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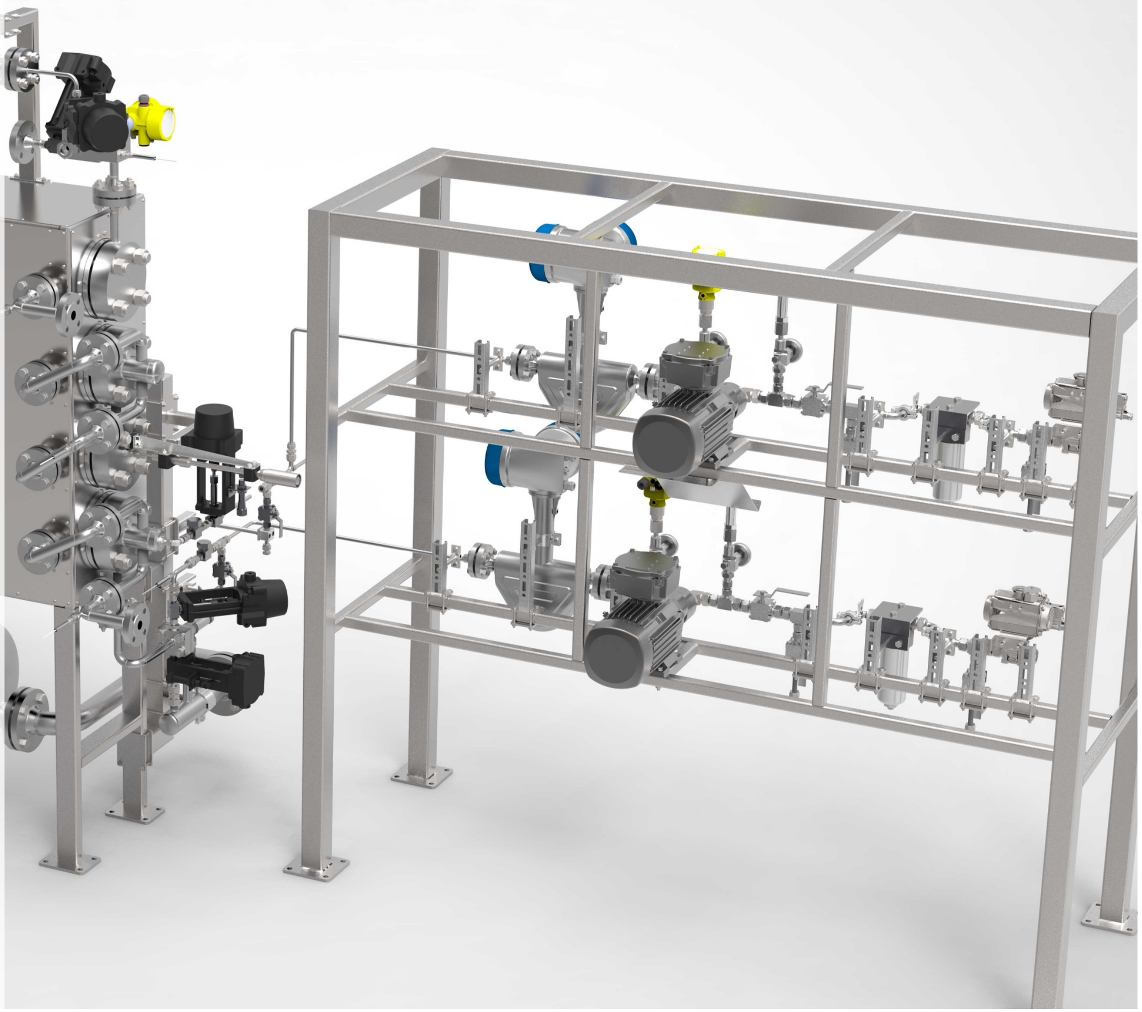
mixing + reaction solutions

Continuous Hydrogenation



Principles, applications & a quick selection guide for the first customer call

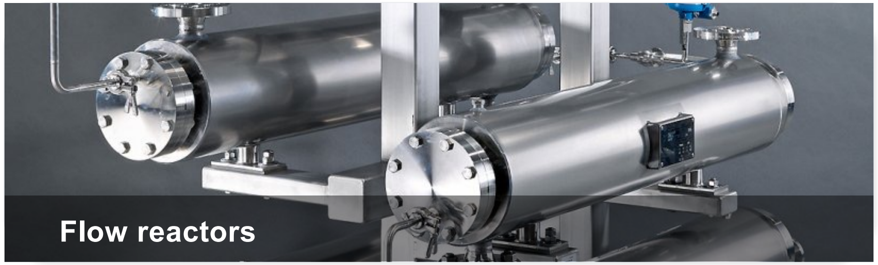
Neftenbach, Switzerland • www.fluitec.ch fluitec mixing + reaction solutions

