4-Dioxane	2.06	18
Esters	Ethylacetate	3.45	18
	<i>n</i> -Butylacetate	3.55	18
Ketones	Acetone	3.15 to 4.10	15, 19, 20
	Cyclohexanone	2.17	21
Alkanes	<i>n</i> -Hexane	4.83	19
	<i>n</i> -Heptane	4.60 to 4.70	15, 19, 20
	<i>n</i> -Octane	4.21	19
	<i>n</i> -Nonane	3.87	19
	Cyclohexane	3.40 to 3.80	17–20
	2,2,4-Trimethylpentane	4.74	19
Alkenes	1-Tetradecene	2.81	18
	Cyclohexene	3.27	21
Aromatics	Aniline	1.08	18
	Nitrobenzene	1.40	18
	Chlorobenzene	2.56	19
	Benzene	2.54 to 2.98	17–20
	1,2,4-Trimethylbenzene	2.59	18
	<i>o</i> -Methylstyrene	2.65	22
	Ethylbenzene	2.69	18
	Toluene	2.81 to 3.50	17, 18
	<i>m</i> -Xylene	2.91 to 3.40	18, 19
	Chloroalkanes	1,2-Dichloroethane	2.25
Tetrachloromethane		3.14 to 3.47	15, 18
1,1,2,2-Tetrachloroethane		3.84	19
Fluorous	1,1,2-Trichloro-1,2,2-trifluoroethane	5.51	19
	<i>n</i> -Perfluoroheptane	6.30 to 6.31	15, 19
Others	Carbon disulfide	2.48	15, 19
	Dimethyl sulfoxide	1.07	19

a) Some values computed from published correlations.



of hydrogen is very small in liquids exhibiting strong cohesion forces such as water and ionic liquids, but it increases in organic solvent and reaches high solubility for fluorinated media (Table 45.3).

Gas solubility in mixed solvents (and, therefore, Henry's constant) varies with solvent composition. The simplest approximation for this is given in Eq. (16) [23]:

$$\ln(H_A^{x,\text{mix}}) = \sum_{j=\text{solvents}} x_j^{\text{mix}} \ln(H_A^{x,j}) \quad (16)$$

where  $x_j^{\text{mix}}$  is the molar fraction of solvent  $j$  in the mixture.

Good approximate values could be obtained using Eq. (16). For a 1:1 mixture of methanol and methyl formate, calculated ( $H_H^{x,\text{calc}} = 520$  MPa) and measured ( $H_H^{x,\text{exp}} = 495$  MPa) Henry coefficients only differ by less than 5% [24].

Very often, solubility and/or Henry's coefficients are determined for each application, preferentially using a liquid phase as close as possible to the real liquid composition, and under the actual operating conditions. Details of experimental methods have been published [16, 25]. Direct measurement of the hydrogen concentration in the liquid phase is also possible using specific probes. Whereas several sensors and techniques have been developed in the past, they cannot generally be applied to processes that may involve high temperature and pressure (up to 500 K and 10 MPa) and corrosive environments. These problems seem to be solved with a new development, albeit the response time is still an issue for very fast processes [26]. Note that solubility could vary during the course of reaction since the composition of the liquid changes [27].

#### 45.2.2.3 Diffusivity

The gas A must transfer from the gas phase to the liquid phase. Equation (1) describes the specific (per  $\text{m}^2$ ) molar flow ( $J_A$ ) of A through the gas-liquid interface. Considering only limitations in the liquid phase, this molar flow notably depends on the liquid molecular diffusion coefficient  $D_{A,L}$  ( $\text{m}^2 \text{s}^{-1}$ ). Based on the liquid state theories,  $D_{A,L}$  can be calculated using the Stokes-Einstein expression, and many correlations have been developed in order to estimate the liquid diffusion coefficients. The best-known example is the Wilke and Chang (W-C) relationship, but many others have been established and compared (Table 45.4) [28–33].

The coefficients are defined for infinitely dilute solution of solute in the solvent L. However, they are assumed to be valid even for concentrations of solute of 5 to 10 mol.%. The relationships are available for pure solvent, and could be used for mixture of solvents composed of molecules of close size and shape. They all refer to the solvent viscosity which can be estimated or measured. Pressure has a negligible influence on liquid viscosity, which decreases with temperature. As a consequence, pressure has a weak influence on liquid diffusion coefficient; conversely, diffusivity increases significantly with temperature (Table 45.4). For mixtures of liquids, an averaged value for the viscosity should be employed.

**Table 45.4** Estimation of the diffusion coefficient in liquid phase.

1	Stokes-Einstein	$D_{A,L} = \frac{kT}{3\pi\mu_L\sigma_A}$	
2	Wilke and Chang	$D_{A,L} = 5.8810^{-17} \frac{T\sqrt{\varphi M_L}}{\mu_L \nu_A^{0.6}}$	$\varphi = 1$ , non-associated liquid $\varphi = 2.6$ , water $\varphi = 1-2$ , liquid with hydrogen bonding
3	Diaz et al.	$D_{A,L}(25^\circ\text{C}) = 1.8610^{-12} \frac{\nu_L^{0.36}}{\nu_A^{0.64} \mu_L^{0.61}}$	$273 < T < 338 \text{ K}$
		$\frac{D_{A,L}(T)}{D_{A,L}(25^\circ\text{C})} = 4996 e^{\frac{-2539}{T}}$	$a = 1, b = -1.15$ , water
4	Sovová	$D_{A,L} = 1.3210^{-15} \frac{a\mu_L^b}{\nu_A^{0.6}}$	$a = 1.8, b = -1.15$ , spherical molecule $a = 203.2, b = -0.5$ , alkane, <i>n</i> -alcohol

Generally, diffusion coefficients at infinite dilution are in the range  $5 \times 10^{-10}$  and  $3 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$  [29, 35, 36]. Since hydrogen is a very small molecule, it diffuses faster than most other dissolved gas. As a result, correlation-based estimates are often underestimated, as shown in Table 45.5.

A wide range of values (one decade!) could be obtained using correlations as well as using different experimental methods [34, 38, 43]. As for solubility, diffusion coefficient at infinite dilution should be determined experimentally using the real liquid phase. Experimental methods are, however, more complex to carry out and correlations are widely used.

#### 45.2.3

##### Coupling Between Mass Transfer and a Single Homogeneous Irreversible Reaction

For a simple hydrogenation reaction between  $\text{H}_2$  transferred from the gas phase with the substrate  $\text{S}$  present in the bulk liquid phase ( $\text{S} + \text{H}_2 \rightarrow \text{P}$ ), considering no mass transfer resistance on the gas side and a gradientless concentration of the molecular catalyst in the liquid phase, various concentration profiles in the liquid boundary layer, or film, exist (Fig. 45.2).

Case 1 in Figure 45.2 refers to a case where the reaction between  $\text{S}$  and  $\text{H}_2$  is very slow. In that case, the rate of hydrogen consumed by the reaction (i.e., the rate of the reaction) is small compared to the maximum rate of mass transfer. Thus, mass transfer feeds the liquid phase easily with dissolved hydrogen. The liquid-phase hydrogen concentration is very close to that at equilibrium given by the Henry's law:

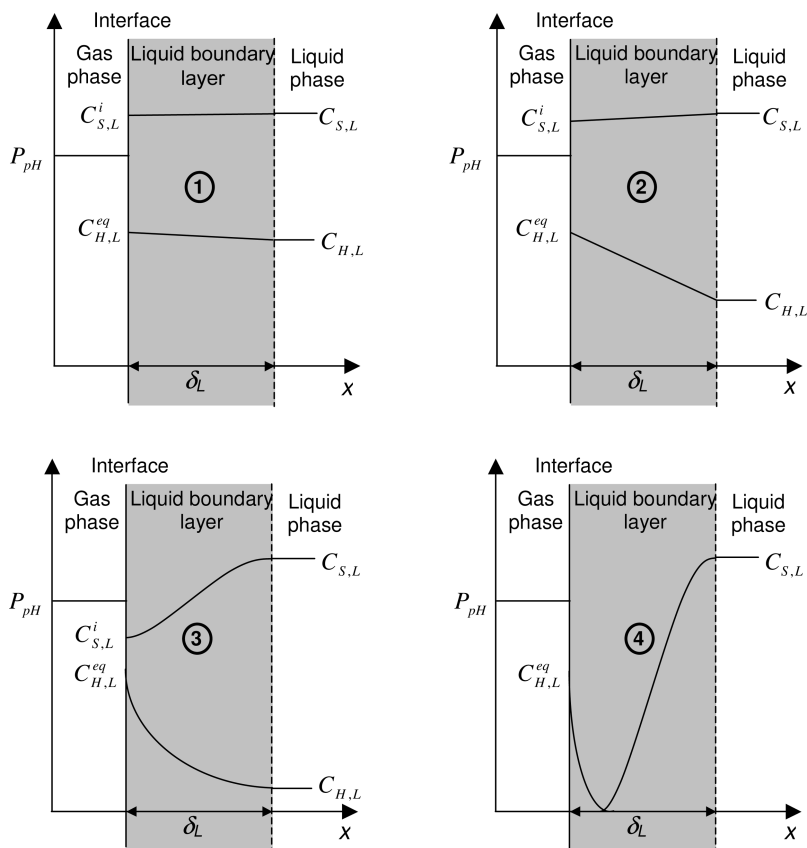
$$C_{\text{H},L} \cong C_{\text{H},L}^{\text{eq}} = \frac{P_{\text{pH}}}{H_{\text{H}}} \quad (17)$$

**Table 45.5** Experimental value of the diffusion coefficient of H<sub>2</sub> ( $D_{\text{H}_2}$ , m<sup>2</sup> s<sup>-1</sup>) in some usual liquids and estimates.