What we deliver

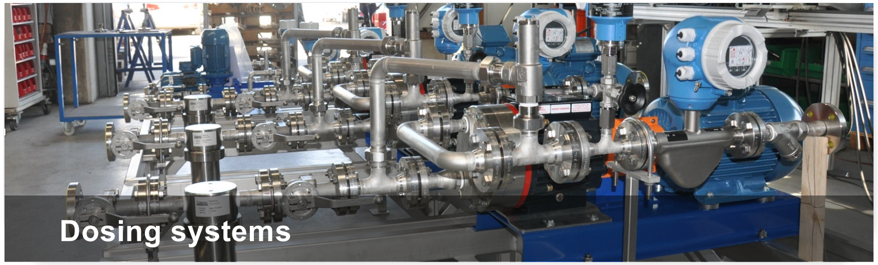
A modular platform for continuous mixing, reaction and scale-up

Solutions tailored for customers who need:

- Flow reactors for process development and production
- Direct scalability from the laboratory to production
- Accurate, cleanable dosing systems (incl. automation)
- Laboratory and pilot plants with data-rich instrumentation
- Modular plants and scalable assemblies / building blocks
- Engineering + fabrication for customer-specific systems



Flow reactors

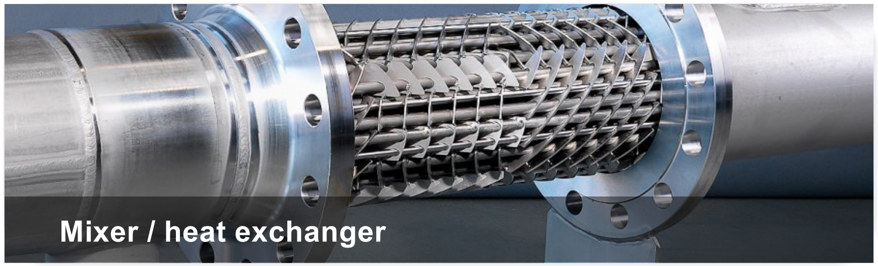


Dosing systems

contiplantPHARMA by fluitec

contiplantLAB by fluitec

Lab & pilot systems



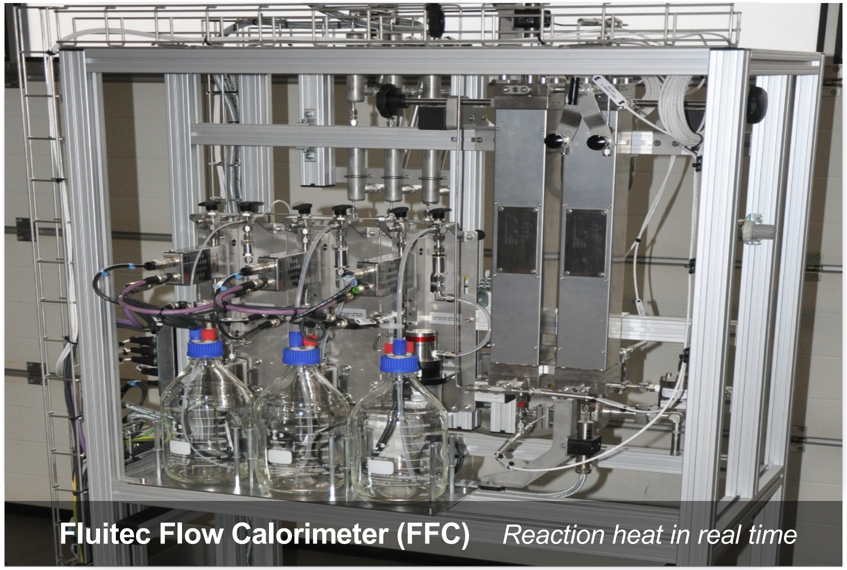
Mixer / heat exchanger

Why continuous flow?

Typical drivers behind flow reactors, modular plants and scalable building blocks

When batch reaches its limits, flow can unlock:

- Safer handling of exothermic and rapid reactions (lower hold-up)
- Improved heat and mass transfer (high surface-to-volume ratio)
- More consistent product quality thanks to defined residence times
- Easy scaling thanks to constant surface-to-volume ratio
- Compact footprint and easier process intensification



Fluitec Flow Calorimeter (FFC) *Reaction heat in real time*

Fast check: Is your process a good fit?

- ✓ Exothermic / fast kinetics
- ✓ Multiphase (gas/liquid, liquid/liquid, slurries)
- ✓ Viscous and/or fouling media
- ✓ Tight quality specifications
- ✓ Need a scalable lab direct production route

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Why continuous hydrogenation?

Safe, scalable and reproducible – especially for exothermic gas/liquid reactions

Safety & exothermicity

- Minimal H_2 inventory in the reactor
- Controlled heat removal → fewer hot spots
- Stable operation even for fast reactions
- H_2 separation downstream of the reactor (no H_2 carryover in the product)
- Suitable for safety-critical processes

Mass transfer

- High k_La through defined bubble flow
- Homogeneous gas distribution upstream of the catalyst
- Precise H2 dosing (also PN100)
- High space-time yield

Scale-up & quality

- Reproducible RTD / plug-flow characteristics
- Continuous temperature and pressure monitoring
- Easy transfer: lab → pilot → production
- Consistent product quality

Continuous hydrogenation combines process safety with high selectivity – and makes scale-up predictable.

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Technology overview

Catalyst form × reactor concept — typical decision paths.

	Static mixer / inline	Loop / CSTR	Fixed bed / cartridge
Homogeneous (dissolved)	**Homogeneous Inline H_2 (“Fast”)**	**Homogeneous Retention (“Recycle”)**	
Nano-/micro-particles	**Nanoparticles + filtration (“Hybrid”)**		
Heterogeneous (solid)	**Slurry (DCR / static mixer) (“Deposits, fouling”)**	**Fixed bed (“Cartridge”)**	**Fixed bed (“Cartridge”)**
Coated (structured)	**Coated CSM (“No filtration”)**	**Coated CSM (“No filtration”)**	

Goal: quickly select the right architecture — then confirm with a lab proof-of-concept.

Heterogeneous hydrogenation in a trickle bed

Industry standard for large throughputs — without catalyst in the product.

Concept

H_2 → Trickle bed reactor (Recycle)

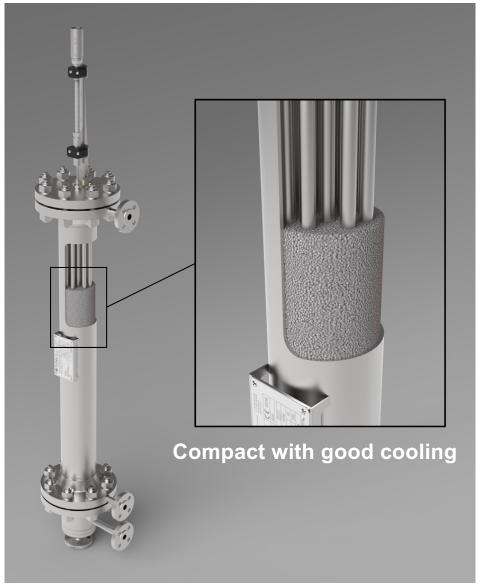
Feed
Substrate (liquid)
→
Trickle bed reactor
Pellets/extrudates in the bed
→
Gas–liquid separator
H_2 disengagement
→
Product

Typical applications

- Bulk chemicals & petrochemicals (hydrogenations, hydroprocessing)
- Fine chemicals when the feed is clean (no solids)
- Multi-bed with interstage cooling/quench for strongly exothermic systems

Limits & risks

- Incomplete wetting → hot spots / selectivity loss
- Plugging with solids / salts / polymer formation
- Catalyst change-out: downtime & regeneration strategy
- Limited residence time behavior



Compact with good cooling

Heterogeneous hydrogenation in a fixed bed

Industry standard for large throughputs — without catalyst in the product.

Concept

Feed
Substrate (liquid) → **Static mixer** (H_2 ↓; Recycle)
H_2 dissolve → **Fixed bed (liquid flow)**
Pellets/extrudates in the bed → **Gas–liquid separator**
H_2 disengagement → **Product**

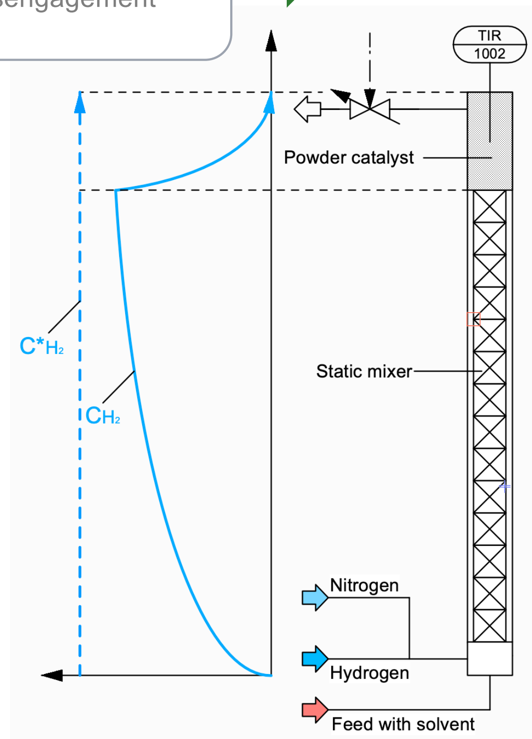
Typical applications

- Hydrogenation of double bonds
- Selective aromatic hydrogenation
- Nitro → amine reductions
- Protective group removal (e.g., benzyl)
- It is particularly suitable for high-quality, controlled applications – less so for simple, cost-driven mass processes.