Solvent/Reference	T [K]	$D_{\text{H}_2}$ [m <sup>2</sup> s <sup>-1</sup> ]	W-C <sup>a)</sup> [m <sup>2</sup> s <sup>-1</sup> ]	e <sup>b)</sup> [%]	Sovová <sup>a)</sup> [m <sup>2</sup> s <sup>-1</sup> ]	e <sup>b)</sup> [%]	Diaz <sup>a)</sup> [m <sup>2</sup> s <sup>-1</sup> ]	e <sup>b)</sup> [%]
Water [37]	294	$5.10 \times 10^{-9}$	$2.92 \times 10^{-9}$	43	$3.13 \times 10^{-9}$	39	$3.23 \times 10^{-9}$	37
Methanol [37, 38]	293	$1.65 \times 10^{-8}$	$1.72 \times 10^{-8}$	65	$8.86 \times 10^{-9}$	46	$5.51 \times 10^{-9}$	67
Ethanol [37, 38]	293	$1.49 \times 10^{-8}$	$1.51 \times 10^{-8}$	80	$6.25 \times 10^{-9}$	58	$4.26 \times 10^{-9}$	71
1-Propanol [37, 38]	298	$1.19 \times 10^{-8}$	$1.28 \times 10^{-8}$	85	$4.55 \times 10^{-9}$	62	$3.25 \times 10^{-9}$	73
2-Methyl-1-propanol [37, 38]	293	$7.90 \times 10^{-9}$	$7.93 \times 10^{-9}$					
1-Pentanol [37, 38]	293	$1.64 \times 10^{-8}$	$2.04 \times 10^{-8}$					
Acetone [38]	298	$4.17 \times 10^{-8}$	$1.08 \times 10^{-8}$	74	$2.03 \times 10^{-8}$	51	$1.04 \times 10^{-8}$	75
Benzene [38]	298	$2.00 \times 10^{-8}$	$6.48 \times 10^{-9}$	68	$9.55 \times 10^{-9}$	52	$7.67 \times 10^{-9}$	62
Cyclohexane [38]	298	$1.73 \times 10^{-8}$	$4.55 \times 10^{-9}$	74	$6.10 \times 10^{-9}$	65	$6.52 \times 10^{-9}$	62
Cyclohexene [38]	298	$2.24 \times 10^{-8}$	$6.13 \times 10^{-9}$	73	$8.71 \times 10^{-9}$	61	$7.70 \times 10^{-9}$	66
<i>o</i> -Methylstyrene [39]	298	$1.10 \times 10^{-8}$						
Cumene [39]	298	$1.30 \times 10^{-8}$						
<i>n</i> -Hexane [38]	298	$6.24 \times 10^{-8}$	$1.41 \times 10^{-8}$	77	$1.26 \times 10^{-8}$	80	$1.37 \times 10^{-8}$	78
<i>n</i> -Heptane [38]	298	$5.01 \times 10^{-8}$	$1.16 \times 10^{-8}$	77	$1.10 \times 10^{-8}$	78	$1.23 \times 10^{-8}$	76
<i>n</i> -Octane [38]	298	$4.49 \times 10^{-8}$	$8.84 \times 10^{-9}$	80	$9.31 \times 10^{-9}$	79	$1.05 \times 10^{-8}$	77
Tetrachloromethane [37, 38, 40]	298	$9.75 \times 10^{-9}$	$1.05 \times 10^{-8}$					
Triperfluorobutylamine [41, 42]	298	$6.52 \times 10^{-9}$	$5.78 \times 10^{-9}$	41	$5.66 \times 10^{-9}$	42	$6.17 \times 10^{-9}$	37

a) See Table 45.4 for expression (W-C; Wilke and Chang).

b) e = 100 × (experimental value - calculated value) / experimental value.



**Fig. 45.2** Possible qualitative concentration profiles in the liquid boundary layer for homogeneous hydrogenations with molecular catalysts.

The concentration of the substrate S is also uniform throughout the boundary layer. This case is often called “chemical regime”, because the limiting phenomenon is the chemical reaction and not the physical process of mass transfer. In that case, the gas–liquid contact area ( $A$ ,  $a$ ,  $a_L \dots$ ) is not a crucial parameter; conversely, the liquid retention ( $\varepsilon_L$ ) must be high to promote the reaction.

Curve 2 in Figure 45.2 depicts the case where the hydrogenation reaction is not that slow. Most of the conversion still takes place in the bulk of the liquid, so that the concentration of S in the film is almost that in the bulk of the liquid; the fall in hydrogen concentration across the film is mainly due to the diffusional resistance coupled to the “pumping” effect of the reaction in the bulk liquid. In that case an efficient reactor must have a high liquid retention,  $\varepsilon_L$ , for the reaction to take place in the bulk, and a high surface area,  $a$ , for hydrogen transfer through the film.

In case 3 in Figure 45.2, the curves give qualitatively the concentrations distributions for a moderately fast reaction. Here, a significant fraction of the gas that dissolves, is converted within the boundary layer before reaching the bulk liquid. Correspondingly, S is also converted in the film and its concentration is lower than in the bulk of liquid phase. Since a significant part of the conversion takes place in the film, the interface area becomes even more important than in the previous cases, and reactors developing a larger specific contact area will drive to higher conversion rates. Finally, in case 4, the reaction is so fast that it occurs completely in the film. No reaction takes place in the bulk liquid phase ( $C_{H,L}=0$ ) and the observed rate of conversion is proportional to the contact area. The liquid retention  $\varepsilon_L$  is of no importance.

The above general qualitative discussion points that at least three important parameters play a role in the coupling of mass transfer with the chemical reaction:

- the ratio between the intrinsic reaction rate and the maximum transfer rate;
- the specific contact area (or interface/volume ratio) of the gas–liquid phases; and
- the concentration ratio  $C_{H,L}^{\text{eq}}/C_{S,L}$ .

Although more fundamental approaches are used in the science of chemical reaction engineering to account for the diffusion/reaction coupling, we rather propose the explanation restricted to rate laws of first order with respect to hydrogen and based on intuition.

The exact composition of the liquid with respect to hydrogen cannot be guessed. Consequently, we can only estimate either transfer or reaction maximum rates and fluxes. From Eq. (12), the maximum mass transfer rate  $\Phi_H^{\text{max}}$  ( $\text{mol s}^{-1}$ ) is obtained when the reaction is so “fast” that the bulk concentration of dissolved hydrogen is zero ( $C_{H,L}=0$ ), as given in Eq. (18).

$$\Phi_H^{\text{max}} = k_L a V_R \frac{P_{\text{pH}}}{H_H} = k_L a V_R C_{H,L}^{\text{eq}} \quad (18)$$

Assuming a first-order rate law with respect to hydrogen, with a kinetic constant  $k_c$ , the maximum rate of chemical reaction ( $\text{mol s}^{-1} \text{mL}^{-3}$ ) is obtained when the hydrogen concentration reaches equilibrium ( $C_{H,L}=C_{H,L}^{\text{eq}}$ ) and the corresponding maximum reaction flux  $\Phi_{\text{Chem}}^{\text{max}}$  ( $\text{mol s}^{-1}$ ) results in Eq. (19).

$\Phi_{\text{Chem}} = r V_R = k_c C_{H,L} V_R$  with  $C_{H,L}=C_{H,L}^{\text{eq}}$  affords:

$$\Phi_{\text{Chem}}^{\text{max}} = r V_R = k_c C_{H,L}^{\text{eq}} V_R \quad (19)$$

If  $\phi^2$  is the ratio of these maximal fluxes, this is rewritten as (Eq. (20)):

$$\phi^2 = \frac{r V_L}{k_L a V_R} \left( \frac{P_{\text{pH}}}{H_H} - C_{H,L} \right)^{-1} = \frac{r}{k_L a_L C_{H,L}^{\text{eq}}} = \frac{k_c}{k_L a_L} = \frac{k_c \varepsilon_L}{k_L a} \quad (20)$$

Three situations arise:

- $k_L a \gg k_c \varepsilon_L \Leftrightarrow \phi^2 \ll 1$ . The mass transfer is very easy compared to the chemical reaction. The latter is thus the limiting process, and the reacting system is described as operating in the “chemical regime” as depicted in Figure 45.2a.
- $k_L a \ll k_c \varepsilon_L \Leftrightarrow \phi^2 \gg 1$ . The mass transfer is difficult compared to the chemical reaction. The mass transfer is the limiting process, and the system is described as operating in the “diffusion controlled regime” (Fig. 45.2, cases 1 to 4).
- $k_L a$  and  $k_c \varepsilon_L$  are close  $\Leftrightarrow \phi^2$  is close to unity. Both the chemical and physical processes are important and contribute to the overall hydrogenation rate.

The reasoning was built using the constants describing the physical and chemical processes. It is often more convenient to compare the characteristic times of the processes involved. Equation (20) transforms into Eq. (21):

$$\phi^2 = \frac{k_c}{k_L a_L} = \frac{t_{\text{diffGL}}}{t_c} \quad (21)$$

where  $t_{\text{diffGL}}$  is the characteristic diffusional gas–liquid mass transfer time ( $t_{\text{diffGL}} = 1/k_L a_L$ ) and  $t_c$  is the characteristic chemical reaction time which, for a first-order reaction, is the reciprocal of the kinetic constant ( $t_c = 1/k_c$ ). Many other physical phenomena that can interfere with the chemical reaction are described by their characteristic times. These include macro- and micro-mixing, mass transport by convection, and heat exchange. Often, a simple comparison of these characteristic times offers a simple and convenient tool to identify the dominant process in the reactor.

The *qualitative* results above are obtained for *first-order* kinetics. The proper quantitative dimensionless criterion describing reaction/diffusion coupling for kinetic laws  $n$ th order with respect to the gas solute and  $m$ th order with respect to the substrate has been derived using more complex mathematics, following the pioneering investigations of Hatta. For homogeneous hydrogenations  $S + H_2 \rightarrow P$ , the rate laws write  $r = k_c (C_{H,L})^n (C_{S,L})^m$  leading to the Hatta number (Eq. (22)).

$$Ha = \frac{1}{k_L} \sqrt{\frac{2}{n+1} D_{H,L} k_c C_{H,L}^{i(n-1)} C_{S,L}^m} \quad (22)$$

where  $D_{H,L}$  is the diffusion coefficient of hydrogen in the liquid and  $C_{H,L}^i$  is the hydrogen concentration at the interface (see Fig. 45.1). It can be easily recognized that both numbers  $Ha$  and  $\phi$  compare the rate of chemical reaction and that of diffusion.

In order to compute  $Ha$ , the first problem is the knowledge of  $C_{H,L}^i$ . It was noted earlier that the resistance to mass transfer on the gas side is negligible, but this assumption is valid only when the gas phase is composed of pure hydrogen – that is, the vapor pressure of the solvent and substrate are negligible and it must be checked. Under this assumption, Eq. (17) applies and Eq. (22) becomes:

$$Ha = \frac{1}{k_L} \sqrt{\frac{2}{n+1} D_{H,L} k_c C_{H,L}^{eq(n-1)} C_{S,L}^m} \quad (23)$$

In general, the intrinsic kinetics, the diffusion, mass transfer and Henry coefficients are either known or can be estimated, while the Hatta number can be determined. This is the first step in assessing the working regime of the reactor.

The Hatta criterion compares the rates of the mass transfer (diffusion) process and that of the chemical reaction. In gas–liquid reactions, a further complication arises because the chemical reaction can lead to an increase of the rate of mass transfer. Intuition provides an explanation for this. Some of the reaction will proceed within the liquid boundary layer, and consequently some hydrogen will be consumed already within the boundary layer. As a result, the molar transfer rate  $J_H$  with reaction will be higher than that without reaction. One can now feel the impact of the rate of reaction not only on the transfer rate but also, as a second-order effect, on the *enhancement* of the transfer rate. In the case of a slow reaction (see case 2 in Fig. 45.2), the enhancement is negligible. For a faster reaction, however, a large part of the conversion occurs in the boundary layer, and this results in an overall increase of mass transfer (cases 3 and 4 in Fig. 45.2).

For a more general and quantitative description of the mass transfer rate and in the absence of mass transfer limitations on the gas side, the enhancement factor  $E \geq 1$  is defined as:

$$J_H = Ek_L(C_{H,L}^{eq} - C_{H,L}) \quad (24)$$

Since  $E$  depends itself on  $C_{H,L}$ , which in turn depends on the intrinsic kinetics, its value is not obvious to compute. For first-order reactions, the system formed with Eqs. (24) to (26), and with the given boundary conditions and corresponding to the qualitative profiles of Figure 45.2, must be solved.

$$\text{Mass balance of hydrogen: } D_{H,L} \frac{d^2 C_H}{dx^2} = k_c C_H C_S \quad (25)$$

$$\text{Mass balance of the substrate: } D_{S,L} \frac{d^2 C_S}{dx^2} = k_c C_H C_S \quad (26)$$

Boundary conditions:  $x=0$ ,  $C_H = C_{H,L}^i$  and  $dC_S/dx = 0$   
 $x=\delta_L$ ,  $C_H = C_{H,L}$  and  $C_S = C_{S,L}$

The boundary conditions require knowledge of the interface concentration of hydrogen  $C_{H,L}^i$  to compute  $E$  (see below). For hydrogenations, the equilibrium concentration ( $C_{H,L}^i = C_{H,L}^{eq}$ ) can be used, albeit with the assumption of no mass transfer resistance on the gas side. Otherwise, it must be determined using Eq. (4). The boundary conditions for the substrate S state that it is not transferred to the gas phase – that is, S is not vaporized. This assumption is most often

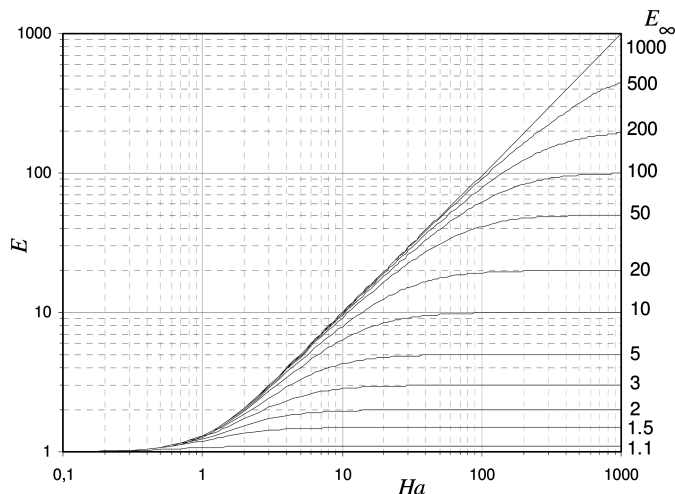


Fig. 45.3 The Van Krevelen and Hoftijzer diagram.

valid since substrates involved in homogeneous hydrogenations are rather large molecules of molecular weight  $\geq 120$  and with high boiling points ( $\geq 150^\circ\text{C}$ ). Key values  $k_L$ ,  $D_{H,L}$ ,  $D_{S,L}$ ,  $k_c$  are of the same type as those required to compute the Hatta number (see above).

An approximate analytical solution to this system has been proposed by van Krevelen and Hoftijzer (Eq. (27) and Fig. 45.3):

$$E = \frac{Ha'}{th(Ha')}, \quad Ha' = Ha \sqrt{\frac{E_\infty - E}{E_\infty - 1}}, \quad E_\infty = 1 + \frac{D_{S,L}C_{S,L}}{D_{H,L}C_{H,L}^i} \quad (27)$$

where  $E_\infty$  is the limiting enhancement factor.

From Eq. (27), the enhancement factor  $E$ , and hence  $J_H$ , is obtained by trial and error. Using the two numbers  $Ha$  and  $E$ , the four situations in Figure 45.2 can be now quantitatively described:

- Situation 1: very slow reaction,  $Ha \rightarrow 0$ ,  $C_{H,L} \cong C_{H,L}^i \cong C_{H,L}^{eq}$  diffusion processes are not limiting, the reactor performances are readily estimated using the intrinsic chemical kinetics.
- Situation 2: slow chemical reaction,  $Ha < 0.3$ ,  $E \cong 1$ . The Hatta number is small, and thus the chemical reaction does not modify the mass transfer process and consequently,  $E \cong 1$ . However, the chemical reaction is not so slow compared to the mass transfer rate. The hydrogen concentration in the bulk is smaller than the equilibrium concentration. The substrate concentration  $A$  is constant in the film and is almost that in the bulk. The consumption of  $H_2$  and  $A$  is negligible in the film and takes place in the bulk of the liquid. The reactor performances are obtained straightforwardly (see below). The mass transfer rate is obtained by  $J_H = k_L(C_{H,L}^{eq} - C_{H,L})$ .