High-demand concept

Limits & risks

- Not suitable for liquids with poor solubility
- Complex gas-liquid management
- Plugging with solids / salts / polymer formation
- Requires robust pressure vessels, fittings, seals
- Higher investment costs with rapid amortization



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Coated static mixers (catalytic cartridges)

A modular platform for continuous mixing, reaction and scale-up

Concept

Feed
Substrate (liquid)

→ H_2 ↓ **CSM / coated mixer**
Catalyst as a coating

→ **Gas–liquid separator**
H_2 disengagement

→ **Product**

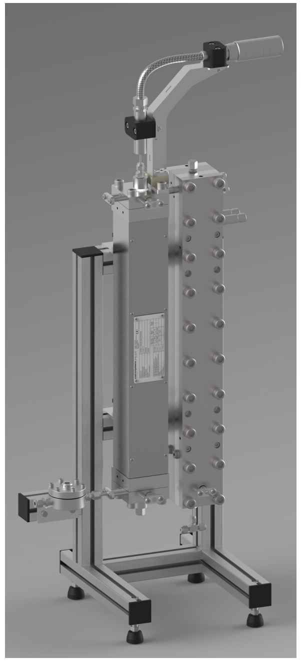
Typical applications

- Fine chemicals/pharma: clean feed, high product quality
- Hydrogenations with very low metal limits
- Campaign operation: cartridge change-out without filtration

High-demand concept

Limits & design points

- Coating: activity vs. lifetime (fouling)
- Avoid erosion/particles in the feed
- Steer selectivity via staging (H_2 splitting / quench)
- Scalable only from 20 ml/min labflow



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Homogeneous hydrogenation in a static mixer (inline)

Best fit for fast reactions without solids — very high gas/liquid mass transfer.

Concept

Feed
Substrate + catalyst (dissolved)

→ H_2 →

Static mixer / tubular section
Homogeneous catalyst in solution

→

Gas–liquid separator
H_2 disengagement

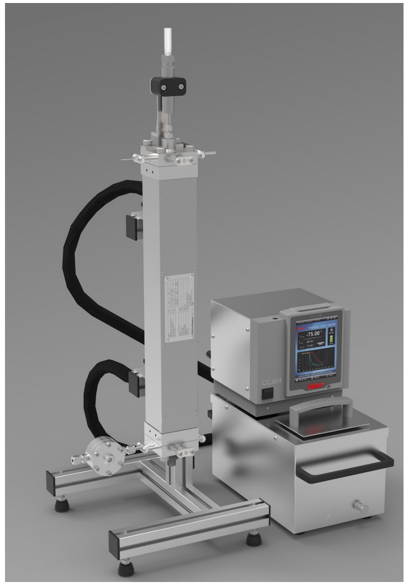
→ **Product**

Typical applications

- C=C and C=N hydrogenations (fine chemicals / pharma)
- Asymmetric hydrogenation (high-value intermediates)
- C=O reductions (transfer hydrogenation often possible)

Limits & key questions

- How will the catalyst be separated / recycled?
- Solvent & ligand stability under H_2/pressure
- Sensitivity to trace impurities (S, P, halogens)



Nanoparticle catalysis + filtration (hybrid)

High activity like homogeneous — separation like heterogeneous (e.g., crossflow/TFF).

Concept

Feed
Substrate + NP catalyst

→ H_2 → **Static mixer / loop**
NP catalyst (colloidal / micro)

→ **Crossflow filter**
Catalyst retention

→ **Product**

Recycle

Typical applications

- Selective hydrogenations (e.g., alkyne → alkene)
- Hydrogenolysis / deprotections (Pd-based systems)
- When filtration is already in place (precious metal recovery)

High-demand concept

Limits & design points

- Particle stability (agglomeration, leaching, activity drift)
- Filter fouling & shear sensitivity (recirculation needed)
- Particle size vs. pressure drop vs. retention efficiency

Liquid catalysts: what happens to the catalyst?