- Situation 3: fast reaction,  $0.3 < Ha < 3$ ,  $E > 1$ . The reaction occurs in the boundary layer to a large extent so that the hydrogen concentration in the bulk of the liquid is very low. The mass transfer rate is obtained by  $J_H = Ek_L(C_{H,L}^{eq} - C_{H,L})$  with  $E \cong \sqrt{1 + Ha^2}$ ,  $E < E_\infty$ .
- Situation 4: very fast reaction,  $Ha > 3$  and  $E < E_\infty$ ,  $E \cong Ha$ . All the conversion occurs in the boundary layer. The hydrogen concentration in the bulk of the liquid falls to zero. Thus, all the catalyst in the bulk is useless. For instantaneous reactions,  $Ha \gg 3$ ,  $E = E_\infty$  and the reaction takes place in a narrow plane located somewhere in the boundary layer; the larger  $E_\infty$  the closer to the interface the reaction plane. If the limiting enhancement factor  $E_\infty$  is very high, it is said that the reaction takes place at the gas–liquid interface. Such a case is referred to as “surface reaction”.

In situations 3 and 4, as much interface area as possible with a minimum volume of bulk liquid is required. However, hydrogenations are not very fast reactions and, in most cases, situations 1 or 2 prevail.

In this section, we have examined how the coupling between mass transfer and the chemical reaction defines the concentration profile of the limiting reagent (i.e., hydrogen), and how the mass or molar flow between the gas and the liquid phase can be computed. In the next section, the estimation of the overall rate of reaction (i.e., the reactor productivity) will be reviewed for different gas–liquid reactors.

#### 45.2.4

#### Coupling of Reaction and Mass Transfer in Ideal Reactors

On a theoretical basis, when considering two fluid phases and the three basic ideal reactors (i.e., a closed stirred tank (batch), continuous stirred tank (CSTR) and plug flow), six ideal reactor types can be listed. Applying the specificity of homogeneous hydrogenations reduces the number to only four cases. Indeed, when considering a gas phase composed of pure hydrogen, perfectly mixed or plug flow considerations for the gas phase are equivalent. Second, as hydrogen is poorly soluble, hydrogenation reactors are conducted under constant hydrogen pressure to achieve high substrate conversion. Thus, the three ideal reactors investigated here are:

- stirred tank reactor, closed to liquid, open to gas feed (batch or B)
- stirred tank reactor, open to the liquid and the gas (CSTR)
- plug flow reactor, open to the liquid and the gas (PF).

(Note here that the term “batch” refers to the liquid phase – that is, to the dissolved reagents.)

Last but not least, the following simplifications and/or assumptions are generally valid and/or can be achieved and checked:

1. The gas phase is pure hydrogen at constant pressure (no need to write gas phase mass balance).

2. The hydrogenation corresponds to a single reaction  $S + \nu H_2 \rightarrow P$  with very high chemo- or regio-selectivity; thus, negligible side reactions and with  $\nu=1$  generally, the ubiquitous case of asymmetric hydrogenations has been investigated [43].
3. The liquid phase volume can be considered as constant (except for the semi-batch!), since the change in molar volume going from the reagent to product is minimal, especially in the case of the rather large molecules used in pharmaceutical applications and/or the reagent is diluted with a solvent.
4. Isothermal conditions prevail.

In the following, the mass balance for substrate S and hydrogen in the liquid phase are written, considering that assumptions 1 to 4 hold. For a more illustrative view, mass balance is proposed with the concentrations as variables. In general, if the reaction stoichiometry is known, then the conversion number is used as the unified single variable.

#### 45.2.4.1 Mass Balance for a Batch Reactor

$$\text{For substrate S: } \frac{dC_{S,L}}{dt} = -r(C_{H,L}, C_{S,L}) \quad (28)$$

$$\text{For hydrogen: } \frac{dC_{H,L}}{dt} = \underbrace{-\nu r(C_{H,L}, C_{S,L})}_{\text{Reaction}} + \underbrace{Ek_L a (C_{H,L}^{\text{eq}} - C_{H,L})}_{\text{Mass transfer}} \quad (29)$$

Clearly, for a very slow reaction ( $Ha < 0.3$ ), the gas to liquid mass transfer is not limiting, which translates into  $C_{H,L} \cong C_{H,L}^{\text{eq}}$  (see above), thus making the contribution of mass transfer negligible. Equation (29) can be discarded as  $C_{H,L} \cong C_{H,L}^{\text{eq}}$  can be used in Eq. (28).

From a production viewpoint, the operating parameter is the time required to achieve a given conversion of S. It is obtained by solving the set of differential Eqs. (28) and (29). This requires knowledge of the intrinsic rate law  $r(C_S, C_H)$ , the volumetric mass transfer coefficient  $k_L a$ , the boundary conditions (initial and final concentrations of hydrogen and substrate S, i.e.,  $C_{H,L}^{\text{in}}, C_{H,L}^{\text{out}}, C_{S,L}^{\text{in}}$ , and  $C_{S,L}^{\text{out}}$ , the two latter being related by the conversion), and a good estimate of the enhancement factor  $E$ . The latter factor is estimated with Eq. (27), and requires knowledge of the hydrogen and substrate S diffusion coefficients in the liquid phase and the Hatta number.

Very often, the quasi steady-state assumption for the hydrogen liquid phase concentration is proposed (Eq. (30)):

$$\frac{dC_{H,L}}{dt} = -\nu r(C_{H,L}, C_{S,L}) + Ek_L a (C_{H,L}^{\text{eq}} - C_{H,L}) \cong 0 \quad (30)$$

This generally leads to a much simpler integration of Eq. (28). Even under a constant hydrogen pressure, this assumption is not valid in the early stages of

the reaction, nor when complete conversion is achieved as hydrogen will still be transferred as long as the hydrogen liquid phase concentration does not reach the equilibrium concentration. However, it is generally valid for most of the reaction course.

When applying, the simplified following expressions are obtained:

$$\text{For substrate S: } t_{\text{Batch}} = \int_{C_{S,L}^{\text{in}}}^{C_{S,L}^{\text{out}}} \frac{dC_{S,L}}{r(C_{H,L}, C_{S,L})} \quad (31)$$

$$\text{For hydrogen: } Ek_L a (C_{H,L}^{\text{eq}} - C_{H,L}) = vr(C_{H,L}, C_{S,L}) \quad (32)$$

#### 45.2.4.2 Mass Balance for a CSTR Reactor

$$\text{For substrate S: } \underbrace{\frac{Q}{V_L} C_{S,L}^{\text{in}}}_{\text{Inlet}} - \underbrace{r(C_{H,L}, C_{S,L})}_{\text{Reaction}} = \underbrace{\frac{Q}{V_L} C_{S,L}^{\text{out}}}_{\text{Outlet}} + \underbrace{\frac{dC_{S,L}}{dt}}_{\text{Accumulation}} \quad (33)$$

$$\text{For hydrogen: } \frac{Q}{V_L} C_{H,L}^{\text{in}} - vr(C_{H,L}, C_{S,L}) + \underbrace{Ek_L a (C_{H,L}^{\text{eq}} - C_{H,L})}_{\text{Mass transfer}} = \frac{Q}{V_L} C_{H,L}^{\text{out}} + \frac{dC_{H,L}}{dt} \quad (34)$$

Similar to the case of the batch reactor,  $C_{H,L} \cong C_{H,L}^{\text{eq}}$  (for  $Ha < 0.3$ ) and Eq. (34) is eliminated.

The operating parameter for the CSTR reactor is the liquid flow rate  $Q$ , which sets the residence time of the liquid through the ratio  $Q/V_L$  and finally the conversion. From a production viewpoint, the (residence) time required to achieve a given conversion of S (or outlet concentration of S) is obtained by solving the set of Eqs. (33) and (34). The characteristics of the reactor  $k_L a$  and  $V_L$  must be known. In general, whereas  $V_L$  is easily determined in a batch reactor, it is not in a CSTR. Rather,  $V_L = \varepsilon_L V_R$  will be used, which requires knowledge of the liquid hold-up  $\varepsilon_L$ . Correlations provide  $k_L a$  (see below) and  $\varepsilon_L$  characteristics for the different reactor types [3].

##### 45.2.4.2.1 Simplified Mass Balances

In most continuous hydrogenations, hydrogen is fed through the gas inlet only ( $C_{H,L}^{\text{in}} = 0$ ). As hydrogen is poorly soluble in liquids, the outlet molar flow of hydrogen in the liquid can be neglected ( $QC_{H,L}^{\text{out}}/V_L \cong 0$ ) compared to the mass transfer flow and the reaction flow. Because the reactor is perfectly mixed, the outlet concentration of S is that in the reactor ( $C_{S,L}^{\text{out}} = C_{S,L}$ ). Finally, CSTRs are operated over production times much longer than the residence time (otherwise there is no point in working with a continuous reactor!); thus, steady-state conditions stand for most of the production, which translate into:

$$\frac{dC_{S,L}}{dt} \cong 0 \quad \text{and} \quad \frac{dC_{H,L}}{dt} \cong 0$$

With these simplifications, Eqs. (33) and (34) reduce to a set of algebraic Eqs. (35) and (36), which can easily be solved.

$$\text{For reagent A:} \quad \frac{Q}{\varepsilon V_R} (C_{S,L}^{\text{in}} - C_{S,L}) = r(C_{H,L}, C_{S,L}) \quad (35)$$

$$\text{For hydrogen:} \quad Ek_L a (C_{H,L}^{\text{eq}} - C_{H,L}) = vr(C_{H,L}, C_{S,L}) \quad (36)$$

Note that these equations allow the residence time and conversion to be computed, but other process issues are neglected. For example, although assumption 1 is considered, any solvent exhibits some vapor pressure and thus can be extracted by the outlet hydrogen feed.