Four robust routes for retention/separation — depending on product requirements.

1) Membrane retention (OSN / NF)

- Catalyst stays in a loop; product passes the membrane
- Good fit for precious-metal complexes (Rh/Ru/Ir/Pd)
- Scalable as a continuous recycle loop

2) Biphasic / thermomorphic

- Catalyst in its own phase (e.g., aqueous / ionic liquid)
- Single phase at reaction temperature; split phases on cooling
- Simple phase split instead of filtration

3) Scavenger / adsorption

- Inline polisher: metal/ligand scavengers
- Good for small catalyst loads and tight metal limits
- As a safety net downstream of the reactor

4) Immobilization (hybrid)

- Complex bound to a support or structured coating
- Less separation effort — similar to heterogeneous processing
- Trade-off: activity/selectivity vs. stability

Slurry hydrogenation in a DCR (staged plug-flow)

When solids must be tolerated.

Concept

Recycle

H_2

Stage 1

DCR – reaction zone
Slurry (Pd/C, Raney Ni, …)

Stage 2

DCR – reaction zone
Heat removal / quench

Stage 3

DCR – reaction zone
Stable RTD (plug-flow-like)

H_2 dosing per stage (control selectivity / exotherm)

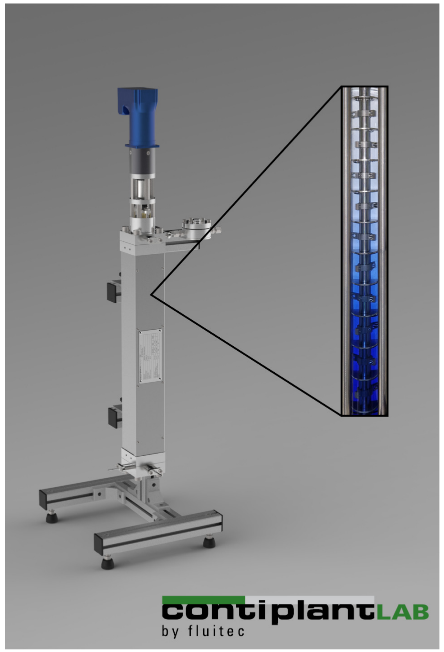
Typical applications

- Nitro → amine (strongly exothermic, solids-tolerant)
- Hydrogenolysis with activated-carbon catalysts
- Feeds with salts/particles (more robust than fixed beds)

High-demand concept

Limits & key questions

- Catalyst separation (filter, centrifuge, magnet, …)
- Wear / attrition (particle management)
- In-operation catalyst regeneration (skid design)



Microparticle catalyst + static mixer + filter

Between slurry and coatings: high activity + controllable separation.

Concept

H_2 → Recycle

Feed
Substrate + micro-catalyst

→ **Static mixer (slurry-capable)**
Microparticles (e.g., 20–60 µm)

→ **Filter (inline/crossflow)**
Catalyst retention

→ **Product**

When does it make sense?

- When coating is not feasible (poisoning/fouling)
- When a fixed bed is too sensitive (particles in the feed)
- When catalyst recovery (Pd, Pt) is economically important

Limits & risks

- Filter cake / fouling (design: crossflow, backpulse)
- Attrition → rising fines fraction (harder to retain)
- Pressure drop & pump sizing (shear, viscosity)

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Application 1: Nitro → amine

Pharma, dyes, fine chemicals — often strongly exothermic & mass-transfer limited.

Customer goals

- High selectivity (avoid hydroxylamine / over-reduction)
- Safe heat removal & avoidance of hot spots
- Robust solids tolerance (Pd/C, Raney, salts)

Best-fit concepts

- Slurry in DCR (staged, exotherm controlled)
- Coated mixers (when the feed is clean)
- Trickle bed / Fixed bed (when there is no solids risk)

Typical first-call questions

- How much heat is released (ΔH) — do we need quench/multiple stages?
- Is there solid formation (salts, crystallization) along the reaction?
- What metal limits apply — is filtration/polishing planned?

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Application 2: C=C saturation (alkene hydrogenation)

Broad use case — from fragrances to API intermediates.

Best-fit concepts

- Coated static mixers (high product quality)
- Fixed bed (scale & long campaigns)
- Homogeneous inline (when very selective / asymmetric)

Why Fluitec

- Excellent temperature control for exothermic saturations
- Modular elements: combine coated + uncoated sections
- Scalable gas/liquid contacting

Limits / watch-outs

- Over-hydrogenation (multiple unsaturations) → staging & H_2 splitting
- Catalyst poisoning (sulfur, amines, halogens)
- Viscosity and gas hold-up at high concentrations

Application 3: Selective alkyne → alkene (partial hydrogenation)

A modular platform for continuous mixing, reaction and scale-up

Best-fit concepts

- Nano-/microparticles + filtration (high activity, controllable)
- Coated static mixers in stages
- Fixed bed only with very clean feed (avoid fouling)

Selectivity levers

- Staging (dose H_2 at multiple points)
- Short, narrow RTD (plug flow)
- Fast quench / cooling at target conversion

Limits / watch-outs

- Over-hydrogenation → narrow operating window
- Catalyst deactivation (deposits/polymers)
- In-line analytics (GC/IR) is often decisive

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Application 4: C=O reduction (aldehyde/ketone → alcohol)

Often homogeneous/transfer — catalyst handling is the core topic.

Best-fit concepts

- Homogeneous in a static mixer (single phase)
- Homogeneous + membrane retention (OSN) for precious-metal recycling
- Transfer hydrogenation when H_2 infrastructure is not desired

First-call questions

- Product requirements: metal limits / ligand residues?
- Donor/solvent: recyclability & by-products
- Selectivity vs. rate (temperature, pressure, ligand)

Limits / watch-outs

- Homogeneous systems can be sensitive to impurities
- Membranes: verify solvent stability and fouling behavior
- Ensure heat removal at high concentrations (ΔT)

Application 5: Imine hydrogenation / reductive amination

Gas/liquid + often water/salt: reactor robustness decides.

Best-fit concepts

- Homogeneous inline (selective & clean)
- Slurry in DCR (if salt/solids formation is possible)
- Coated mixers (when filtration should be avoided)

Process levers

- Staging for pH / imine equilibria
- Minimize gas excess — separate H_2 after the reactor
- Inline quench + polisher (metals, ammonium salts)

Limits / watch-outs

- Exotherm + water content → verify heat removal & corrosion
- Amine substrates can inhibit catalysts
- Clarify solids management (salts, crystals) early

Application 6: Hydrogenolysis & deprotections

Cbz/Bn — often Pd/C; particles & filtration become the bottleneck.

Best-fit concepts

- Slurry in DCR (robust for Pd/C, activated carbon)
- Microparticles + filtration (Pd recovery)
- Coated CSM (only if feed is very clean and low-fouling)

Why continuous?

- Safer operation with minimal H_2 hold-up
- Inline degassing & controlled quench
- Consistent product quality over the campaign

Limits / watch-outs

- Catalyst fines → filtration design (crossflow/TFF)
- Catalyst poisoning from protecting-group by-products
- Metal limits: plan polishing (scavenger)

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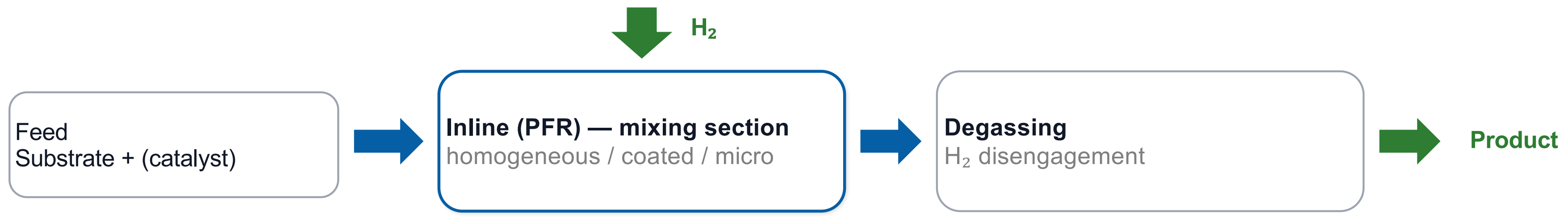
Process mode: Fast reactions “in line”

Single-pass plug flow — minimal hold-up and narrow residence-time distribution.



Best fit

- Reactions < 1–5 min residence time
- Selectivity benefits from narrow RTD
- Exotherms manageable with fast heat removal

Limits / watch-outs

- Solids/salts → plugging risk (clarify upfront)
- Pressure drop rises with length/internals
- In-line analytics helps keep quality stable
- Scalable only from 20 ml/min