#### 45.2.4.3 Mass Balance for a Plug Flow Reactor

Beside assumptions 1 to 4, a further operating condition is required (and is most often valid!) which simplifies the analysis. The hydrogen flow rate is large compared to the hydrogen consumption by the chemical reaction, and this translates into assuming the liquid hold-up  $\varepsilon_L$  constant over the reactor length. Under these conditions, and considering the simplifications ( $C_{H,L}^{\text{in}}=0$ ,  $QC_{H,L}^{\text{out}}/V_L=0$  and steady state) proposed in Section 45.2.4.2 on CSTR, the simplified mass balances for S and hydrogen in the liquid phase become:

$$\text{For substrate S:} \quad \frac{\varepsilon_L V_R}{Q} = \int_{C_{S,L}^{\text{in}}}^{C_{S,L}^{\text{out}}} \frac{dC_{S,L}}{r(C_{H,L}, C_{S,L})} \quad (37)$$

$$\text{For hydrogen:} \quad Ek_L a (C_{H,L}^{\text{eq}} - C_{H,L}) = vr(C_{H,L}, C_{S,L}) \quad (38)$$

### 45.3

#### Industrial Reactor and Scale-Up Issues

Many types of reactor may be used for gas–liquid reactions, including bubble columns, mechanically stirred tanks, plate columns, counter- or co-current packed bed columns, falling films, venturi ejectors, and spray columns. These types of equipment differ in properties such as shape, size, arrangement of internal components used to promote gas–liquid contact and heat removal. They also cover a wide variety of fields, including chemistry, biochemistry, refining, petro-chemistry, food processing, environment, and pharmaceuticals [3, 5]. Selective hydrogenation processes are generally carried out in stirred tank batch reactors (“Batch”), with some examples using CSTRs [44a] or jet-loop venturi re-

actors [44b]. Loop reactors are suited to the efficient removal of heat while maintaining good gas to liquid mass transfer capabilities.

Stirred tank reactors are mostly used because they provide a rapid means of obtaining a uniform composition and temperature throughout the reaction mixture; they also offer the flexibility required for the small-scale production of many different molecules. Companies such as Biazzi, Davy Process Technology (Buss loop technology), DeDietrich and others provide technology adapted to hydrogenations (i.e., pressures up to 100 bar and temperatures up to 200 °C) [45–47]. Here, some scale-up issues related to stirred tank reactors are described.

Mechanically stirred gas–liquid reactor performances are affected by the degree of mixing, apparatus geometry, stirring power, flow rate, discharge and feed locations for the gas and liquid. For a correct design, the following requirements must be satisfied:

- satisfactory reactants and catalyst homogeneity in the liquid phase;
- satisfactory dissipation of the reaction heat to insure reactor stability and a reasonable uniform reactor temperature; and
- optimal gas hold-up and sufficient bubble break up to guarantee adequate gas–liquid mass transfer.

Quantitative design correlations to meet these requirements are available in the literature [1–3].

The scale-up of mechanically stirred gas–liquid reactors mainly involves reactor size and stirrer size, and is generally based on homothetic designs from pilot tests. The similitude in the scale-up means that the following parameters are – or at least should be – kept constant:

- (i) power dissipation of the stirrer per unit volume (or mass) of liquid;
- (ii) heat transfer capability per unit reactor volume; and
- (iii) gas–liquid volumetric mass transfer coefficient.

Point (i) only requires the assumption that the power input per unit volume is constant. Items (ii) and (iii) are further discussed below. Most often, these three conditions are difficult to satisfy simultaneously, and a choice must be made between them.

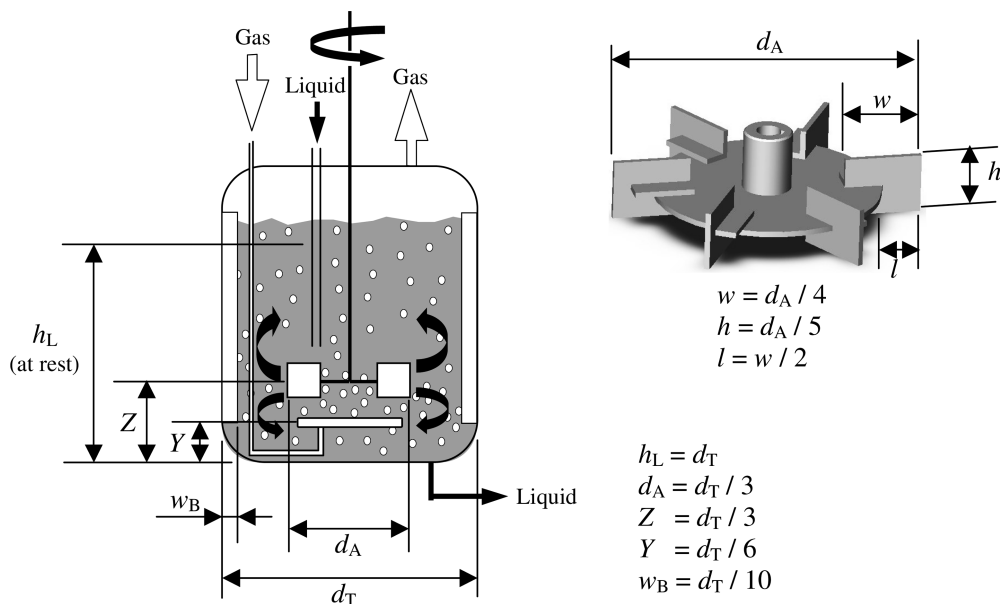
For most homogeneous hydrogenations, heat transfer is generally not an issue. With heat of reactions in the range 100 to 150 kJ mol<sup>-1</sup> (see above), and considering that dilute (0.5 to 2 kmol m<sup>-3</sup>) solutions of the substrate are most often used, the maximum adiabatic temperature rise can be estimated (Eq. (39)):

$$\Delta T_{\text{adiab}}^{\text{max}} = \frac{C_{\text{A,L}}^{\text{in}} (-\Delta H)}{\rho_L c_{\text{pm}}} \quad (39)$$

For organic liquids,  $\rho_L$  and  $c_{\text{pm}}$  are in the range 800 to 1100 kg m<sup>-3</sup> and 2000 to 3000 J kg<sup>-1</sup> K<sup>-1</sup>, respectively; this leads to maximum adiabatic temperature rises of 15 to 150 K. Conventional mechanically agitated tank reactors can deal with  $\Delta T_{\text{adiab}}^{\text{max}}$  in the range 0 to 20 K, but from  $20 < \Delta T_{\text{adiab}}^{\text{max}} < 50$ , the boiling tem-

perature of the solvent must be checked for safety as a rise of the total pressure may be large depending on the solvent. A pressure-resistant liquid condenser may be used as a simple heat exchanger. From  $50 < \Delta T_{\text{adiab}}^{\text{max}} < 150$ , specifically designed reactors displaying good to excellent heat transfer capacity must be used. Two technologies are available for this: (i) stirred tanks equipped with high surface internals to improve heat exchange (Biazzi); or (ii) loop reactors equipped with an external heat exchanger (Buss loop reactor) [45–47]. While most hydrogenators are stirred tanks, loop reactors are also used for asymmetric hydrogenations [48, 49]. It should be noted, however, that the mass transfer capability of such loop reactors was questioned [50].

The schematic illustration in Figure 45.4 shows that, beside the gas injection, the gas–liquid stirred tank is very similar to devices used for single liquid-phase operations. However, both good mixing and good mass transfer between the gas and the liquid phase are required. Thus, high-shear impellers are preferred to propellers, which are less efficient for promoting a large interfacial area. Rushton-type turbines satisfy these requirements, and are largely used in industry. Typical aspect ratios are given in the figure for the tank, equipped with internals (three to four baffles, gas-sparger) and for the widely used six flat-blades turbine (Rushton-type). Similar turbines equipped with hollow shaft and impellers – the so-called “self-inducing gas effect turbines” such as the Cavitator<sup>®</sup> – allow better gas–liquid mass transfer.



**Fig. 45.4** Left: Schematic diagram of a continuous stirred tank reactor with gas and liquid inlet and outlet. Right: A Rushton-type turbine (adapted from [3]).