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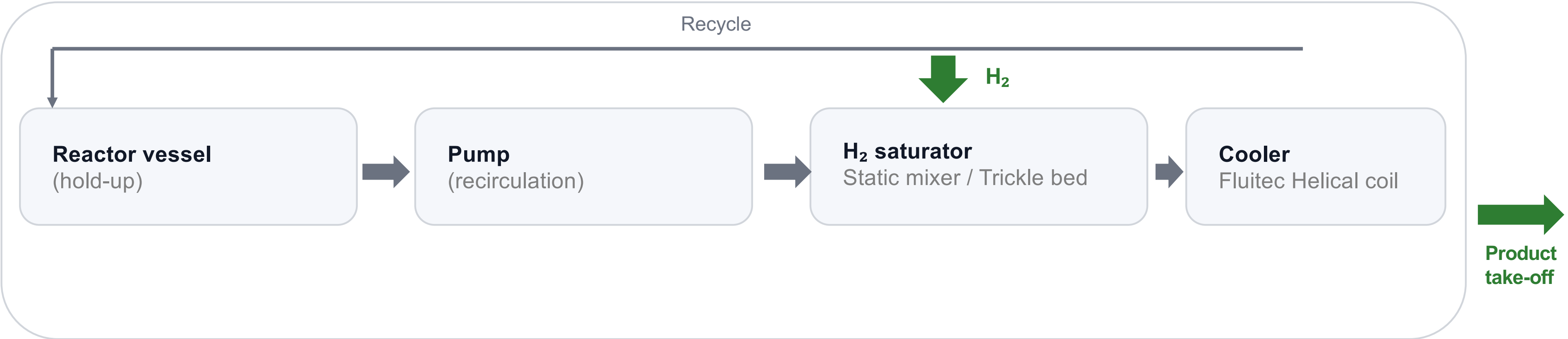
Process mode: Long residence times (loop / recycle)

For slower kinetics, low catalyst loading or strict selectivity.



When is a loop ideal?

- Long reaction times (minutes to hours)
- H_2 mass transfer limiting → high kLa via recirculation
- Keep catalyst in the loop (homogeneous/NP/slurry)

Limits / watch-outs

- RTD becomes more CSTR-like → consider cascade/staging
- Pumps/filters set availability
- Design gas management (degassing, recycle) properly

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Where are the limits?

A quick reality check — so the first concept is right the first time.

Limits (typical)

- Heat removal: ΔT / hot spots for strongly exothermic systems
- Mass transfer: kLa and wetting set the rate
- Solids: abrasion, settling, plugging, filter fouling

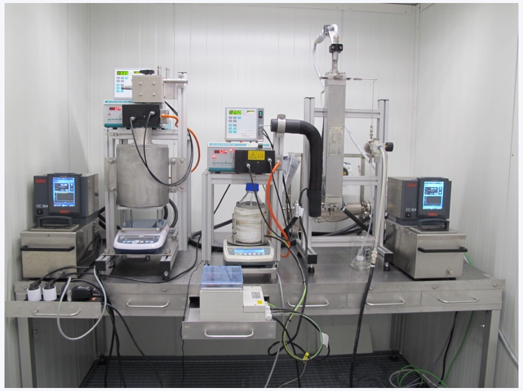
Limits (catalyst-related)

- Poisoning (S, P, halogens), deactivation/fouling
- Leaching (coated) & metal limits
- Selectivity: over-hydrogenation at “too long” residence time

First-pass design rules

- Start with data: ΔH, H_2 solubility, viscosity, solids risk
- Then pick a reactor: inline (fast) vs loop/CSTR (long) vs fixed bed (scale)
- Always include: degassing + (filter/polisher) + safety concept

Why no trials at Fluitec?



Fluitec lab → scale: key specs & test set-up

Test fast, then scale reliably (plug-and-play).

Operating window (lab system)

Temperature	−15 °C … 200 °C
Pressure	0 … 60 bar
Flow rate (liquid)	5–10 / 20–40 / 100–500 mL·min^{-1} (size-dependent)
Operation	Slurry capable • calorimetry capable • scalable design

Recommended starting conditions for tests

- Liquid: 20 mL/min
- H_2: 50 NmL/min

→ Operate the system with good dispersion

Configurable modules

- Gas/liquid contacting (gasser + mixer)
- Reaction zone: coated / uncoated / slurry
- Heat removal: internal heat exchangers / quench

What we need for a quick assessment

- Reaction (class) + target product/spec
- Solvent, concentration, solids risk
- ΔH (or batch data), desired throughput

Approach for the first project

In 3 steps to a robust process architecture.

1 Scoping (1–2 weeks)

- Collect reaction data
- Risk check (ΔH, solids, selectivity)
- Initial concept selection (inline/loop/fixed bed)

2 Lab PoC (days)

- Screen catalyst form & solvent
- Define the window for T/P/residence time
- Metal limits & separation concept

3 Scale & skid

- Scale via modules/cartridges
- Safety & degassing concept
- Automation + analytics

Next step: 30-min scoping call + data exchange (reaction, spec, throughput).

Why Fluitec

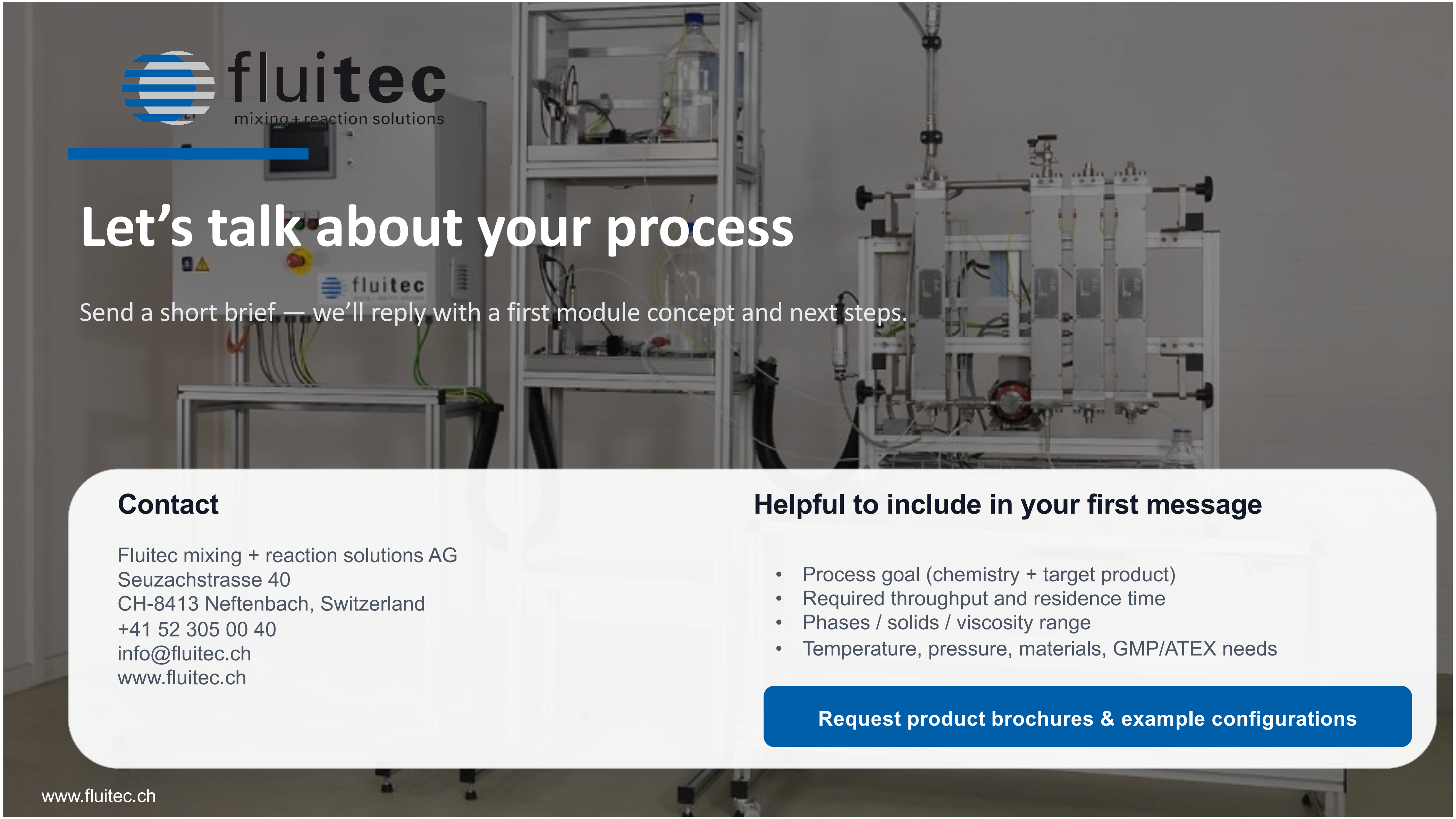
A partner for mixing, heat transfer and in-line reaction technology

What customers value

- Established expertise since 1993 in static mixing, heat transfer and reaction systems
- Modular Contiplant platform for fast development and safe scale-up
- Integrated dosing and PLC process visualisation for repeatable operation
- Options for sterile / GMP-oriented designs and demanding process requirements
- Swiss engineering with in-house manufacturing capabilities

Bring your toughest mixing or reaction task — we'll propose a module set-up and a pragmatic testing plan.

Measure – Consult - Treat



Let’s talk about your process

Send a short brief — we’ll reply with a first module concept and next steps.

Contact

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Helpful to include in your first message

- Process goal (chemistry + target product)
- Required throughput and residence time
- Phases / solids / viscosity range
- Temperature, pressure, materials, GMP/ATEX needs

Request product brochures & example configurations