Batch operations are usually performed in a similar vessel without liquid and gas outlet. In such a set-up (batch) the hydrogen is still fed to the tank, at a flow rate corresponding to the chemical consumption, and possibly to heat removal capability.

Many correlations allow estimation of the gas-liquid volumetric mass transfer coefficient  $k_{L}a$  in mechanically stirred tank reactors. The following intends not to provide a comprehensive review but rather a critical evaluation of selected correlations adapted to hydrogenations [Eqs. (40) to (43)] [25, 51–53].

$$k_{L}a = 0.06 \left( \frac{D_{A,L}}{d_A^2} \right) \left( \frac{N_R d_A^2 \rho_L}{\mu_L} \right)^{1.5} \left( \frac{N_R^2 d_A}{g} \right)^{0.19} \left( \frac{\mu_L}{\rho_L D_{H,L}} \right)^{0.5} \left( \frac{\mu_L V_{SG}}{\sigma_L} \right)^{0.6} \left( \frac{N_R d_A}{V_{SG}} \right)^{0.32} \quad (40)$$

$$k_{L}a = 0.026 \left( \frac{P}{V_L} \right)^{0.4} V_{SG}^{0.5} \quad (41)$$

$$k_{L}a = 55.2 \left( \frac{D_{A,L}}{d_A^2} \right) \left( \frac{N_R^2 d_A}{g} \right)^{2.07} \left( \frac{N_R d_A^2 \rho_L}{\mu_L} \right)^{1.2} \left( \frac{N_R^2 d_A^3 \rho_L}{\sigma_L} \right)^{-1.34} \quad (42)$$

$$k_{L}a = 0.0003 \left( \frac{D_{A,L}}{d_A^2} \right) \left( \frac{\mu_L}{\rho_L D_{A,L}} \right)^{0.5} \left( \frac{N_R d_A^2 \rho_L}{\mu_L} \right)^{1.45} \left( \frac{N_R^2 d_A^3 \rho_L}{\sigma_L} \right)^{0.5} \quad (43)$$

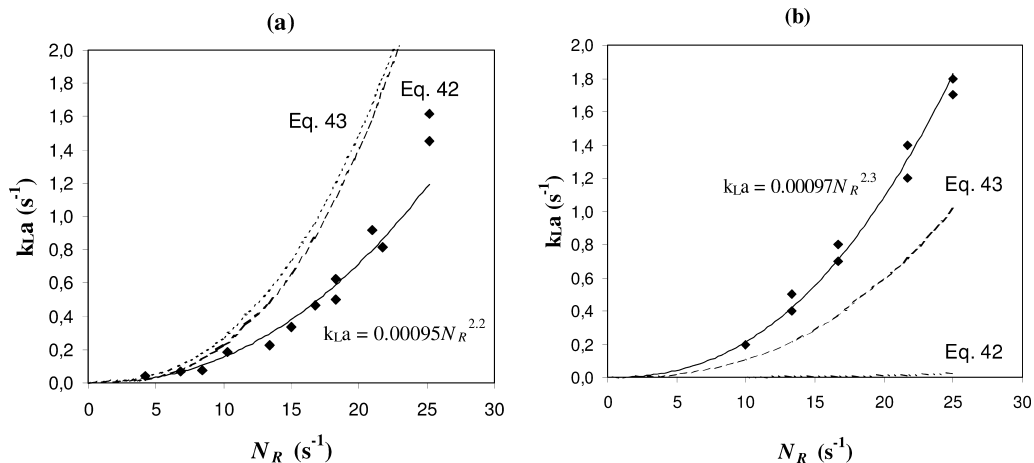
All correlations exhibit a dependence of the volumetric mass transfer coefficient  $k_{L}a$  towards: (i) the properties of the fluids such as those of the liquid ( $\mu_L$ ,  $\rho_L$ ,  $\sigma_L$ ) and of the gas ( $D_{A,L}$ ); (ii) the vessel geometry ( $d_A$  thus  $d_T$  and others; see Fig. 45.4); and (iii) the agitation speed ( $N_R$ ). All of these data are easy to collect, and the determination of  $k_{L}a$  should not be problematic.

However, correlations have been established using some experimental investigations, and thus are checked for a restricted range of operating conditions (reactor volume, nature of the liquid, of the gas, pressure and temperature range) and reactor set-up.

For example, the first and second correlations [Eqs. (40) and (41)] were established using a continuous flow of air/oxygen in an open-end gas set-up which resulted in an important contribution of the superficial gas velocity ( $V_{SG}$ ) to the

**Table 45.6** Reactor and experimental conditions used for the correlations.

	$V_R$	Turbine	Baffles	Gas "A"	Liquid	Temp. [°C]	P [MPa]	Reference
Eq. (40)	12'L	6×Rushton	4	O <sub>2</sub>	glycerol-water mixtures	30	0.1	51
Eq. (42)	2.25'L	6×Rushton	2	H <sub>2</sub>	propylene	24–60	1.1–5.5	53
Eq. (43)	0.5'L	6×Rushton gas-effect	4	H <sub>2</sub> N <sub>2</sub>	water ethanol	20–80	1–5	25



**Fig. 45.5** Dependence of the volumetric mass transfer coefficient with the speed of agitation for correlations of Eqs. (42) and (43) and comparison with experimental data for: (a) a 25-cm<sup>3</sup> tank reactor equipped with a four-blade impeller; and (b) a 300-cm<sup>3</sup> tank reactor equipped with a four-blade gas-inducing turbine.

mass transfer process. A correlation close to that in Eq. (41) has been used for the scale-up of Jacobsen hydrolytic kinetic resolution [54]. However, such correlations cannot be used for batch reactors equipped with a hydrogen delivery system, a set-up often encountered in batch production for fine chemicals. Consequently, before any further investigations are made it is highly advisable to check the numerical values obtained, using the three proposed correlations.

A comparison between the two last correlations and experimental data for small laboratory reactors (25 to 300 cm<sup>3</sup>) equipped with a magnetic stirrer or a traditional six-blade impeller (not Rushton-type) and using a catalytic hydrogenation in organic solvent has been published (Fig. 45.5) [55].

Three conclusions can be made:

- The two correlations can yield very similar predictions when used inappropriately (i.e., without consideration of the very small size of the reactor; Fig. 45.5 a), but they give different results when larger tank dimensions are reached (Fig. 45.5 b).
- The experimental data are not well fitted by the correlations, thus demonstrating the importance of the stirrer shape and dimensions.
- In the case where no correlations are available (i.e., the application involves an exotic fluid, a non-traditional stirrer or a very small reactor), experimental measurements of  $k_L a$  must be performed to afford power law correlations valid for very similar reactor, turbines and fluids. Several techniques for  $k_L a$  determination have been published [56].



## 45.4 Future Developments

In the future, it is possible that homogeneous hydrogenations will develop to a point where continuous processes are required [44 b]. This will not necessarily be due to large-scale production but, rather, to technological pressures from the pharmaceutical industry. The driving force behind this will be the need for a more rational use of expensive catalysts (asymmetric hydrogenations), for homogeneous catalyst recovery (ionic liquids, other bi-phase systems), or supported catalyst technology. The CSTR might not represent the best choice when switching to continuous processes.

Batch or semi-batch reactors are used in fine chemical and pharmaceutical productions because the production rates are small enough to allow quenching of the reaction, and because a single reactor system may be used for many products. In some cases, continuous operation may be mandatory for reasons dictated by the scale of production, economics, kinetics and safety. For asymmetric hydrogenations, expensive molecular catalysts are often used in gas-liquid systems for which precise control of reaction conditions is necessary. Capital costs in term of occupancy might also be an issue. Some hydrogenations display strong exotherms, such as the hydrogenation of nitro-derivatives, and this requires specific scale-up design that is not easy to achieve with traditional reactor technology. Last – and by no means least – hydrogen is considered to be a dangerous reagent, and any design aiming at reducing the hydrogen inventory inside the reaction medium would be beneficial.

New reactor technologies are currently under development, and these include meso- and micro-structured reactors or the use of membranes. Among meso-structured reactors, monolithic catalysts play a pre-eminent role in environmental applications, initially in the cleaning of automotive exhaust gases. Beside this gas-solid application, other meso-structures such as membranes [57, 58], corrugated plate or other “arranged catalysts” and, of course, monoliths can be used as multiphase reactors [59, 60]. These reactors also offer a real potential for process intensification, which has already been demonstrated in commercial applications such as the production of hydrogen peroxide.

In recent years, micro-structured reactors have attracted considerable attention for a variety of applications [61, 62]. Such micro devices are characterized by a laminar flow, and the very high surface-to-volume ratio they provide leads to increased mass and heat transfer, offering the potential for process intensification. It has also been recognized that micro-structured components, because of their low mass and thermal inertia, are able to offer short response times for unsteady state periodic operations. Micro-reactors have been used successfully for fluorination, oxidations and both heterogeneous [63–65] and homogeneous hydrogenations [66]. A review on gas-liquid micro-structured reactors has been published [67]. The very small material inventory when using micro devices offers another advantage, notably as a laboratory tool for screening applications, kinetics determination and process data acquisition, where the main concern is

to gain as much information as possible with minimal reagent inventory [66, 68].

While batch reactors remain the “workhorse” in fine chemical production, the need to switch to continuous processes will increase the use of meso- and micro-structured reactors both at the laboratory scale (for discovery, process data determination, demonstration, small-scale production) and at the production level.

### Nomenclature

Symbol	Definition	Unit
$A$	Interfacial area	$\text{m}^2$
$a$	Specific interfacial area per volume of gas–liquid emulsion	$\text{m}^2 \text{m}_{\text{G+L}}^{-3}$
$a_{\text{L}}$	Specific interfacial area per volume of liquid	$\text{m}^2 \text{m}_{\text{L}}^{-3}$
$C_{\text{A,G}}$	Concentration of gas A in the gas phase	$\text{mol m}_{\text{G}}^{-3}$
$C_{\text{A,L}}$	Concentration of gas A in the bulk of the liquid	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{A,G}}^{\text{i}}$	Concentration of gas A at the interface, gas side	$\text{mol m}_{\text{G}}^{-3}$
$C_{\text{A,L}}^{\text{i}}$	Concentration of gas A at the interface, liquid side	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{A,L}}^{\text{eq}}$	Concentration of gas A in the liquid at equilibrium	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{H,L}}$	Concentration of hydrogen dissolved in the bulk of the liquid	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{H,L}}^{\text{eq}}$	Concentration of hydrogen in the liquid at equilibrium	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{S,L}}$	Concentration of substrate S in the bulk of the liquid	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{S,L}}^{\text{i}}$	Concentration of substrate S at the interface, liquid side	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{H}}$	Hydrogen concentration in the intrinsic kinetic law	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{S}}$	Substrate concentration in the intrinsic kinetic law	$\text{mol m}_{\text{L}}^{-3}$
$C_{\text{L}}$	Total concentration of the liquid	$\text{mol m}_{\text{L}}^{-3}$
$c_{\text{pm}}$	Global specific heat of the liquid	$\text{J kg}^{-1} \text{K}^{-1}$
$d_{\text{A}}$	Diameter of the turbine, of the agitation device	$\text{m}$
$D_{\text{A,G}}$	Diffusion coefficient of gas A in the gas phase	$\text{m}^2 \text{s}^{-1}$
$D_{\text{A,L}}$	Diffusion coefficient of dissolved gas A in the liquid phase	$\text{m}^2 \text{s}^{-1}$
$D_{\text{H,L}}$	Diffusion coefficient of hydrogen in the liquid phase	$\text{m}^2 \text{s}^{-1}$
$D_{\text{S,L}}$	Diffusion coefficient of substrate S in the liquid phase	$\text{m}^2 \text{s}^{-1}$

Symbol	Definition	Unit
$E$	Enhancement factor	–
$g$	Acceleration due to gravity	$9.81 \text{ m s}^{-2}$
$H_A$ or $H_H$	Henry constant for gas A or hydrogen related to concentration	$\text{MPa m}^3 \text{ mol}^{-1}$
$H_A^x$ or $H_H^x$	Henry constant for gas A or hydrogen related to molar fraction	MPa
in	Superscript related to initial (Batch) or inlet (CSTR, PF) concentration	–
$J_A, J_H$	Mass transfer rate of gas A, of hydrogen	$\text{mol s}^{-1} \text{ m}_L^{-3}$
$k_c$	Reaction rate constant	variable
$k_L$	Mass transfer coefficient of the gas being transferred, liquid side	$\text{m s}^{-1}$
$k_L a$	Volumetric mass transfer coefficient of the gas being transferred	$\text{s}^{-1}$
$M_L$	Molar weight of the liquid (in Table 45.3)	$\text{kg mol}^{-1}$
$n, m$	Reaction order in intrinsic kinetic law	–
$N_R$	Rotational speed of turbine, of agitation device	$\text{s}^{-1}$
out	Superscript related to final (Batch) or outlet (CSTR, PF) concentration	–
P	Power dissipated in reactor	W
$P_{pA}, P_{pH}$	Partial pressure of gas A, or hydrogen, in the gas phase	MPa or Pa
$Q$	Volumetric liquid flow rate	$\text{m}_L^3 \text{ s}^{-1}$
$r$	Intrinsic rate of reaction	$\text{mol m}_L^{-3} \text{ s}^{-1}$
$V_G$	Volume of gas in the gas–liquid emulsion	$\text{m}_G^3$
$V_L$	Volume of liquid in the gas–liquid emulsion	$\text{m}_L^3$
$V_R$	Volume of the gas–liquid emulsion in the reactor	$\text{m}_{G+L}^3$
$V_{SG}$	Superficial gas velocity	$\text{m s}^{-1}$
$x$	Spatial coordinate	m
$x_A$	Molar fraction of dissolved gas A in the liquid phase	–
$x_i$	Molar fraction of compound $i$ in the liquid phase (general)	–
$x_j^{\text{mix}}$	Molar fraction of solvent $j$ in the liquid mixture	–
$\Delta H$	Heat of reaction (unit to be used in equations)	$\text{J mol}^{-1} \text{ K}^{-1}$
$\varepsilon_L$	Volume fraction of the gas–liquid emulsion occupied by the gas	–
$\mu_L$	Dynamic viscosity of the liquid	Pa s
$v_A$	Molar volume of dissolved gas A at its normal boiling temperature	$\text{m}^3 \text{ mol}^{-1}$
$v_L$	Molar volume of the liquid L at its normal boiling temperature	$\text{m}^3 \text{ mol}^{-1}$

Symbol	Definition	Unit
$\nu$	Stoichiometric coefficient	–
$\rho_L$	Density of the liquid phase	$\text{kg m}_L^{-3}$
$\sigma_A$	Spherical diameter of dissolved A molecule	m
$\sigma_L$	Superficial or interfacial tension of the liquid	$\text{N m}^{-1}$

### Abbreviations

CSTR	continuous stirred tank reactor
PFR	plug flow reactor
STR	stirred tank reactor (batch reactor)

### References

- 1 K. R. Westerterp, W. P. M. van Swaaij, A. A. C. M. Beenackers, *Chemical Reactor Design and Operation*. John Wiley, New York, 1984.
- 2 O. Levenspiel, *Chemical Reaction Engineering*, 2nd edn. John Wiley, New York, 1972.
- 3 P. Trambouze, J.-P. Euzen, R. Bononno, *Chemical Reactors: From Design to Operation*. Technip, Paris, 2004.
- 4 A. Giannetto, P. L. Silveston, *Multiphase Catalytic Reactors: Theory, Design, Scale-up*. Hemisphere Publishing Corp., 1986.
- 5 P. Mills, R. V. Chaudhari, *Catal. Today* 1997, 37, 367.
- 6 M. Baerns, P. Claus, in: B. Cornils, W. A. Herrmann (Eds.), *Applied Homogeneous Catalysis with Organometallic Compounds*. VCH, Weinheim, 1996, vol. 2.
- 7 O. Wachsena, K. Himmlerb, B. Cornils, *Catal. Today* 1998, 42, 373.
- 8 J. C. Charpentier, Solubility and diffusivity of gases in liquids, in: A. Giannetto, P. L. Silveston, *Multiphase Catalytic Reactors: Theory, Design, Scale-up*. Hemisphere Publishing Corp., 1986, p. 81.
- 9 B. E. Poling, J. M. Prausnitz, J. P. O'Connell, *The Properties of Gases and Liquids*, 5th edn. McGraw-Hill, New York, 2000.
- 10 E. D. Snijder, G. F. Versteeg, W. P. M. van Swaaij, *J. Chem. Eng. Data* 1994, 39, 405.
- 11 V. Meille, C. de Bellefon, D. Schweich, *Ind. Eng. Chem. Res.* 2002, 41, 1711.
- 12 H. U. Blaser, H.-P. Jalett, M. Garland, M. Studer, H. Thies, A. Wirth-Tijani, *J. Catal.* 1998, 173, 282.
- 13 B. Fillion, B. I. Morsi, *Ind. Eng. Chem. Res.* 2000, 39, 2157.
- 14 Q. Liu, F. Takemura, A. Yabe, *J. Chem. Eng. Data* 1996, 41, 1141.
- 15 C. L. Young (Ed.), *IUPAC Solubility Data Series*. Pergamon Press, Oxford, UK, 1981, Vols. 5–6.
- 16 G. T. Hefter, R. P. T. Tomkins, *The Experimental Determination of Solubilities – IUPAC*. Wiley & Sons, 2003.
- 17 P. J. Dyson, G. Laurency, C. A. Ohlin, J. Vallance, T. Welton, *Chem. Commun.* 2003, 19, 2418.
- 18 E. Wilhelm, R. Battino, *Chem. Rev.* 1973, 73, 1.
- 19 P. Lühring, A. Schumpe, *J. Chem. Eng. Data* 1989, 34, 250.
- 20 J. L. Anthony, E. J. Maginn, J. F. Brennecke, *J. Phys. Chem. B* 2002, 106, 7315.
- 21 M. Herskowitz, J. Wisniak, L. Skiadman, *J. Chem. Eng. Data* 1983, 28, 164.
- 22 M. Herskowitz, S. Morita, J. M. Smith, *J. Chem. Eng. Data* 1978, 23, 227.
- 23 J. M. Prausnitz, R. N. Lichtenthaler, E. G. Azevedo, *Molecular Thermodynamics of Fluid-Phase Equilibria*, 3rd edn. Prentice-

- Hall PTR, Upper Saddle River, New Jersey, USA, 1999.
- 24 M. S. Wainwright, T. Ahn, D. L. Trimm, N. W. Cant, *J. Chem. Eng. Data* **1987**, *32*, 22.
  - 25 E. Dietrich, C. Mathieu, H. Delmas, J. Jenck, *Chem. Eng. Sci.* **1992**, *47*, 3597.
  - 26 M. Meyberg, F. Roessler, *Ind. Eng. Chem. Res.* **2005**, *44*, 9705–9711. See also [www.fugatron.com](http://www.fugatron.com).
  - 27 V. R. Choudhary, M. G. Sane, H. Vadgaonkar, *J. Chem. Eng. Data* **1986**, *31*, 294.
  - 28 C. R. Wilke, P. Chang, *AIChE J.* **1955**, *1*, 264.
  - 29 E. L. Cussler, *Diffusion, Mass Transfer in Fluid Systems*, 2nd edn. Cambridge University Press, 1997.
  - 30 D. L. Wise, G. Houghton, *Chem. Eng. Sci.* **1966**, *21*, 999.
  - 31 M. Diaz, A. Vega, J. Coca, *Chem. Eng. Commun.* **1987**, *52*, 271.
  - 32 H. Sovova, *Coll. Czech. Chem. Commun.* **1976**, *41*, 3715.
  - 33 D. M. Himmelblau, *Chem. Rev.* **1964**, *64*, 527.
  - 34 D. Schweich, *Génie de la réaction chimique*. Tec&Doc, Paris, 2001.
  - 35 J. Lieto, *Le génie chimique à l'usage des chimistes*, 1998.
  - 36 K. Sporka, J. Hanika, V. Ruzicka, *Coll. Czech. Chem. Commun.* **1969**, *34*, 3145.
  - 37 K. Sporka, J. Hanika, V. Ruzicka, M. Halousek, *Coll. Czech. Chem. Commun.* **1971**, *36*, 2130.
  - 38 C. N. Satterfield, Y. H. Ma, T. K. Sherwood, *Inst. Chem. Eng. Symp. Ser.* **1968**, *28*, 22.
  - 39 M. Ross, J. H. Hildebrand, *J. Chem. Physics* **1964**, *40*, 2397.
  - 40 K. Nakanishi, E. M. Voigt, J. H. Hildebrand, *J. Chem. Physics* **1965**, *42*, 1860.
  - 41 R. J. Powell, J. H. Hildebrand, *J. Chem. Physics* **1971**, *55*, 4715.
  - 42 G. Wild, J. C. Charpentier, *Techniques de l'ingénieur* **1987**, *P*, 605.
  - 43 (a) C. de Bellefon, in: E. Derouane, et al. (Eds.), *Principles and Methods for Accelerated Catalyst Design*. NATO ASI, Kluwer, **2002**, p. 71. (b) N. Pestre, V. Meille, C. de Bellefon, *J. Mol. Catal. A*: **2006**.
  - 44 (a) S. Wang, F. Kienzle, *Org. Proc. Res. Dev.* **1998**, *2*, 226; (b) B. Chen, U. Dingerdissen, J. G. E. Krauter, H. G. J. Lankink, K. Möbus, D. J. Ostgard, P. Panster, T. H. Riermeier, S. Seebald, T. Tacke, H. Trauthwein, *Appl. Catal.* **2005**, *280*, 17.
  - 45 J.-P. Landert, T. Scubla, *Chem. Eng. (New York)* **1995**, *102*, 118.
  - 46 P. Cramers, C. Selinger, *PharmaChem* **2002**, *1*, 7.
  - 47 See on the internet: [www.biazzi.ch](http://www.biazzi.ch), [www.davyprotech.com](http://www.davyprotech.com), [www.dedietrichddz.com](http://www.dedietrichddz.com).
  - 48 J. F. McGarrity, W. Brieden, R. Fuchs, H.-P. Mettler, B. Schmidt, O. Werbitzky, in: H.-U. Blaser, E. Schmidt (Eds.), *Asymmetric Catalysis on Industrial Scale*. Wiley-VCH, **2004**, p. 283.
  - 49 H.-U. Blaser, R. Hanreich, H.-D. Schneider, F. Spindler, B. Steinacher, in: H.-U. Blaser, E. Schmidt (Eds.), *Asymmetric Catalysis on Industrial Scale*. Wiley-VCH, **2004**, p. 55.
  - 50 R. Imwinkelried, *Chimia* **1997**, *51*, 300.
  - 51 H. Yagi, F. Yoshida, *Ind. Eng. Chem., Process Des. Dev.* **1975**, *14*, 488.
  - 52 S. Y. Lee, Y. P. Tsui, *Chem. Eng. Prog.* **1999**, *23*.
  - 53 T. I. Mizan, J. Li, B. I. Morsi, M.-Y. Chang, *Chem. Eng. Sci.* **1994**, *49*, 821.
  - 54 L. Aouni, K. E. Hemberger, S. Jasmin, H. Kabir, J. F. Larrow, I. Le-Fur, Ph. Morel, T. Schlama, in: H.-U. Blaser, E. Schmidt (Eds.), *Asymmetric Catalysis on Industrial Scale*. Wiley-VCH, **2004**, p. 165.
  - 55 V. Meille, N. Pestre, P. Fongarland, C. de Bellefon, *Ind. Chem. Eng. Res.* **2004**, *43*, 924.
  - 56 A. L. Mårques, G. Wild, N. Midoux, *Chem. Eng. Sci.* **1994**, *33*, 247.
  - 57 L. Greiner, D. H. Mueller, E. C. D. van den Ban, J. Woeltinger, C. Wandrey, A. Liese, *Adv. Synth. Catal.* **2003**, *345*, 679.
  - 58 V. Diakov, A. Varma, *AIChE J.* **2003**, *49*, 2933.
  - 59 A. Cybulski, J. A. Moulijn, *Structured Catalysts and Reactors*. Dekker, New York, **1998**.
  - 60 S. Roy, T. Bauer, M. Al-Dahhan, P. Lehner, T. Turek, *AIChE J.* **2004**, *50*, 2918.
  - 61 K. Jähnisch, V. Hessel, H. Löwe, M. Baerns, *Angew. Chem. Int. Ed.* **2004**, *43*, 406.
  - 62 (a) V. Hessel, S. Hardt, H. Löwe, *Chemical Micro Process Engineering (Fundamen-*

- tals, *Modelling and reactions*). Wiley-VCH, **2004**; (b) V. Hessel, H. Löwe, A. Müller, G. Kolb, *Micro Chemical Process Engineering (Processing and Plants)*. Wiley-VCH, **2005**.
- 63** K. K. Yeong, A. Gavriilidis, R. Zapf, V. Hessel, *Chem. Eng. Sci.* **2004**, *59*, 3491.
- 64** R. Abdallah, V. Meille, J. Shaw, D. Wenn, C. de Bellefon, *Chem. Commun.* **2004**, 372.
- 65** J. Kobayashi, Y. Mori, K. Okamoto, R. Akiyama, M. Ueno, T. Kitamori, S. Kobayashi, *Science* **2004**, *304*, 1305.
- 66** (a) C. de Bellefon, N. Tanchoux, S. Caravieilhès, P. Grenouillet, V. Hessel, *Angew. Chem. Int. Ed.* **2000**, *39*, 3442; (b) R. Abdallah, V. Meille, J. Shaw, D. Wenn, C. de Bellefon, *Chem. Commun.* **2004**, 372; (c) C. de Bellefon, T. Lamouille, N. Pestre, F. Bornette, F. Neumann, V. Hessel, *Catal. Today* **2005**, *110*, 179.
- 67** V. Hessel, P. Angeli, A. Gavriilidis, H. Löwe, *Ind. Eng. Chem. Res.* **2005**, *44*, 9750.
- 68** (a) C. de Bellefon, N. Pestre, T. Lamouille, P. Grenouillet, V. Hessel, *Adv. Synth. Cat.* **2003**, *345*, 190; (b) C. de Bellefon, R. Abdallah, T. Lamouille, N. Pestre, S. Caravieilhès, P. Grenouillet, *Chimia* **2002**, *56*, 621.